UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

FORM 20-F

(Mark One)

☐ **REGISTRATION STATEMENT PURSUANT TO SECTION 12(b) OR 12 (g) OF THE SECURITIES EXCHANGE ACT OF 1934**

OR

☒ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the fiscal year ended December 31, 2024

OR

☐ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

OR

☐ **SHELL COMPANY REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

Date of event requiring this shell company report_____

For the transition period from _____ to _____

Commission file number: 001-41115

Genenta Science S.p.A.
(Exact name of Registrant as specified in its charter)

N/A
(Translation of Registrant's name into English)

Italy
(Jurisdiction of incorporation or organization)

Via Olgettina No. 58
20132 Milan, Italy
(Address of principal executive offices)

Via Olgettina No. 58
20132 Milan, Italy
Attn: Pierluigi Paracchi
Tel: +39-02-2643-4681
Email: pierluigi.paracchi@genenta.com
(Name, Telephone, E-mail and/or Facsimile number and Address of Company Contact Person)

Securities registered or to be registered pursuant to Section 12(b) of the Act:

Title of each class	Trading symbol(s)	Name of each exchange on which registered
American depositary shares (each American depositary share representing one ordinary share)	**GNTA**	**The Nasdaq Stock Market LLC (The Nasdaq Capital Market)**
Ordinary shares, no par value*		**The Nasdaq Stock Market LLC (The Nasdaq Capital Market)**

* Not for trading, but only in connection with the listing of American depositary shares on The Nasdaq Capital Market.

Securities registered or to be registered pursuant to Section 12(g) of the Act:

None
(Title of Class)

Securities for which there is a reporting obligation pursuant to Section 15(d) of the Act:

None
(Title of Class)

Indicate the number of outstanding shares of each of the Issuer's classes of capital or common stock as of the close of the period covered by the annual report.

The registrant had 18,289,866 ordinary shares outstanding as of December 31, 2024.

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. ☐ Yes ☒ No

If this report is an annual or transition report, indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934. ☐ Yes ☒ No

Note — Checking the box above will not relieve any registrant required to file reports pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934 from their obligations under those Sections.

Indicate by check mark whether the registrant: (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. ☒ Yes ☐ No

Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit such files).
☒ Yes ☐ No

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer or an emerging growth company. See definition of "large accelerated filer," "accelerated filer," and "emerging growth company" in Rule 12b-2 of the Exchange Act. (Check one):

Large accelerated filer ☐ Accelerated filer ☐ Non-accelerated filer ☒ Emerging growth company ☒

If an emerging growth company that prepares its financial statements in accordance with U.S. GAAP, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards† provided pursuant to Section 13(a) of the Exchange Act. ☐

† The term "new or revised financial accounting standard" refers to any update issued by the Financial Accounting Standards Board to its Accounting Standards Codification after April 5, 2012.

Indicate by check mark whether the registrant has filed a report on and attestation to its management's assessment of the effectiveness of its internal control over financial reporting under Section 404(b) of the Sarbanes-Oxley Act (15 U.S.C. 7262(b)) by the registered public accounting firm that prepared or issued its audit report. ☐

If securities are registered pursuant to Section 12(b) of the Act, indicate by check mark whether the financial statements of the registrant included in the filing reflect the correction of an error to previously issued financial statements. ☐

Indicate by check mark whether any of those error corrections are restatements that required a recovery analysis of incentive-based compensation received by any of the registrant's executive officers during the relevant recovery period pursuant to §240.10D-1(b). ☐

Indicate by check mark which basis of accounting the registrant has used to prepare the financial statements included in this filing:

U.S. GAAP ☒ International Financial Reporting Standards as issued by the International Accounting Standards Board ☐ Other ☐

If "Other" has been checked in response to the previous question, indicate by check mark which financial statement item the registrant has elected to follow. ☐ Item 17 ☐ Item 18

If this is an annual report, indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). ☐ Yes ☒ No

(APPLICABLE ONLY TO ISSUERS INVOLVED IN BANKRUPTCY PROCEEDINGS DURING THE PAST FIVE YEARS)

Indicate by check mark whether the registrant has filed all documents and reports required to be filed by Sections 12, 13 or 15(d) of the Securities Exchange Act of 1934 subsequent to the distribution of securities under a plan confirmed by a court. ☐ Yes ☐ No

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CERTAIN INFORMATION

As used in this Annual Report on Form 20-F (this "Annual Report"), unless otherwise indicated or the context otherwise requires, references to

- "we," "Genenta," "us," "our," "the Company," or "our company" are to Genenta Science S.p.A., including its subsidiaries;
- "ordinary shares" are to our ordinary shares, no par value;
- "ADSs" or "American Depositary Shares" are to our American depositary shares, each representing one ordinary share;
- "Nasdaq" are to the Nasdaq Capital Market;
- "Italy" are to the Republic of Italy, "E.U." are to the European Union, and "U.S." are to the United States of America;
- "$," "USD," "dollars," "USD$" or "U.S. dollars" are to the legal currency of the U.S.; and
- "€," "EURO," or "Euros" are to the legal currency of the E.U.

Solely for the convenience of the reader, this Annual Report contains translations of certain U.S. dollar amounts into Euros at specified rates. Except as otherwise stated in this Annual Report, all foreign currency transactions are translated into Euros through a specific application embedded in our accounting system, which is powered by the official exchange rates provided by HSBC (Hongkong and Shanghai Banking Corporation) in the City of London, United Kingdom. Specifically, the Consolidated Balance Sheet balances resulting from our financial statement as of December 31, 2024, are translated at the spot exchange rate as of December 31, 2024, that is $1.00 per €0.9603, while the Consolidated Statements of Operations and Comprehensive Loss balances are translated at the weighted average exchange rate of non-Euro currency transactions during the reporting period.. No representation is made that such U.S. dollar amounts referred to in this Annual Report could have been or could be converted into Euros at such rates or any other rates. Any discrepancies in any table between totals and sums of the amounts listed are due to rounding.

The audited consolidated financial statements and notes thereto as of and for fiscal 2024, 2023 and 2022 included elsewhere in this Annual Report have been prepared in accordance with U.S. generally accepted accounting principles ("US GAAP"). Our fiscal semi-annual year-end is June 30th and our fiscal year-end is December 31st.

FORWARD-LOOKING STATEMENTS

This Annual Report contains many statements that are "forward-looking" and uses forward-looking terminology such as "anticipate," "believe," "could," "estimate," "expect," "future," "intend," "may," "ought to," "plan," "possible," "potentially," "predicts," "project," "should," "will," "would," negatives of such terms or other similar statements. You should not place undue reliance on any forward-looking statement due to its inherent risk and uncertainties, both general and specific. Although we believe the assumptions on which the forward-looking statements are based are reasonable and within the bounds of our knowledge of our business and operations as of the date of this Annual Report, any or all of those assumptions could prove to be inaccurate. As a result, the forward-looking statements based on those assumptions could also be incorrect. The forward-looking statements in this Annual Report include, without limitation, statements relating to:

- our goals and strategies;
- our future business development, results of operations and financial condition;
- our ability to protect our intellectual property rights;
- projected revenues, profits, earnings and other estimated financial information;
- our ability to maintain strong relationships with our customers and suppliers;
- our planned use of proceeds; and
- governmental policies regarding our industry.

The forward-looking statements included in this Annual Report are subject to known and unknown risks, uncertainties and assumptions about our business and business environment. These statements reflect our current views with respect to future events and are not a guarantee of future performance. Actual results of our operations may differ materially from information contained in the forward-looking statements as a result of risk factors, some of which are described under the headings "Risk Factors", "Operating and Financial Review and Prospects," "Information on our Company" and elsewhere in this Annual Report.

These risks and uncertainties are not exhaustive. Other sections of this Annual Report include additional factors which could adversely impact our business and financial performance. The forward-looking statements contained in this Annual Report speak only as of the date of this Annual Report or, if obtained from third-party studies or reports, the date of the corresponding study or report, and are expressly qualified in their entirety by the cautionary statements in this Annual Report. Since we operate in an emerging and evolving environment and new risk factors and uncertainties emerge from time to time, you should not rely upon forward-looking statements as predictions of future events. Except as otherwise required by the securities laws of the U.S., the E.U. and Italy, we undertake no obligation to update or revise any forward-looking statements to reflect events or circumstances after the date of this Annual Report or to reflect the occurrence of unanticipated events.

PART I

ITEM 1. IDENTITY OF DIRECTORS, SENIOR MANAGEMENT AND ADVISERS

A. Directors and Senior Management

Not required.

B. Advisers

Not required.

C. Auditors

Not required.

ITEM 2. OFFER STATISTICS AND EXPECTED TIMETABLE

A. Offer Statistics

Not applicable.

B. Method and Expect

Not applicable.

ITEM 3. KEY INFORMATION

A. [Reserved]

B. Capitalization and Indebtedness

Not required.

C. Reasons for the Offer and Use of Proceeds

Not required.

D. Risk Factors

You should carefully consider all of the information in this report, including various changing regulatory, competitive, economic, political and social risks and conditions described below, before making an investment in our ordinary shares. One or more of a combination of these risks could materially impact our business, results of operations and financial condition. In any such case, the market price of our ADSs or ordinary shares could decline, and you may lose all or part of your investment.

Summary of Risk Factors

Risks relating to our business include issues arising from the following matters and related adverse developments:

- We have a limited operating history and have incurred significant losses since our inception. We have never generated revenue and will require significant additional funds, which may not be available on acceptable terms or at all. As a result, you could lose your entire investment.

- Our lentiviral-based gene therapy product candidates are based on a novel technology that is in preliminary stages of evaluation, which makes it difficult to predict the time and cost of product candidate development or the likelihood of receiving required regulatory approvals. Our rights to the intellectual property underlying our novel technology derive solely from our license agreement with San Raffaele Hospital ("OSR") and any failure to comply with the terms of such license agreement could have a material adverse effect on our intellectual property position and our ability to seek approval for and ultimately commercialize such product candidates.

- Even if we do receive regulatory approvals for our product candidates, they may face commercialization issues from significantly larger oncology competitors, unfavorable pricing regulations or lack of acceptance by doctors, hospitals, patients and insurers. Our product candidates and the process for administering them may also cause undesirable side effects or have other properties that could delay or prevent their regulatory approval, limit their commercial potential, or result in significant negative consequences following any potential marketing approval.

- We currently have very few employees and rely almost entirely on the efforts of third parties over which we have limited control and in certain cases are reliant on a sole supplier for our materials. Our contract research organizations ("CROs") may fail to observe the standards to which our studies must be conducted, and our product candidates may not be approved as a result. Likewise, our contract manufacturing organizations ("CMOs") may not produce the needed materials for preclinical and clinical testing, whether as a result of their commitments to other customers or otherwise. Any failure of these third parties to meet our expectations would have a materially adverse effect on our product development efforts.

- Our clinical trials for Temferon must be successful if we are to seek and obtain regulatory marketing application through the submission of a new Biological License Application ("BLA") and marketing authorization application ("MAA") with the U.S. Food and Drug Administration ("FDA") and the European Medicines Agency ("EMA"), respectively. Advanced clinical trials are often not successful even if prior trials were successful, and even if we are able to conduct advanced clinical trials and those trials are successful, we may not obtain necessary regulatory approvals for Temferon or we may be unable to successfully commercialize our products even if we receive the necessary regulatory approvals.

- Our Chief Executive Officer, directors and shareholders who own more than 5% of our outstanding ordinary shares currently own approximately 39% of our ordinary shares and will therefore be able to exert significant control over matters submitted to our shareholders for approval.

- As a public company, we will need to comply with extensive additional U.S. and Italian governmental regulations and Nasdaq rules, which will be expensive, and require significant management attention.

- As a company organized under the laws of Italy and whose shares are represented by ADSs, the rights of investors in the Company differ in several material respects from the rights of holders of shares of common stock of a U.S. domestic company and may not provide investors the same protections.

Risks Related to Our Financial Position and Capital Requirements

We will need additional capital in the future. Raising additional capital by issuing securities may cause dilution to existing shareholders. Financing may not be available on acceptable terms, or at all. Failure to obtain this necessary capital when needed may force us to delay, limit, or terminate our product candidate development efforts or other operations.

As of December 31, 2024, our cash and cash equivalents and marketable securities were approximately €12.7 million. If we continue to use cash at our historical rates of use, we will need significant additional financing, which we may seek through a combination of private and public equity offerings, debt financings and collaboration, in-licensing arrangements, joint ventures, strategic alliances or partnerships. For example, on May 12, 2023, we filed with the Securities and Exchange Commission (the "SEC") a shelf registration statement, which was declared effective by the SEC on May 24, 2023 and permits us to sell from time to time additional ordinary shares, ordinary shares represented by ADSs or rights exercisable for ordinary shares or ADSs in one or more offerings in amounts, at prices and on the terms that we will determine at the time of offering for aggregate gross sales proceeds of up to $100.0 million. As of December 31, 2024, approximately $99.7 million of securities remained available under this registration statement. Further, we have entered into an ATM sales agreement, as amended (the "Sales Agreement"), with Virtu Americas LLC and Rodman & Renshaw LLC (the "Sales Agents") pursuant to which we may, but are not obligated to, offer and sell, from time to time, ADSs with an aggregate offering price up to $29,696,999 through the Sales Agents, subject to the terms and conditions described in the Sales Agreement and SEC rules and regulations (our "ATM offering"). As of December 31, 2024, approximately $29.7 million of capacity remained available under this ATM offering. To the extent that we raise additional capital through the sale of equity or convertible debt securities, your ownership interest will be diluted, and the terms of any such offerings may include liquidation or other preferences that may adversely affect the then existing shareholders' rights. Debt financing, if available, would result in increased fixed payment obligations, and we may be required to agree to certain restrictive covenants, such as limitations on our ability to incur additional debt, limitations on our ability to acquire, sell or license intellectual property rights and other operating restrictions that could adversely impact our ability to conduct our business. If we raise additional funds through collaborations, licensing arrangements, joint ventures, strategic alliances, or partnerships with third parties, we may be required to relinquish rights to some of our technologies or product candidates or otherwise agree to terms unfavorable to us. Even if we believe that we have sufficient funds for our current or future operating plans, we may seek additional capital if market conditions are favorable, or if we have specific strategic considerations.

Our future funding requirements will depend on many factors, including but not limited to:

- the scope, progress, results and costs of drug discovery, laboratory testing, pre- and non-clinical development and clinical trials for our product candidates, including Temferon;

- the cost, timing, and outcome of regulatory review of our product candidates;

- the costs of future activities, including product sales, marketing, manufacturing and distribution, for any of our product candidates for which we receive marketing approval;
- the cost of preparing, filing and prosecuting patent and trademark applications, maintaining and enforcing our intellectual property rights and defending our intellectual property-related claims;
- any product liability or other lawsuits related to our products;
- the expenses needed to attract and retain skilled personnel; and
- the costs associated with being a public company.

Any additional fundraising efforts may divert our management from their day-to-day activities, which may adversely affect our ability to develop and commercialize our product candidates. In addition, we cannot guarantee that future financing will be available in sufficient amounts or on terms acceptable to us, if at all. Moreover, the terms of any financing may adversely affect the holdings or the rights of holders of our securities and the issuance of additional securities, whether equity or debt, by us, or the possibility of such issuance, may cause the market price of our securities to decline.

If we are unable to obtain funding on a timely basis, we may be required to significantly curtail, delay or discontinue one or more of our research or development programs or the development or commercialization, if any, of any product candidates or be unable to expand our operations or otherwise capitalize on our business opportunities, as desired, which could materially affect our business, financial condition and results of operations.

Clinical drug development involves a lengthy and expensive process with uncertain timelines and uncertain outcomes, and results of earlier trials may not be predictive of future trial results. If clinical studies of our product candidates are prolonged or delayed, we may be unable to obtain the required regulatory approvals, and therefore be unable to commercialize our product candidates on a timely basis or at all.

We have a limited history of conducting large-scale or pivotal clinical studies, and no history commercializing pharmaceutical products, which may make it difficult to evaluate the prospects for our future viability. Our operations to date have been limited to financing and staffing our company, developing our technology, and developing Temferon for glioblastoma multiforme. We have not yet demonstrated an ability to successfully complete a large-scale or pivotal clinical study, obtain marketing approval, manufacture a commercial scale product, or conduct sales and marketing activities necessary for successful product commercialization. Consequently, predictions about our future success or viability may not be as accurate as they could be if we had a history of successfully developing and commercializing pharmaceutical products.

If clinical studies for our product candidates are prolonged, delayed or stopped, we may be unable to obtain regulatory approval and commercialize our product candidates on a timely basis, which would require us to incur additional costs and delay or restrict our receipt of any product revenue. There have been significant developments in the highly dynamic field of immuno-oncology such as the earlier availability of product candidates or earlier approval of drugs for the same indications as our product candidates, which may lead us to adapt or alter our clinical programs. At this stage, we cannot assure you of the safety or tolerability of Temferon as a monotherapy, or of its ability to demonstrate efficacy in humans. The commencement of planned clinical studies could be substantially delayed or prevented by several factors, including:

- discussions with the Italian Medicines Agency (Agenzia italiana del farmaco, or "AIFA"), FDA, EMA, or other regulatory agencies regarding the scope or design of our clinical studies;
- the limited number of, and competition for, suitable sites to conduct our clinical studies, many of which may already be engaged in other clinical study programs, including some that may be for the same indication as our product candidates;
- approval of drugs for the same indications as our product candidates;
- any delay or failure to obtain regulatory approval or agreement to commence a clinical study in any of the countries where enrollment is planned;
- inability to obtain sufficient funds required for a clinical study;

- clinical holds on, or other regulatory objections to, a new or ongoing clinical study;
- delay or failure in the testing, validation, manufacture and delivery of sufficient supplies of product candidate for our clinical studies;
- delay or failure to reach agreement on acceptable clinical study agreement terms with prospective sites or CROs, the terms of which can be subject to extensive negotiation and may vary significantly among different sites or CROs; and
- delay or failure to obtain institutional review board ("IRB") or ethics committee approval to conduct a clinical study at a prospective site.

The completion of our clinical studies could in the future be substantially delayed or prevented by several factors, including:

- slower than expected rates of patient recruitment and enrollment, due to factors including, but not limited to, the availability of other drugs to treat potential patients, the unwillingness of patients to participate in low-dose groups of dose-ranging studies and lack of recruitment by clinical study sites;
- delays relating to adding new clinical study sites;
- failure of patients to complete the clinical study or return for post-treatment follow-up;
- failure of our collaborators to provide us with products necessary for us to conduct our combination studies;
- safety issues, including severe or unexpected drug-related adverse effects experienced by patients, including possible deaths;
- the AIFA, FDA, EMA, or other regulatory authorities requiring us to suspend or terminate a clinical study, or requiring us to submit additional data or imposing other requirements before permitting us to continue a clinical study;
- lack of efficacy during clinical studies;
- errors in trial design or conduct;
- termination of our clinical studies by one or more clinical study sites;
- inability or unwillingness of patients or clinical investigators to follow our clinical study protocols, including clinical investigators' failure to comply with our clinical study protocols without our notice;
- inability to monitor patients adequately during or after treatment by us and/or our CROs; and
- the need to repeat or terminate clinical studies as a result of inconclusive or negative results or unforeseen complications in testing.

Changes in regulatory requirements and guidance may also occur and we may need to significantly amend clinical study protocols or submit new clinical study protocols to reflect these changes with the appropriate regulatory authorities. In addition, changes in the competitive environment have occurred and may continue to occur. Amendments may require us to renegotiate terms with CROs or resubmit clinical study protocols to IRBs or ethics committees for re-examination, which may impact the costs, timing or successful completion of a clinical study.

Our clinical studies may be suspended or terminated at any time by the AIFA, FDA, EMA, other regulatory authorities, the IRBs or ethics committees overseeing the clinical study at issue, any of our clinical study sites, or us, due to a number of factors, including:

- failure to conduct the clinical study in accordance with regulatory requirements or our clinical protocols;
- safety issues or any determination that a clinical study presents unacceptable health risks;
- lack of adequate funding to continue the clinical study due to unforeseen costs or other business decisions;
- upon a breach or pursuant to the terms of any agreement with, or for any other reason by, current or future collaborators that have responsibility for the clinical development of any of our product candidates; and
- availability of a new effective treatment for the respective disease or condition that would be considered to be standard of care by regulatory bodies.

Our research, development and clinical costs will increase if we experience delays in clinical studies or marketing approvals or if we are required to conduct additional clinical studies or other testing of our product candidates. We may be required to obtain additional funding to conduct and complete such clinical studies. We cannot assure you that our clinical studies will begin as planned or be completed on schedule, if at all, or that we will not need to restructure our trials after they have begun. Significant clinical study delays also could shorten any periods during which we may have the exclusive right to commercialize our product candidates or allow our competitors to bring products to market before we do, which may harm our business and results of operations. Any failure or significant delay in completing clinical studies for our product candidates would adversely affect our ability to obtain regulatory approval and our commercial prospects and ability to generate product revenue will be diminished.

We are a clinical-stage biopharmaceutical company with limited operating history, which may make it difficult for you to evaluate the success of our business to date and to assess our future viability.

We are an emerging biotechnology company with a limited operating history. Investment in biopharmaceutical product development is highly speculative because it entails substantial upfront capital expenditures and significant risk that any potential product candidate will fail to demonstrate adequate effect or an acceptable safety profile, gain regulatory approval and become commercially viable. All of our product candidates are in early development, and none have been approved for commercial sale. We have not demonstrated an ability to successfully complete late-stage clinical trials, obtain regulatory approvals, manufacture our product candidates at commercial scale or arrange for a third-party to do so on our behalf, conduct sales and marketing activities necessary for successful commercialization, or obtain reimbursement in the countries of sale. We may encounter unforeseen expenses, difficulties, complications, and delays in achieving our business objectives. Our short history as an operating company makes any assessment of our future success or viability subject to significant uncertainty. If we do not address these risks successfully or are unable to transition at some point from a company with a research and development focus to a company capable of supporting commercial activities, then our business will be materially harmed.

We have incurred significant losses in every year since our inception. We expect to continue to incur losses over the next several years and may never achieve or maintain profitability.

We have no products approved for commercial sale, have not generated any revenue from commercial sales of our product candidates, and have incurred losses each year since our inception. Our losses for the years ended December 31, 2024, 2023, and 2022, were approximately €8.9 million, €11.6 million, and €8.5 million, respectively. As of December 31, 2024, we had an accumulated deficit of approximately €56.0 million. Substantially all of our operating losses resulted from costs incurred in connection with our research and development activities, including pre- and non-clinical development of our gene therapy product candidates, namely our leading product candidate Temferon, and from general and administrative costs associated with our operations.

We expect that it will be several years, if ever, before we have any product approved for commercial sale. We have funded our operations to date primarily through proceeds from our mandatory convertible bond financing in March 2025 and our initial public offering of ADSs and ordinary shares in December 2021 (the "IPO") and, prior to our IPO, the private placement of ordinary shares to our founding shareholders. We expect to continue to incur significant expenses and increasing operating losses for the foreseeable future. We anticipate that our expenses will increase substantially if, and as, we:

- continue the research and development of our gene therapy product candidates, including continuing and conducting preclinical studies and clinical trials of Temferon and conducting preclinical studies and clinical trials for any additional product candidates that we may pursue in the future;
- develop and obtain regulatory approval for registration studies for our current product candidate, Temferon, and any additional product candidates that we may pursue in the future;
- seek regulatory and marketing approvals for our product candidates that successfully complete clinical studies, including obtaining orphan drug designation;
- establish a sales, marketing, and distribution infrastructure to commercialize any product candidates for which we may obtain marketing approval;

- industrialize our lentivirus *ex-vivo* gene therapy approach into a robust, scalable and, if approved, commercially viable process;
- maintain, protect, and expand our intellectual property portfolio;
- hire and retain qualified technical personnel, such as clinical, quality control, commercial and scientific personnel;
- expand our infrastructure and facilities to support our operations, including adding equipment and physical infrastructure to support our research and development; and
- incur additional legal, accounting, and other expenses associated with operating as a public company.

We have not generated revenue from product sales and may never be profitable.

Our ability to generate revenue from product sales and achieve profitability depends on our ability, alone or with partners, to successfully complete the development of, and obtain the regulatory approvals necessary to commercialize, our product candidates. We do not anticipate generating revenues from product sales for the next several years, if ever, and our ability to do so depends heavily on our success in many areas, including but not limited to:

- completing research and pre- and non-clinical development of our product candidates;
- seeking and obtaining regulatory and marketing approvals for product candidates for which we complete clinical studies, if any;
- establishing and maintaining supply and manufacturing processes and relationships with third parties that can provide adequate (in amount and quality) products and services, at acceptable cost, to support clinical development and market demand for our product candidates, if marketing approval is received;
- negotiating favorable terms in any collaboration, licensing or other arrangements into which we may enter; and
- obtaining market acceptance of our product candidates, if approved for marketing, as viable treatment options.

Even if one or more of the product candidates we develop is approved for commercial sale, we anticipate incurring significant costs associated with commercialization, with all associated risks and uncertainties. Therefore, we cannot predict when, or if, we will be able to achieve profitability. Additional clinical trials or delays in the initiation and completion of clinical trials could cause our expenses to increase significantly and profitability to be further delayed.

Our failure to become and remain profitable would decrease the value of our company and could impair our ability to raise capital, maintain our research and development efforts, expand our business or continue our operations. A decline in the value of our Company also could cause you to lose all or part of your investment.

Risks Related to Product Development, Regulatory Approval, and Commercialization

Our lentivirus ex-vivo gene transfer therapy product candidates are based on a novel technology, which makes it difficult to predict the time and cost of product candidate development and likelihood of subsequently obtaining regulatory approval.

We have concentrated our research and development efforts on our lentivirus *ex-vivo* gene transfer strategy approach, and our future success is highly dependent upon our successful development of commercially viable gene therapy product candidates. There can be no assurance that we will not experience problems or delays in developing new product candidates and that such problems or delays will not cause unanticipated costs, or that any such development problems can be solved. Because lentivirus *ex-vivo* gene transfer cell therapies represent a relatively new field of cellular immunotherapy and cancer treatment generally, developing and commercializing our product candidates subjects us to a number of risks and challenges, including:

- obtaining regulatory approval for our product candidates, as the AIFA, FDA, EMA, and other regulatory authorities have limited experience with lentivirus *ex-vivo* gene transfer therapies for cancer;
- developing and deploying consistent and reliable processes for engineering a patient's hemapoietic stem progenitor cells ("HSPCs") *ex vivo* and infusing the engineered HSPCs back into the patient;

- sourcing clinical and, if approved, commercial supplies of the materials used to manufacture our product candidates;
- developing programming modules with the desired properties, while avoiding adverse reactions;
- creating viral vectors capable of delivering multiple programming modules;
- developing a reliable and consistent *ex vivo* gene modification and manufacturing process;
- securing manufacturing capacity suitable for the manufacture of our product candidates in line with expanding enrollment in our clinical studies and our projected commercial requirements;
- minimizing and avoiding infection and contamination during production of product candidates;
- developing protocols for the safe administration of our product candidates;
- educating medical personnel regarding our lentivirus *ex-vivo* gene transfer technologies and the potential side effect profile of each of our product candidates, such as potential adverse effects related to pyrexia and infections;
- establishing integrated solutions in collaboration with specialty treatment centers in order to reduce the burdens and complex logistics commonly associated with the administration of lentivirus *ex-vivo* gene transfer cell therapies;
- if and when we obtain any required regulatory approvals, establishing sales and marketing capabilities or partnerships to successfully launch and commercialize our product candidates and gaining market acceptance of a novel therapy; and
- the availability of coverage and adequate reimbursement from third-party payors.

We may not be able to successfully develop our lentivirus *ex-vivo* gene transfer product candidates or our technology in a manner that will yield products that are safe, effective, scalable, or profitable. Additionally, because our technology involves the genetic modification of patient cells *ex vivo*, we are subject to additional regulatory challenges and risks, including:

- regulatory requirements governing gene and cell therapy products are evolving in response to new clinical data. To date, several cell therapy products that involve the genetic modification of patient cells have been approved in the United States and/or the European Union, including two lentivirus *ex-vivo* gene transfer products;
- genetically modified products could lead to lymphoma, leukemia or other cancers, or other aberrantly functioning cells in the event of improper insertion of a gene sequence into a patient's chromosome, or due to other unknown causes;
- although our viral vectors are not able to replicate, there is a risk with the use of lentiviral vectors that they could lead to new or reactivated pathogenic strains of virus or other infectious diseases; and,
- the FDA recommends a 15-year follow-up observation period for patients who receive treatment using gene therapies and guidance promulgated by the EMA requires a similar follow-up observation period for patients who receive cell therapeutic products, which has to be sufficient to observe the subjects for risks that may be due to the characteristics of the product, the nature and extent of the exposure, and the anticipated time of occurrence of delayed adverse reactions and could be as long as life-time, and we may need to adopt an observation period for our product candidates.

Moreover, public perception and awareness of cell and gene therapy safety issues may adversely influence the willingness of subjects to participate in clinical trials of our product candidates, or if approved, of physicians to prescribe our products. Physicians, hospitals, and third-party payors often are slow to adopt new products, technologies, and treatment practices that require additional upfront costs and training. Treatment centers may not be willing or able to devote the personnel and establish other infrastructure required for the administration of lentivirus *ex-vivo* gene transfer cell therapies. Physicians may not be willing to undergo training to adopt this novel and personalized therapy, may decide the therapy is too complex to adopt without appropriate training, and may choose not to administer the therapy. Based on these and other factors, hospitals and payors may decide that the benefits of this new therapy do not or will not outweigh its costs.

Our gene therapy product candidates and the process for administering our product candidates may cause undesirable side effects or have other properties that could delay, prevent their regulatory approval, limit their commercial potential, or result in significant negative consequences following any potential marketing approval.

Following treatment with our gene therapy product candidates, patients may experience changes in their health, including illnesses, injuries, discomforts or a fatal outcome. It is possible that as we study and test Temferon or other product candidates in larger, longer, and more extensive clinical programs, or as use of our product candidates becomes more widespread if they receive regulatory approval, illnesses, injuries, discomforts, side effects, and other adverse events that were observed in earlier clinical trials, as well as conditions that did not occur or went undetected in previous clinical trials, will be reported by patients. Gene therapies are also subject to the potential risk that occurrence of adverse events will be delayed following administration of the gene therapy due to persistent biological activity of the genetic material or other components of the vectors used to carry the genetic material. Many times, additional safety risks, contraindications, drug interactions, adverse events and side effects are only detectable after investigational products are tested in larger scale clinical trials or, in some cases, after they are made available to patients on a commercial scale after approval. Moreover, as noted above, the FDA generally requires a long-term follow-up of study subjects for potential gene therapy-related adverse events for a 15-year period, including a minimum of five years of annual examinations followed by ten years of annual queries, either in person or by questionnaire, of study subjects. If additional clinical experience indicates that Temferon or any other product candidates or similar products developed by other companies has side effects or causes serious or life-threatening side effects, the development of the product candidate may fail or be delayed, or, if the product candidate has received regulatory approval, such approval may be revoked or limited.

There have been several significant adverse side effects in gene therapy treatments in the past, including reported cases of leukemia with the use of gammaretrovirus vector and patient deaths in other clinical trials. There have been recent case reports of suspected unexpected serious adverse reactions (“SUSARs”) involving an ex-vivo transduced lentivirus vector (“LVV”) gene therapy product, Bluebird Bio, Inc.’s (“Bluebird Bio”) elivaldogene autotemcel (“Lenti-D”), involving two SUSARs for cases of acute myeloid leukemia (“AML”), and one case involving myelodysplastic syndrome.

In July 2021, the EMA safety committee (Pharmacovigilance Risk Assessment Committee – PRAC) announced that there is no evidence the LVV used in both Lenti-D and the E.U.-approved gene therapy Zynteglo spurred the AML cases.

Bluebird Bio announced on August 9, 2021 that the SUSAR involving myelodysplastic syndrome occurred in one patient treated with Lenti-D over a year previously, that this SUSAR “is likely mediated by Lenti-D lentiviral vector (LVV) insertion,” and that “[e]vidence currently available suggests that specific design features of Lenti-D LVV likely contributed to this event.” As a result of this SUSAR, the FDA placed a clinical hold on Bluebird Bio’s Lenti-D phase 3 trial for cerebral adrenoleukodystrophy. Post-approval, on November 24, 2024, the FDA announced that the FDA is investigating the known risk of hematologic malignancies with serious outcomes, including those such as hospitalization, the requirement for allogeneic hematopoietic stem cell transplantation, and death, and is evaluating the need for further regulatory action.

Gene therapy is still a relatively new approach to disease treatment and additional adverse side effects could develop. Possible adverse side effects that may occur with treatment with gene therapy products include an immunologic reaction early after administration that could substantially limit the effectiveness of the treatment or represent safety risks for patients. Another safety concern for gene therapies using viral vectors has been the possibility of insertional mutagenesis by the vectors, leading to malignant transformation of transduced cells. While our lentivirus *ex-vivo* gene transfer therapy approach is designed to avoid immunogenicity after administration, there can be no assurance that patients would not create antibodies that may impair treatment. Our approach involves the use of integrating vectors which have the potential for genomic disruption and therefore could interfere with other genes with adverse clinical effects. If any of our gene therapy product candidates demonstrates adverse side effects, we may decide or be required to halt or delay clinical development of such product candidates.

Potential risks for gene therapy products can be identified, in addition to side effects caused by the product candidate itself, as part of the entire process required for their manufacturing and administration. For Temferon manufacturing, each patient needs to be subjected to a mobilization and harvesting process for HSPC collection. This procedure is associated with risks linked to the administration of mobilization agents. The conditioning regimen required for administering our product candidate and the associated procedures can also cause adverse side effects. A gene therapy patient is generally administered with cytotoxic drugs to remove stem cells from the bone marrow to create sufficient space for the modified stem cells to engraft and produce their progeny. This procedure compromises the patient's immune system, and adverse events related to preconditioning have been observed in our ongoing clinical trials. If in the future we are unable to demonstrate that such adverse events were caused by the conditioning regimens used, or by their administration process or related procedure, the FDA, EMA or other regulatory authorities could order us to cease further development of, or deny the approval of, Temferon or our other product candidates for any or all target indications. Even if we can demonstrate that adverse events are not related to our drug product, such occurrences could affect the ability to enroll patients to complete the clinical trials, or the commercial viability of any product candidates that obtain regulatory approval.

To date, Temferon has only been administered to a small number of glioblastoma multiforme (GBM) patients in our Phase 1/2a clinical trial. Only one serious adverse reaction has been attributed to Temferon (abnormal liver enzyme) that occurred early in a patient who subsequently survived more than three years. Adverse events that have occurred in this clinical trial have been attributed either to the autologous stem cell transplant procedures (which include conditioning chemotherapy), concomitant medications or disease progression. The majority of these adverse events resolved. Three patients with GBM died within 122 days of Temferon administration due to complications resulting from conditioning chemotherapy and possibly concomitant steroid use.

Patient deaths and severe adverse events caused by any investigational product candidates could result in the delay, suspension, clinical hold, or termination of clinical trials by sponsors, ethics committees and regulatory authorities. If we elect or are required to delay, suspend, or terminate any clinical trial of any product candidates that we develop, the commercial prospects of such product candidates will be harmed and our ability to generate product revenue from any of these product candidates would be delayed or eliminated. Serious adverse events observed in clinical trials could hinder or prevent market acceptance of the product candidate at issue. Any of these occurrences may harm our business, prospects, financial condition, and results of operations significantly.

Additionally, if any of our product candidates receives marketing approval, the FDA could require us to adopt a Risk Evaluation and Mitigation Strategy ("REMS") and EMA or other non-U.S. regulatory authorities could impose other specific obligations as a condition of approval to ensure that the benefits outweigh its risks, which may include, among other things, a medication guide outlining the risks of the product for distribution to patients, a communication plan to health care practitioners, and restrictions on how or where the product can be distributed, dispensed or used. Furthermore, if we or others later identify undesirable side effects caused by Temferon or any of our other product candidates, several potentially significant negative consequences could result, including:

- regulatory authorities may suspend or withdraw approvals of such a product candidate;
- regulatory authorities may require additional warnings or limitations of use in product labeling;

- we may be required to change the way a product candidate is distributed, dispensed, or administered or conduct additional clinical trials;
- we could be sued and held liable for harm caused to patients; and
- our reputation may suffer.

Any of these events could prevent us from achieving or maintaining market acceptance of our product candidates and could significantly harm our business, prospects, financial condition and results of operations.

We are evaluating Temferon in a Phase 1/2a clinical trial in newly diagnosed unmethylated MGMT gene promoter glioblastoma tumor patients (the "TEM-GBM Study") and in a Phase 1/2a clinical trial in metastatic Renal Cell Carcinoma ("mRCC") patients (the "TEM GU Study"). To date, we have completed Phase 1 of the TEM-GBM Study, and the TEM GU Study is ongoing and not complete.

We are at a very early stage of development for all our gene therapy product candidates. At this stage, our lead product candidate Temferon has been authorized by AIFA to be evaluated in two Phase 1/2a clinical trials in Italy. A study testing Temferon in multiple myeloma study was also approved by AIFA, but we closed the study because of enrollment feasibility.

To commence a clinical trial in the U.S., we will be required to seek FDA acceptance of an investigational new drug application ("IND") for each of our product candidates, including Temferon. We cannot be sure any IND we submit to the FDA, or any similar clinical trial application we submit in other countries, will be accepted. If we will be required by regulatory authorities to conduct additional preclinical testing prior to filing an IND or similar application to clinically evaluate any of our product candidates, including Temferon, this may result in delay in our product candidate development. The results of any such preclinical testing may not be positive and may not support an application to study Temferon or any of our other product candidates in additional clinical trials. Currently, we do not have plans to conduct clinical trials outside of Italy.

It is possible that the FDA or EMA will not view our ongoing or planned trials as providing adequate support for future clinical trials or for an application for marketing approval, for any one or more reasons, including elements of the design or execution of the trials or safety concerns or other trial results. If we are unable to confirm or replicate the results of our trials in larger patient group or if negative results are obtained, we would likely be further delayed or prevented from advancing further clinical development of Temferon or any of our other product candidates.

Additionally, the FDA or EMA may disagree with the sufficiency of our proposed reliance upon the preclinical, manufacturing, or clinical data generated by third-party academic-sponsored trials, or our interpretation of preclinical, manufacturing, or clinical data from our ongoing trials with AIFA. If so, the FDA or EMA may require us to obtain and submit additional preclinical, manufacturing, or clinical data.

We need to complete our Phase 2 of the TEM-GBM Study and Phase 1/2a of the TEM GU Study, as well as additional clinical trials to obtain regulatory approvals to market Temferon. Carrying out later-stage clinical trials is a complicated process. We are a small organization with limited experience in preparing, submitting, and prosecuting regulatory filings, and we have not previously submitted a BLA to the FDA or the equivalent application to EMA for any product candidate.

In addition, we have not yet conducted clinical trials of any our product candidates in the U.S. or Europe (outside of Italy), and we cannot be certain how many clinical trials of Temferon or any of our other product candidates will be required or how such trials should be designed. Consequently, we may be unable to successfully and efficiently execute and complete necessary clinical trials in a way that leads to a BLA submission (or its equivalent for EMA) and approval of Temferon or any of our other product candidates. We may require more time and incur greater costs than our competitors and may not succeed in obtaining regulatory approvals of product candidates that we develop. Failure to commence or complete, or delays in, our planned clinical trials, could prevent us from or delay us in commercializing Temferon.

We may encounter substantial delays in commencement and completion of clinical trials.

Before obtaining marketing approval from regulatory authorities for the sale of our product candidates, we must conduct extensive clinical studies to demonstrate the safety and efficacy of the product candidates in humans. Clinical development is a long, expensive, and uncertain process, and delay or failure can occur at any stage of any of our clinical trials. We cannot guarantee that any clinical studies will be conducted or completed on schedule, if at all. Clinical trials can be delayed or prevented for several reasons, including:

- delays in reaching a consensus with regulatory agencies on study design;
- changes in regulatory requirements and guidance that require amending or submitting new clinical protocols;
- difficulties obtaining regulatory approval to commence a clinical trial or complying with conditions imposed by a regulatory authority regarding the scope or term of a clinical trial;
- difficulties obtaining IRB approval to conduct a clinical trial at a prospective site in the U.S.;
- failure to perform in accordance with the FDA's good clinical practices ("GCP") or applicable regulatory guidelines in other countries;
- delays in reaching or failing to reach agreement on acceptable terms with prospective CROs and trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
- failure by CROs, other third parties or us to adhere to clinical trial protocol and record keeping requirements;
- trial sites or patients dropping out of a study;
- the occurrence of serious adverse events associated with the product candidate that are viewed to outweigh its potential benefits;
- insufficient or inadequate supply or quality of a product candidate or other materials necessary to conduct our clinical trials;
- delays in the testing, validation, manufacturing and delivery of our product candidates to the clinical sites; and,
- if the FDA or EMA or other regulatory authorities elect to enact policy changes.

Clinical trials may also be delayed or terminated because of ambiguous or negative interim results. In addition, a clinical trial may be suspended or terminated by us, AIFA, the FDA, EMA, the IRBs at the sites where the IRBs are overseeing a trial, a data safety monitoring board overseeing the clinical trial at issue or by other regulatory authorities due to a number of factors, including:

- failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols;
- inspection of the clinical trial operations or trial sites by AIFA, the FDA, EMA or other regulatory authorities;
- unforeseen safety issues or lack of effectiveness; and,
- lack of adequate funding to continue the clinical trial.

Any inability to successfully complete preclinical and clinical development could result in additional costs to us or impair our ability to generate revenues. This could result in increased costs, delays in advancing our product candidates, delays in testing the effectiveness of our product candidates or termination of the clinical trials altogether.

In addition, if we make changes to our product candidates, we may need to conduct additional studies to bridge our modified product candidates to earlier versions, this will increase the costs and could delay our clinical development plan, or marketing approval for our product candidates. For example, among our preclinical candidates, we are developing a "switchable" system. This system has the potential to be a "switchable" on/off system that may limit the long-term exposure to any selected therapeutic payloads, but it requires further preclinical testing as well as additional manufacturing validation. Moreover, our platform is designed to allow us to use other therapeutic payloads, other than IFN-α. This has the potential to open a multitude of therapeutic indications but further preclinical testing as well as additional manufacturing validation are required. Any modification of our product candidates will likely require updates to our clinical trial applications and INDs with the relevant regulatory authorities, which may result in delay, suspension, or termination of ongoing or future clinical trials pending our submission, and the agencies' review, of such updates. Clinical study delays could also shorten any periods during which we may have the exclusive right to commercialize our product candidates or allow our competitors to bring products to market before we do, which could impair our ability to successfully commercialize our product candidates and may harm our business and results of operations.

The results of preclinical studies, early-stage clinical trials, data obtained from real-world use, and published third-party studies may not be indicative of results in future clinical trials and we cannot assure you that any clinical trials will lead to results sufficient for the necessary regulatory approvals.

The results of preclinical studies may not be predictive of the results of clinical trials, and the results of any completed clinical trials, including studies derived from real-world use and studies in published literature, or clinical trials we commence may not be predictive of the results of later-stage clinical trials. Additionally, interim results and analyses from our ongoing clinical trials do not necessarily predict final results. Moreover, preliminary data and analyses from our ongoing clinical trials may change as more patient data becomes available. In general, we conduct interim analyses at pre-specified times, which do not include data after the cut-off date and will not be available until the next planned interim analysis. From time to time, preliminary data and analyses might be presented, typically by academic investigators at scientific conferences or in scientific publications. Interim data and analyses are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and/or more patient data becomes available to us. Interim and preliminary data/analyses also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data available to us or that we previously published. As a result, preliminary and interim data/analyses should be viewed with caution until the final data are available. Material adverse changes in the final data compared to the preliminary or interim data/analyses could significantly harm our business prospects.

Indeed, our product candidates may fail to show the desired safety and efficacy in clinical development despite demonstrating positive results in preclinical studies or having successfully advanced through initial clinical trials. Later clinical trial results may not replicate earlier clinical trials for a variety of reasons, including differences in trial design, different trial endpoints (or lack of trial endpoints in exploratory studies), subject population, number of subjects, subject selection criteria, trial duration, drug dosage and formulation and lack of statistical power in the earlier studies. Our company has limited experience in designing and conducting clinical trials and we may be unable to design and execute a clinical trial to support regulatory approval. There can be no assurance that any of our clinical trials will ultimately be successful or support further clinical development of any of our product candidates. Several companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in clinical development even after achieving promising results in earlier studies, and any such setbacks in our clinical development could have a negative impact on our business. Any of our product candidates, including Temferon, may fail to show the desired safety and efficacy in clinical development despite positive results in preclinical studies. Any such failure would cause us to abandon the product candidate.

Additionally, our ongoing clinical trials utilize, and our planned clinical trials may utilize, an "open-label" trial design. An "open-label" clinical trial is one where both the patient and investigator know whether the patient is receiving the investigational product candidate or either an existing approved drug or placebo. Most typically, open-label clinical trials test only the investigational product candidate and sometimes may do so at different dose levels. Open-label clinical trials are subject to various limitations that may exaggerate any therapeutic effect as patients in open-label clinical trials are aware when they are receiving treatment. Open-label clinical trials may be subject to a "patient bias" where patients perceive their symptoms to have improved merely due to their awareness of receiving an experimental treatment. In addition, open-label clinical trials may be subject to an "investigator bias" where those assessing and reviewing the physiological outcomes of the clinical trials are aware of which patients have received treatment and may interpret the information of the treated group more favorably given this knowledge. The results from an open-label trial may not be predictive of future clinical trial results with any of our product candidates for which we include an open-label clinical trial when studied in a controlled environment with a placebo or active control.

We may find it difficult to enroll patients in our clinical trials, which could delay or prevent us from proceeding with clinical trials of our product candidates.

Identifying and qualifying patients to participate in clinical trials of our product candidates is critical to our success. The timing of our clinical trials depends on our ability and on the speed at which we can recruit patients to participate in testing our product candidates, as well as the completion of required follow-up periods. We may experience delays in our clinical trials if we encounter difficulties in enrollment. Patients may be unwilling to participate in our gene therapy clinical trials because of negative publicity from adverse events related to the biotechnology or gene therapy fields, the safety profile of our product candidate under study, the perceived risks and benefits of the product candidate under study; the perceived risks and benefits of gene therapy-based approaches to treatment of diseases, including any required pretreatment conditioning regimens, the existence of competitive clinical trials for similar patient populations.

In addition, we may not be able to identify, recruit and enroll a sufficient number of patients due to the existence of efficacious alternative treatments, the size of the patient population and process for identifying subjects, the design of the trial protocol, the exclusion/inclusion criteria that we are currently targeting may limit the pool of patients that may be enrolled in our ongoing or planned clinical trials. Additional challenges include the proximity and availability of clinical trial sites for prospective subjects, and the patient referral practices of physicians, and the ability to obtain and maintain subject consent. Furthermore, there is a risk of high screening failure rates due to patient ineligibility and a significant number of withdrawals from consideration for the trial caused by the rapid deterioration of patients' clinical conditions, along with the risk that enrolled subjects will drop out before completion of the trial.

If patients are unwilling to participate in our studies for any reason, the timeline for recruiting patients, conducting studies, and obtaining regulatory approval of potential product candidates will be delayed.

If we experience delays in the commencement or completion or termination of any clinical trial of our product candidates, the commercial prospects of our product candidates will be harmed, and our ability to generate product candidate revenue from any of these product candidates could be delayed or prevented. In addition, any delays in completing our clinical trials will increase our costs, slow down our product candidate development and approval process and jeopardize our ability to commence product candidate sales and generate revenue. Any of these occurrences may harm our business, financial condition, and prospects significantly. In addition, many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval of our product candidates.

The results of clinical trials conducted at clinical sites outside the U.S. may not be accepted by the FDA and the results of clinical trials conducted at clinical sites in the U.S. may not be accepted by international regulatory authorities.

To date our only ongoing recruiting clinical trials have been conducted in Italy but we are eventually planning to globally develop Temferon, including in the U.S. Although the FDA may accept data from clinical trials conducted outside the U.S., acceptance of this data is subject to certain conditions imposed by the FDA. For example, the clinical trial must be well-designed and conducted and performed by qualified investigators in accordance with GCPs, ethical principles such as or IRB or ethics committee approval and informed consent. Generally, the subject population for any clinical trials conducted outside of the U.S. must be representative of the U.S. population, and the data must be applicable to the U.S. population and U.S. medical practice in ways that the FDA deems clinically meaningful. In addition, while these clinical trials are subject to the applicable local laws, FDA acceptance of the data will be dependent upon its determination that the trials were conducted consistent with all applicable U.S. laws and regulations. There can be no assurance the FDA or international regulatory authorities will accept data from trials conducted in Italy or outside of the location in which each regulatory authority is based as adequate support of a marketing application in each jurisdiction. If the FDA does not accept the data from sites in our Italian conducted clinical trials, or if international regulatory authorities do not accept the data from our future U.S. clinical trials, it would likely result in the need for additional trials, which would be costly and time-consuming and could delay or permanently halt the development of one or more of our product candidates.

Our ability to successfully initiate, enroll and complete a clinical trial in any foreign country including the U.S., is subject to numerous risks unique to conducting business in foreign countries, including:

- difficulty in establishing or managing relationships with CROs and physicians;
- different standards for the conduct of clinical trials;
- the absence in some countries of established groups with sufficient regulatory expertise for review of gene therapy protocols;
- our inability to locate qualified local consultants, physicians and partners; and,
- the potential burden of complying with a variety of laws, medical standards and regulatory requirements, including the regulation of pharmaceutical and biotechnology products and treatment.

Changes in methods of product candidate manufacturing or formulation may result in additional costs or delay.

As product candidates proceed through preclinical studies to late-stage clinical trials towards potential approval and commercialization, it is common that various aspects of the development program, such as manufacturing methods and formulation, are altered along the way to optimize processes and results. Such changes carry the risk that they will not achieve these intended objectives. We may also experience delays in developing a sustainable, reproducible, and scalable manufacturing process or delays in transferring that process to commercial partners, which may prevent us from initiating, completing, or expanding our clinical trials or commercializing our products, if any, on a timely or profitable basis, if at all. For example, the anticipated transition of our cell processing to a different commercial partner in the U.S., or to a commercial partner(s) relying on automated closed system, if available, using all disposable supplies would require regulatory approvals, may not be successful or may experience unforeseen delays, which may cause shortages or delays in the supply of our products available for clinical trials and future commercial sales, if any. In addition, there is no assurance that products manufactured using a different commercial partner or an automated closed system, if and when available, will achieve the same results observed to date in Temferon clinical and preclinical and non-clinical studies. Any of these changes could cause our product candidates to perform differently and affect the results of planned clinical trials or other future clinical trials conducted with the materials manufactured using altered processes. Such changes may also require additional testing such as comparability studies, FDA or EMA notification or FDA approval. This could delay completion of clinical trials, require the conduct of bridging clinical trials or the repetition of one or more clinical trials, increase clinical trial costs, delay approval of our product candidates and jeopardize our ability to commence sales and generate revenue.

Even if we complete the necessary preclinical and clinical studies, we cannot predict when or if we will obtain regulatory approval to commercialize a product candidate and the approval may be for a narrower indication than we seek.

We cannot commercialize a product until the appropriate regulatory authorities have reviewed and approved the product candidate. Even if our product candidates demonstrate safety and efficacy in preclinical and clinical studies, the regulatory agencies may not complete their review processes in a timely manner, or we may not be able to obtain regulatory approval. Many companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in late-stage clinical trials even after achieving promising results in preclinical testing and earlier-stage clinical trials. Additional delays may result if an FDA Advisory Committee or other regulatory authority does not recommend approval or recommends restrictions on approval. In addition, we may experience delays or rejections based upon additional government regulation from future legislation or administrative action, or changes in regulatory agency policy during the period of product development, clinical studies, and the review process. Regulatory agencies also may approve a product candidate for fewer or more limited indications than requested or may grant approval subject to the performance of post-marketing studies. In addition, regulatory agencies may not approve the labeling claims that are necessary or desirable for the successful commercialization of our product candidates. If we are unable to obtain necessary regulatory approvals, our business, prospects, financial condition, and results of operations may suffer.

In addition, the U.S. Supreme Court recently overruled the Chevron doctrine, which gives deference to U.S. regulatory agencies' statutory interpretations in litigation against U.S. federal government agencies, such as the FDA, where the law is ambiguous. This landmark Supreme Court decision may invite more companies and other stakeholders to bring lawsuits against the FDA to challenge longstanding decisions and policies of the FDA, including the FDA's statutory interpretations of market exclusivities and the "substantial evidence" requirements for drug approvals, which could undermine the FDA's authority, lead to uncertainties in the industry, and disrupt the FDA's normal operations, any of which could delay the FDA's review of our regulatory submissions. We cannot predict the full impact of this decision, future judicial challenges brought against the FDA, or the nature or extent of government regulation that may arise from future legislation or administrative action.

We may seek designations for our product candidates with the FDA, EMA and other comparable regulatory authorities that are intended to confer benefits such as a faster development process or an accelerated regulatory pathway, but there can be no assurance that we will successfully obtain such designations. In addition, even if one or more of our product candidates are granted such designations, we may not be able to realize the intended benefits of such designations.

The FDA, EMA, and other comparable regulatory authorities, offer certain designations for product candidates that are intended to encourage the research and development of pharmaceutical and biotechnology products addressing conditions with significant unmet medical need. These designations may confer benefits such as additional interaction with regulatory authorities, a potentially accelerated regulatory pathway and priority review. There can be no assurance that we will successfully obtain such a designation for Temferon. In addition, while such designations could expedite the development or approval process, they do not change the standards for approval. Even if we obtain such designations for one or more of our product candidates, there can be no assurance that we will realize their intended benefits.

For example, we may seek a Breakthrough Therapy Designation from the FDA for one or more of our product candidates. A Breakthrough Therapy Designation is defined as a therapy that is intended, alone or in combination with one or more other therapies, to treat a serious or life-threatening disease or condition, if preliminary clinical evidence indicates that the therapy may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. For therapies that have Breakthrough Therapy Designation, interaction and communication between the FDA and the sponsor of the trial can help to identify the most efficient path for clinical development while minimizing the number of patients placed in ineffective control regimens. Therapies with Breakthrough Therapy Designation from the FDA are also eligible for accelerated approval. Designation as a breakthrough therapy is within the discretion of the FDA. Accordingly, even if we believe one of our product candidates meets the criteria for Breakthrough Therapy Designation, the FDA may disagree and instead determine not to make such designation. In any event, the receipt of a Breakthrough Therapy Designation for a product candidate may not result in a faster development process, review or approval compared to therapies considered for approval under conventional FDA procedures and does not assure ultimate approval by the FDA. In addition, even if one or more of our product candidates qualify for Breakthrough Therapy Designation, the FDA may later decide that such product candidates no longer meet the conditions for qualification.

We may also seek Fast Track Designation from the FDA for some of our product candidates. If a therapy is intended for the treatment of a serious or life-threatening condition and the therapy demonstrates the potential to address unmet medical needs for this condition, the therapy sponsor may apply for Fast Track Designation. The FDA has broad discretion whether or not to grant this designation, so even if we believe a particular product candidate is eligible for this designation, there can be no assurance that the FDA would decide to grant it. Even if we do receive Fast Track Designation, we may not experience a faster development process, review or approval compared to conventional FDA procedures and receiving a Fast Track Designation does not provide assurance of FDA ultimate approval. The FDA may withdraw Fast Track Designation if it believes that the designation is no longer supported by data from our clinical development program.

In addition, we may seek a regenerative medicine advanced therapy ("RMAT") designation for some of our product candidates. An RMAT is defined as a cell therapy, therapeutic tissue engineering products, human cell and tissue products, or any combination products using any such therapies or products. Gene therapies, including genetically modified cells that lead to a durable modification of cells or tissues may meet the definition of regenerative medicine therapy. The RMAT program is intended to facilitate efficient development and expedite review of RMATs, which are intended to treat, modify, reverse, or cure a serious or life-threatening disease or condition, and for which preliminary clinical evidence indicates that the candidate has potential to address unmet medical needs for such disease or condition. A new drug application or a BLA for an RMAT may be eligible for priority review or accelerated approval through (1) surrogate or intermediate endpoints reasonably likely to predict long-term clinical benefit or (2) reliance upon data obtained from a meaningful number of sites. Benefits of such designation also include early interactions with FDA to discuss any potential surrogate or intermediate endpoint to be used to support accelerated approval. A regenerative medicine therapy that is granted accelerated approval and is subject to post-approval requirements may fulfill such requirements through the submission of clinical evidence, clinical studies, patient registries, or other sources of real-world evidence, such as electronic health records; the collection of larger confirmatory data sets; or post-approval monitoring of all patients treated with such therapy prior to its approval. RMAT designation is within the discretion of the FDA. Accordingly, even if we believe one of our product candidates meets the criteria for designation as a regenerative medicine advanced therapy, the FDA may disagree and instead determine not to make such designation. In any event, the receipt of RMAT designation for a product candidate may not result in a faster development process, review or approval compared to product candidates considered for approval under conventional FDA procedures and does not assure ultimate approval by the FDA. In addition, even if one or more of our product candidates qualify for RMAT designation, the FDA may later decide that the biological products no longer meet the conditions for qualification.

We may seek a conditional marketing authorization in Europe for some or all of our current product candidates, but we may not be able to obtain or maintain such a designation.

As part of its marketing authorization process, EMA may grant marketing authorizations for certain categories of medicinal products based on less complete data than is normally required, where the benefit of immediate availability of the medicine outweighs the risk inherent in the fact that additional data are still required or in the interests of public health. In such cases, it is possible for the Committee for Medicinal Products for Human Use ("CHMP") to recommend the granting of a marketing authorization, subject to certain specific obligations to be reviewed annually, which is referred to as a conditional marketing authorization. This may apply to medicinal products for human use that fall under the jurisdiction of the EMA, including those that aim at the treatment, the prevention, or the medical diagnosis of seriously debilitating or life-threatening diseases and those designated as orphan medicinal products.

A conditional marketing authorization may be granted when the CHMP finds that, although comprehensive clinical data referring to the safety and efficacy of the medicinal product have not been supplied, all the following requirements are met:

- the risk-benefit balance of the medicinal product is positive;
- the applicant will provide the comprehensive clinical data post-authorization;
- unmet medical needs will be fulfilled; and
- the benefit to public health of the immediate availability on the market of the medicinal product concerned outweighs the risk inherent in the fact that additional data is still required.

The granting of a conditional marketing authorization is restricted to situations in which only the clinical part of the application is not yet fully complete. Incomplete preclinical or quality data may only be accepted if duly justified and only in the case of a product intended to be used in emergency situations in response to public health threats. Conditional marketing authorizations are valid for one year, on a renewable basis. The holder will be required to complete ongoing trials or to conduct new trials with a view to confirming that the benefit-risk balance is positive. In addition, specific obligations may be imposed in relation to the collection of pharmacovigilance data.

Granting a conditional marketing authorization allows medicines to reach patients with unmet medical needs earlier than might otherwise be the case and will ensure that additional data on a product is generated, submitted, assessed, and acted upon. Although we may seek a conditional marketing authorization for one or more of our product candidates by the EMA, the CHMP may ultimately not agree that the requirements for such conditional marketing authorization have been satisfied and hence delay the commercialization of our product candidates.

We have received orphan drug designation for Temferon for the treatment of GBM and we may seek orphan drug designation for additional indications and for other product candidates. We may be unable to obtain orphan drug designation for our product candidates and, even if we obtain such designation, we may not be able to realize the benefits of such designation, including potential marketing exclusivity of our product candidates, if approved.

Regulatory authorities in some jurisdictions, including the U.S. and E.U., may designate drugs for relatively small patient populations as "orphan drugs." Under the Orphan Drug Act, the FDA may designate a product as an orphan drug if it is a drug intended to treat a rare disease or condition, which is generally defined as a patient population of fewer than 200,000 individuals in the U.S. or a patient population of 200,000 or more individuals in the U.S., but for which there is no reasonable expectation that the cost of developing the drug will be recovered from sales in the U.S. In the E.U., the European Commission grants orphan drug designation to promote the development of products that are intended for the diagnosis, prevention, or treatment of a life-threatening or chronically debilitating condition affecting not more than five in 10,000 people in the E.U. community. Additionally, designation is granted for products intended for the diagnosis, prevention, or treatment of a life-threatening, seriously debilitating, or serious and chronic condition and when, without incentives, it is unlikely that sales of the drug in the E.U. would be sufficient to justify the necessary investment in developing the drug or biologic product. In either case, the applicant for orphan designation must also demonstrate that no satisfactory method of diagnosis, prevention, or treatment for the condition has been authorized (or, if a method exists, the new product would be a significant benefit to those affected compared to the product available).

Temferon has been granted orphan drug designation in the U.S. and E.U. for the treatment of GBM. If we request orphan drug designation from the FDA for Temferon for additional indications, if we request the international equivalent from the applicable regulatory authorities for Temferon or if we request orphan drug designation or the international equivalent for any of our other product candidates, there can be no assurances that the FDA or international regulatory authorities will grant any of our product candidates such designation. This designation of a product candidate as an orphan product does not mean that any regulatory agency will accelerate regulatory review of, or ultimately approve, that product candidate, nor does it limit the ability of any regulatory agency to grant orphan drug designation to product candidates of other companies that treat the same indications as our product candidates prior to our product candidates receiving exclusive marketing approval.

Generally, if a product candidate with an orphan drug designation subsequently receives the first marketing approval for the indication for which it has such designation, the drug may be entitled to a period of marketing exclusivity, which precludes the FDA or EMA from approving another marketing application for the same drug for the same indication for that time period, except in limited circumstances. If another sponsor receives such approval before we do (regardless of our orphan drug designation), we will be precluded from receiving marketing approval for our product for the applicable exclusivity period. The applicable period is seven years in the U.S. and ten years in the E.U. The exclusivity period in the E.U. can be reduced to six years if a drug no longer meets the criteria for orphan drug designation or if the drug is sufficiently profitable so that market exclusivity is no longer justified. Orphan drug exclusivity may be revoked if any regulatory agency determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the drug to meet the needs of patients with the rare disease or condition.

Even if we obtain orphan drug exclusivity for a product candidate, that exclusivity may not effectively protect the product candidate from competition because different drugs can be approved for the same indication. Even after an orphan drug is approved, the FDA may subsequently approve another drug for the same condition if the FDA concludes that the latter drug is not the same drug or is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care. In the E.U., marketing authorization may be granted to a similar medicinal product for the same orphan indication if:

- the second applicant can establish in its application that its medicinal product, although similar to the orphan medicinal product already authorized, is safer, more effective or otherwise clinically superior;
- the holder of the marketing authorization for the original orphan medicinal product consents to a second orphan medicinal product application; or
- the holder of the marketing authorization for the original orphan medicinal product cannot supply enough orphan medicinal product.

Even if we obtain and maintain regulatory approval for a product candidate, our products will remain subject to ongoing regulatory oversight.

Even if we obtain any regulatory approval for our product candidates, they will be subject to ongoing regulatory requirements for manufacturing, labeling, packaging, storage, advertising, promotion, sampling, record-keeping and submission of safety and other post-market information. Any regulatory approvals that we receive for our product candidates also may be subject to a REMS, limitations on the approved indicated uses for which the product may be marketed or to the conditions of approval, or contain requirements for potentially costly post-marketing testing, including Phase 4 clinical trials, and surveillance to monitor the quality, safety, and efficacy of the product. For example, as noted above in the U.S., the holder of an approved BLA is obligated to monitor and report adverse events and any failure of a product to meet the specifications in the BLA. FDA guidance advises that patients treated with some types of gene therapy undergo follow-up observations for potential adverse events for as long as 15 years. The holder of an approved marketing application also must submit new or supplemental applications and obtain FDA approval for certain changes to the approved product, product labeling or manufacturing process.

We must comply with requirements concerning advertising and promotion for any product candidates for which we obtain marketing approval. Promotional communications with respect to therapeutics are subject to a variety of legal and regulatory restrictions and continuing review by the FDA, EMA, or comparable foreign regulatory authorities, Department of Justice, Department of Health and Human Services' Office of Inspector General, state attorneys general, members of Congress, and the public. When the FDA, EMA, or comparable foreign regulatory authorities issue regulatory approval for a product candidate, the regulatory approval is limited to those specific uses and indications for which a product is approved. If we are not able to obtain FDA, EMA, or comparable foreign regulatory authority approval for desired uses or indications for our current product candidates and any future product candidates, we may not market or promote them for those indications and uses, referred to as off-label uses, and our business, financial condition, results of operations, stock price and prospects will be materially harmed. We also must sufficiently substantiate any claims that we make for our products, including claims comparing our products to other companies' products, and must abide by the FDA, EMA, or a comparable foreign regulatory authority's strict requirements regarding the content of promotion and advertising.

While physicians may choose to prescribe products for uses that are not described in the product's labeling and for uses that differ from those tested in clinical trials and approved by the regulatory authorities, we and any third parties engaged on our behalf are prohibited from marketing and promoting the products for indications and uses that are not specifically approved by the FDA, EMA, or comparable foreign regulatory authorities. Regulatory authorities in the U.S. generally do not restrict or regulate the behavior of physicians in their choice of treatment within the practice of medicine. Regulatory authorities do, however, restrict communications by biopharmaceutical companies concerning off-label use.

If we are found to have impermissibly promoted any of our current product candidates and any future product candidates, we may become subject to significant liability and government fines. The FDA and other agencies actively enforce the laws and regulations regarding product promotion, particularly those prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted a product may be subject to significant sanctions. The U.S. federal government has levied large civil and criminal fines against companies for alleged improper promotion and has enjoined several companies from engaging in off-label promotion. The FDA has also requested that companies enter consent decrees or permanent injunctions under which specified promotional conduct is changed or curtailed.

In the E.U., the advertising and promotion of our products are subject to E.U. laws governing promotion of medicinal products, interactions with physicians, misleading and comparative advertising, and unfair commercial practices. In addition, other legislation adopted by individual E.U. Member States may apply to the advertising and promotion of medicinal products. These laws require that promotional materials and advertising for medicinal products are consistent with the product's Summary of Product Characteristics ("SmPC") as approved by the competent authorities. The SmPC is a document that provides information to physicians concerning the safe and effective use of the medicinal product. It forms an intrinsic and integral part of the marketing authorization granted for the medicinal product. Promotion of a medicinal product that does not comply with the SmPC is considered to constitute off-label promotion. The off-label promotion of medicinal products is prohibited in the E.U. The applicable laws at the E.U. level and in the individual E.U. Member States also prohibit the direct-to-consumer advertising of prescription-only medicinal products. Violations of the rules governing the promotion of medicinal products in the E.U. could be penalized by administrative measures, fines, and imprisonment. These laws may further limit or restrict the advertising and promotion of our products to the general public and may also impose limitations on our promotional activities with health care professionals.

In addition, product manufacturers and their facilities are subject to payment of user fees and continual review and periodic inspections by the FDA, EMA, and other regulatory authorities for compliance with current good manufacturing practices ("GMP") requirements and adherence to commitments made in the BLA or foreign marketing application. If we, or a regulatory authority, discover previously unknown problems with a product, such as adverse events of unanticipated severity or frequency, or problems with the facility where the product is manufactured or disagrees with the promotion, marketing or labeling of that product, a regulatory authority may impose restrictions relative to that product, the manufacturing facility or us, including requiring recall or withdrawal of the product from the market or suspension of manufacturing.

If we fail to comply with applicable regulatory requirements, a regulatory authority may:

- issue an untitled letter or warning letter that we are in violation of the law;
- seek an injunction or impose administrative, civil or criminal penalties or monetary fines;
- suspend or withdraw regulatory approval;
- suspend any ongoing clinical trials;
- refuse to approve BLA or comparable foreign marketing application (or any supplements thereto) submitted by us or our strategic partners;
- restrict the marketing or manufacturing of the product;
- seize or detain the products or require the withdrawal of the product from the market;
- refuse to permit the import or export of the products; or
- refuse to allow us to enter supply contracts, including government contracts.

Any government investigation of alleged violations of law could require us to expend significant time and resources in response and could generate negative publicity. The occurrence of any event or penalty described above may inhibit our ability to commercialize our product candidates and adversely affect our business, financial condition, results of operations and prospects.

In addition, the FDA's policies, and those of the EMA and other regulatory authorities, may change and additional government regulations may be enacted that could prevent, limit, or delay regulatory approval of our product candidates. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the U.S. or abroad. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained and we may not achieve or sustain profitability, which would materially and adversely affect our business, financial condition, results of operations and prospects.

Both marketing authorization holders and manufacturers of medicinal products are subject to comprehensive regulatory oversight by the EMA and the competent authorities of the individual E.U. Member States both before and after grant of the manufacturing and marketing authorizations. This includes control of compliance with GMP rules, which govern quality control of the manufacturing process and require documentation policies and procedures. We and our third-party manufacturers would be required to ensure that all our processes, quality systems, methods, and equipment are compliant with GMP. Failure by us or by any of our third-party partners, including suppliers, manufacturers, and distributors to comply with E.U. laws and the related national laws of individual E.U. Member States governing the conduct of clinical trials, manufacturing approval, marketing authorization of medicinal products, both before and after grant of marketing authorization, and marketing of such products following grant of authorization may result in administrative, civil, or criminal penalties. These penalties could include delays in or refusal to authorize the conduct of clinical trials or to grant marketing authorization, product withdrawals and recalls, product seizures, suspension, or variation of the marketing authorization, total or partial suspension of production, distribution, manufacturing, or clinical trials, operating restrictions, injunctions, suspension of licenses, fines, and criminal penalties. operating restrictions, injunctions, suspension of licenses, fines, and criminal penalties.

In addition, E.U. legislation related to pharmacovigilance, or the assessment and monitoring of the safety of medicinal products, provides that EMA and the competent authorities of the E.U. Member States have the authority to require companies to conduct additional post-approval clinical efficacy and safety studies. The legislation also governs the obligations of marketing authorization holders with respect to additional monitoring, adverse event management and reporting. Under the pharmacovigilance legislation and its related regulations and guidelines, we may be required to conduct a burdensome collection of data regarding the risks and benefits of marketed products and may be required to engage in ongoing assessments of those risks and benefits, including the possible requirement to conduct additional clinical trials, which may be time-consuming and expensive and could impact our profitability. Non-compliance with such obligations can lead to the variation, suspension or withdrawal of marketing authorization or imposition of financial penalties or other enforcement measures.

We do not have sales, distribution, and marketing capabilities. If we are unable to develop these capabilities or enter into agreements with third parties to market and sell Temferon and our other product candidates, we will be unable to generate any product revenue.

We currently have no sales, distribution, or marketing organization. To successfully commercialize any of our current or future product candidates, if approved, we will need to develop these capabilities, either on our own or with others. The establishment and development of our own commercial team or the establishment of a contract sales force to market any product candidate we may develop will be expensive and time-consuming and could delay any product launch. Moreover, we cannot be certain that we will be able to successfully develop this capability. We may enter collaborations or alternative transactions and arrangements regarding any approved product candidates with other entities to utilize their established marketing and distribution capabilities, but we may be unable to enter into such agreements on favorable terms, if at all. If any future collaborators do not commit sufficient resources to commercialize our product candidates, or we are unable to develop the necessary capabilities on our own, we will be unable to generate sufficient product revenue to sustain our business. We compete with many companies that currently have extensive, experienced, and well-funded sales, distribution, and marketing operations to recruit, hire, train and retain marketing and sales personnel. We also face competition in our search for third parties to assist us with the sales and marketing efforts of our product candidates, if approved. Without an internal team or the support of a third party to perform marketing and sales functions, we may be unable to compete successfully against these more established companies.

Even if any of our product candidates receives marketing approval, it may fail to achieve the degree of market acceptance by physicians, patients, third party payors and others in the medical community necessary for commercial success.

The commercial success of Temferon will depend upon the acceptance of each product by the medical community, including physicians, patients, and third-party payors. The degree of market acceptance of any approved product will depend on a number of factors, including:

- the efficacy and safety of the product;
- the potential advantages of the product compared to available therapies;
- the convenience and ease of administration compared to alternative treatments;
- limitations or warnings, including use restrictions contained in the product's approved labeling;
- distribution and use restrictions imposed by the FDA, the EMA or other regulatory authority or agreed to by us as part of a mandatory or voluntary risk management plan;
- availability of alternative treatments, including competitive products expected to be commercially launched in the near future;
- pricing and cost effectiveness in relation to alternative treatments;
- if the product is included under physician treatment guidelines as a first-, second-, or third line therapy;
- the strength of sales, marketing and distribution support;
- the availability of third-party coverage and adequate reimbursement and the willingness of patients to pay out-of-pocket in the absence of coverage by third-party payors;
- the strength of sales, marketing and distribution support;
- the willingness of patients to pay for drugs out of pocket in the absence of third party coverage; and,
- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies.

If Temferon is approved but does not achieve an adequate level of acceptance by physicians, third party payors and patients, we may not generate sufficient revenue from the product, and we may not become or remain profitable. In addition, our efforts to educate the medical community and third-party payors on the benefits of the product may require significant resources and may never be successful.

In addition, we may choose to collaborate with third parties that have direct sales forces and established distribution systems, either to augment our own sales force and distribution systems or in lieu of our own sales force and distribution systems. If we enter collaborations or alternative transactions or arrangements with third parties to perform sales, marketing and distribution services for our products, the resulting revenues, or the profitability from these revenues to us are likely to be lower than if we had sold, marketed, and distributed our products ourselves. If we are unable to enter such arrangements on acceptable terms or at all, we may not be able to successfully commercialize any of our product candidates that receive regulatory approval. Depending on the nature of the third party relationship, we may have little control over such third parties, and any of these third parties may fail to devote the necessary resources and attention to sell, market and distribute our products effectively. If we are not successful in commercializing our product candidates, either on our own or through collaborations with one or more third parties, our future product revenue will suffer, and we may incur significant additional losses.

Even if we can commercialize any product candidates, the products may become subject to unfavorable pricing regulations or third-party coverage and reimbursement policies, any of which could harm our business.

Our ability to commercialize any product candidates successfully will depend, in part, on the extent to which coverage and reimbursement for these products and related treatments will be available from government health administration authorities, private health insurers and other organizations. Government authorities and third-party payors, such as private health insurers and health maintenance organizations, decide which medications they will pay for and impact reimbursement levels.

Obtaining and maintaining adequate reimbursement for our products may be difficult. We cannot be certain if we will obtain an adequate level of reimbursement for our products by third party payors. Even if we do obtain adequate levels of reimbursement, third-party payors, such as government or private healthcare insurers, carefully review and increasingly question the coverage of, and challenge the prices charged for, drugs. Reimbursement rates from private health insurance companies vary depending on the company, the insurance plan, and other factors. A primary trend in the U.S. healthcare industry, and elsewhere around the world, is cost containment. Government authorities and third party payors have attempted to control costs by limiting coverage and the amount of reimbursement for medications. Increasingly, third party payors are requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for drugs. We may also be required to conduct expensive pharmacoeconomic studies to justify coverage and reimbursement or the level of reimbursement relative to other therapies. If coverage and reimbursement are not available or reimbursement is available only to limited levels, we may not be able to successfully commercialize any product candidate for which we obtain marketing approval, and the royalties resulting from the sales of those products may also be adversely impacted.

There may be significant delays in obtaining reimbursement for newly approved drugs, and coverage may be more limited than the purposes for which the drug is approved by the FDA, EMA, or other regulatory authorities outside the U.S. Moreover, eligibility for reimbursement does not imply that a drug will be paid for in all cases or at a rate that covers our costs, including research, development, manufacture, sale, and distribution. Interim reimbursement levels for new drugs, if applicable, may also not be sufficient to cover our costs and may not be made permanent. Reimbursement rates may vary according to the use of the drug and the clinical setting in which it is used, may be based on reimbursement levels already set for lower cost drugs and may be incorporated into existing payments for other services. Net prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the U.S. Our inability to promptly obtain coverage and adequate reimbursement rates from both government-funded and private payors for any approved products that we develop could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize products and our overall financial condition.

The regulations that govern marketing approvals, pricing, coverage, and reimbursement for new drug products vary widely from country to country. Current and future legislation may significantly change the approval requirements in ways that could involve additional costs and cause delays in obtaining approvals. Some countries require approval of the sale price of a drug before it can be reimbursed. In many countries, the pricing review period begins after marketing or product licensing approval is granted. In some foreign markets, prescription drug pricing remains subject to continuing governmental control, including possible price reductions, even after initial approval is granted. As a result, we might obtain marketing approval for a product in a particular country, but then be subject to price regulations that delay our commercial launch of the product, possibly for lengthy time periods, and negatively impact the revenues we are able to generate from the sale of the product in that country. Adverse pricing limitations may hinder our ability to recoup our investment in one or more product candidates, even if our product candidates obtain marketing approval. There can be no assurance that our product candidates, if they are approved for sale in the U.S. or in other countries, will be considered medically necessary or cost-effective for a specific indication, or that coverage or an adequate level of reimbursement will be available.

Obtaining and maintaining regulatory approval of our product candidates in one jurisdiction does not mean that we will be successful in obtaining regulatory approval of our product candidates in other jurisdictions. Our failure to obtain regulatory approval in international jurisdictions would prevent our product candidates from being marketed around the world, and any approval we are granted for our product candidates in Italy would not assure approval of product candidates in other jurisdictions, including the U.S.

To market any products outside of Italy, we must establish and comply with numerous and varying regulatory requirements of other countries, including but not limited to the U.S., regarding clinical trial design, safety, and efficacy. The research, testing, manufacturing, labeling, approval, sale, marketing, and distribution of drugs are subject to extensive regulation by regulatory authorities. These regulations differ from country to country. Even if we obtain and maintain regulatory approval of our product candidates in one jurisdiction, such approval does not guarantee that we will be able to obtain or maintain regulatory approval in any other jurisdiction, but a failure or delay in obtaining regulatory approval in one jurisdiction may have a negative effect on the regulatory approval process in others. For example, even if AIFA grants marketing approval of a product candidate, comparable regulatory authorities in foreign jurisdictions, including the FDA, must also approve the manufacturing, marketing, and promotion of the product candidate in those countries.

Approval procedures vary among jurisdictions and can involve requirements and administrative review periods different from those in Italy, including additional non-clinical studies or clinical trials as investigations conducted in one jurisdiction may not be accepted by regulatory authorities in other jurisdictions. In many jurisdictions, a product candidate must be approved for reimbursement before it can be approved for sale in that jurisdiction. In some cases, the price that we intend to charge for our products is also subject to approval. These regulatory procedures can result in substantial delays in such countries. In other countries, product approval depends on showing superiority to an approved alternative therapy. This can result in significant expense for conducting complex clinical trials.

Approval of a product candidate in Italy by AIFA does not ensure approval of such product candidate by the FDA, EMA, or other regulatory authorities in other countries or jurisdictions, and approval by EMA or another regulatory authority does not ensure approval by regulatory authorities in other foreign countries or by the FDA. Sales of our product candidates outside of the U.S. will be subject to foreign regulatory requirements governing clinical trials and marketing approval. Even if the FDA grants marketing approval for a product candidate, comparable regulatory authorities of foreign countries also must approve the manufacturing and marketing of the product candidates in those countries. Approval procedures vary among jurisdictions and can involve requirements and administrative review periods different from, and more onerous than, those in the U.S., including additional preclinical studies or clinical trials. In many countries outside the U.S., a product candidate must be approved for reimbursement before it can be approved for sale in that country. In some cases, the price that we intend to charge for our products, if approved, is also subject to approval. We intend to submit an MAA to EMA for approval of our product candidates in the E.U. but obtaining such approval from the European Commission following the opinion of EMA is a lengthy and expensive process. Even if a product candidate is approved, the FDA or the European Commission may limit the indications for which the product may be marketed, require extensive warnings on the product labeling or require expensive and time consuming additional clinical trials or reporting as conditions of approval. Regulatory authorities in countries outside of the U.S. and E.U. also have requirements for approval of product candidates with which we must comply prior to marketing in those countries. Obtaining foreign regulatory approvals and compliance with foreign regulatory requirements could result in significant delays, difficulties, and costs for us and could delay or prevent the introduction of our product candidates in certain countries.

Finally, we do not have any products approved for sale in any jurisdiction, including international markets, and we do not have experience in obtaining regulatory approval. If we, or any third parties with whom we work, fail to comply with regulatory requirements in the U.S. or international markets or to obtain and maintain required approvals or if regulatory approvals in international markets are delayed, our target market may be reduced and our ability to realize the full market potential of our products will likely be harmed. The inability to meet continuously evolving regulatory standards for approval may result in our failing to obtain regulatory approval to market our current product candidates, which could significantly harm our business, results of operations and prospects.

We operate in a rapidly changing industry and face significant competition, which may result in others discovering, developing, or commercializing products before or more successfully than we do.

The development and commercialization of new biopharmaceutical products is highly competitive and subject to rapid and significant technological advancements. We face competition from major multi-national pharmaceutical companies, biotechnology companies and specialty pharmaceutical companies with respect to our current and future product candidates that we may develop and commercialize in the future. There are several large pharmaceutical and biotechnology companies that currently market and sell products or are pursuing the development of product candidates for the treatment of cancer. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large, established companies. Potential competitors also include academic institutions, government agencies and other public and private research organizations. Our competitors may succeed in developing, acquiring, or licensing technologies and products that are more effective, more effectively marketed and sold or less costly than any product candidates that we may develop, which could render our product candidates noncompetitive and obsolete.

Many of our competitors, either alone or with their strategic collaborators, have substantially greater financial, technical, and human resources than we do. Accordingly, our competitors may be more successful than we are in obtaining approval for treatments and achieving widespread market acceptance, which may render our treatments obsolete or noncompetitive. Mergers and acquisitions in the biotechnology and pharmaceutical industries may result in even more resources being concentrated among a smaller number of our competitors. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical study sites and patient registration for clinical studies, as well as in acquiring technologies complementary to, or necessary for, our programs.

Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive or better reimbursed than any products that we may commercialize. Our competitors also may obtain EMA, FDA, or other regulatory approval for their products more rapidly than we do, which could result in our competitors establishing a strong market position for either the product or a specific indication before we are able to enter the market.

Our product candidates may face competition sooner than anticipated from biosimilar products.

Even if we are successful in achieving regulatory approval to commercialize a product candidate faster than our competitors, our product candidates may face competition from biosimilar products. In the U.S., our product candidates are regulated by the FDA as biologic products, and we intend to seek approval for these product candidates pursuant to the BLA pathway. The Biologics Price Competition and Innovation Act of 2009 (the "BPCIA") created an abbreviated pathway for the approval of biosimilar and interchangeable biologic products. The abbreviated regulatory pathway establishes legal authority for the FDA to review and approve biosimilar biologics, including the possible designation of a biosimilar as "interchangeable" based on its similarity to an existing brand product. Under the BPCIA, an application for a biosimilar product cannot be approved by the FDA until 12 years after the original branded product was approved under a BLA. The law is complex and is still being interpreted and implemented by the FDA. As a result, its ultimate impact, implementation, and meaning are subject to uncertainty.

There is a risk that any exclusivity we may be afforded if any of our product candidates are approved as a biologic product under a BLA could be shortened due to congressional action, the results of recent litigation, or otherwise, or that the FDA will not consider our product candidates to be reference products for competing products, potentially creating the opportunity for generic or biosimilar competition sooner than anticipated. Moreover, the extent to which a biosimilar product, once approved, will be substituted for any one of our reference products in a way that is like traditional generic substitution for non-biologic products is not yet clear, and will depend on a number of marketplace and regulatory factors that are still developing. In addition, a competitor could decide to forego the biosimilar approval path and submit a full BLA after completing its own preclinical studies and clinical trials. In such cases, any exclusivity to which we may be eligible under the BPCIA would not prevent the competitor from marketing its product as soon as it is approved.

In addition, critics of the 12-year exclusivity period in the biosimilar pathway law will likely continue to seek to shorten the data exclusivity period and/or to encourage the FDA to interpret narrowly the law's provisions regarding which new products receive data exclusivity. In December 2019, the U.S. agreed to remove from the United States-Mexico-Canada Agreement a requirement for at least 10 years of data exclusivity for biologic products. Also, the FDA is considering whether subsequent changes to a licensed biologic would be protected by the remainder of the reference product's original 12-year exclusivity period (a concept known in the generic drug context as "umbrella exclusivity"). If the FDA were to decide that umbrella exclusivity does not apply to biological reference products or were to make other changes to the exclusivity period, this could expose us to biosimilar competition at an earlier time. There also have been, and may continue to be, legislative and regulatory efforts to promote competition through policies enabling easier generic and biosimilar approval and commercialization, including efforts to lower standards for demonstrating biosimilarity or interchangeability, limit patents that may be litigated and/or patent settlements and implement preferential reimbursement policies for biosimilars.

In Europe, the European Commission has granted marketing authorizations for several biosimilar products pursuant to a set of general and product class-specific guidelines for biosimilar approvals issued over the past few years. In the European Economic Area ("EEA"), innovative medicinal products generally receive eight years of data exclusivity and an additional two years of marketing exclusivity. Data exclusivity prevents biosimilar applicants from referencing the innovator's preclinical and clinical trial data when applying for a biosimilar marketing authorization, during a period of eight years from the date on which the reference product was first authorized in the EEA. During the additional two-year period of market exclusivity, biosimilar marketing authorization can be submitted, and the innovator's data may be referenced, but no biosimilar product can be marketed until the expiration of the market exclusivity period. This 10-year marketing exclusivity period may be extended to 11 years if, during the first eight of those 10 years, the marketing authorization holder obtains an approval for one or more new therapeutic indications that bring significant clinical benefits compared with existing therapies. However, even if an innovative medicinal product gains the prescribed period of data exclusivity, another company may market another version of the product if such company obtained marketing authorization based on an application with a complete independent data package of pharmaceutical tests, preclinical tests and clinical trials. In addition, companies may be developing biosimilar products in other countries that could compete with our products, if approved.

If competitors can obtain marketing approval for biosimilars referencing our product candidates, if approved, such products may become subject to competition from such biosimilars, with the attendant competitive pressure and potential adverse consequences. Such competitive products may be able to immediately compete with us in each indication for which our product candidates may have received approval.

If product liability lawsuits are brought against us, we may incur substantial liabilities, even if we have appropriate insurance policies, and we may be required to limit commercialization of our product candidates.

We are exposed to potential product liability and professional indemnity risks that are inherent in the research, development, manufacturing, marketing, and use of biopharmaceutical and biotechnology products. Currently, we have no products that have been approved for marketing or commercialization; however, the use of our product candidates in clinical trials, and the sale of these product candidates, if approved, in the future, may expose us to liability claims. Product liability claims may be brought against us or our partners by participants enrolled in our clinical trials, patients, health care providers, biotechnology and pharmaceutical companies, our collaborators or others using, administering, or selling any of our future approved products. If we cannot successfully defend ourselves against any such claims, we may incur substantial liabilities, even if we have product liability or other applicable insurance policies in effect. We may not be able to maintain adequate levels of insurance for these liabilities at reasonable cost and/or reasonable terms. Excessive insurance costs or uninsured claims would add to our future operating expenses and adversely affect our financial condition. As a result of such lawsuits and their potential results, we may be required to limit commercialization of our product candidates. Regardless of the merits or eventual outcome, liability claims may result in:

- decreased demand for our product candidates;
- termination of clinical trial sites or entire trial programs;
- injury to our reputation and negative media attention;
- product recalls or increased warnings on product labels;
- withdrawal of clinical trial participants;
- costs of to defend the related litigation;
- diversion of management and our resources;
- substantial monetary awards to, or costly settlements with, clinical trial participants, patients or other claimants;
- higher insurance premiums;
- loss of initiation of investigations by regulators or other authorities; and,
- the inability to successfully commercialize our product candidates, if approved.

Gene therapies are novel, complex and difficult to manufacture. We could experience production problems that result in delays in our development or commercialization programs or otherwise adversely affect our business.

Biological products are inherently difficult to manufacture, and gene therapy products are complex biological products, the development and manufacture of which necessitates substantial expertise and capital investment.

Temferon is individually manufactured for each patient using complex processes in specialized facilities. Our production process requires a variety of raw materials, some of which are highly specialized, including the viral vector that encodes for the therapeutic payload. Some of these raw materials have limited and, in some cases, sole suppliers. Even though we plan to have back-up supplies of raw materials whenever possible, we cannot be certain such supplies will be sufficient if our primary sources are unavailable. A shortage of a critical raw material or a technical issue during manufacturing may lead to delays in clinical development or commercialization of our product candidates.

Our product candidate, Temferon, is being studied for GBM patients with unmethylated methylguanine methyltransferase ("MGMT") status, as determined by a laboratory test. If approved for use only in uMGMT-GBM patients, use of such a laboratory test would be required for each patient before treatment with Temferon. There are several currently marketed, CE-marked tests for uMGMT status in the E.U., one or more of which may be used in our clinical trials and which we would expect to be used in clinical practice upon approval of Temferon. If a regulatory authority were, however, to deem that no currently-available tests are appropriate for use with Temferon, or if appropriate tests were to become commercially unavailable, we might be required to develop and obtain regulatory approval for our own version of such a companion diagnostic test, or work with another entity to develop such a test, in which case we could experience significant delays in obtaining regulatory approval or interruptions in our ability to market Temferon.

Several factors could cause production interruptions, including equipment malfunctions, facility contamination, raw material shortages or contamination, natural disasters, disruption in utility services, human error, or disruptions in the operations of our suppliers. We have limited experience manufacturing our product candidates. We have contracted with a third party CMO for the manufacture of our viral vectors and certain of our drug products for clinical trials. We expect this CMO will be capable of providing enough of our viral vectors and gene therapy products to meet the anticipated scales for our clinical trials, in due course, and commercial demands, if approved. However, to meet our projected needs for further commercial manufacturing and large-scale clinical trials, third parties with whom we currently work might need to increase their scale and frequency of production, and we will likely need to secure alternate suppliers or develop our own capabilities. We believe that there are alternate sources of supply that can satisfy our requirements, although we cannot be certain that identifying and establishing relationships with such sources, if necessary, would not result in significant delay or material additional costs.

All manufacturers of pharmaceutical products must comply with strictly enforced requirements and complex regulations. Any failure by our CMO to adhere to or document compliance to such regulatory requirements could lead to a delay or interruption in the availability of our product candidate for clinical trials or result in sanctions, including clinical holds, fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of raw materials, product candidates or products, operating restrictions and criminal prosecutions, any of which could have significant adverse consequences on us. Our potential future dependence upon others for the manufacture of our gene therapies may also adversely affect our future profit margins and our ability to commercialize any product candidates that receive regulatory approval on a timely and competitive basis.

Delays in obtaining regulatory approval of our or our CMOs' manufacturing process and facility or disruptions in our manufacturing process may delay or disrupt our commercialization efforts.

Before we can begin to commercially manufacture our viral vector or product candidates in our own facility, or the facility of a CMO, we must obtain regulatory approval from AIFA and eventually the FDA, EMA, or other regulatory authorities for our manufacturing processes and for the facility in which manufacturing is performed. A manufacturing authorization must also be obtained from the appropriate regulatory authorities. In addition, we must pass a pre-approval inspection of our or our CMOs manufacturing facility by AIFA, the FDA, EMA, or other relevant regulatory authorities before any of our gene therapy product candidates can obtain marketing approval. To obtain approval, we will need to ensure that all of our processes, quality systems, methods, equipment policies and procedures are compliant with GMP, and perform extensive audits of vendors, contract laboratories, CMOs and suppliers. If any of our vendors, contract laboratories, CMOs or suppliers is found to be out of compliance with GMP, we may experience delays or disruptions in manufacturing while we work with these third parties to remedy the violation or while we work to identify suitable replacement vendors. The GMP requirements govern quality control of the manufacturing process and documentation policies and procedures. In complying with GMP, we will be obligated to expend time, money and effort in production, record keeping and quality control to assure that the product meets applicable specifications and other requirements. If we fail to comply with these requirements, we will be subject to possible regulatory action and may not be permitted to sell any products that we may develop.

Failure to comply with ongoing regulatory requirements could cause us to suspend production or put in place costly or time-consuming remedial measures.

The regulatory authorities may, at any time following approval of a product for sale, audit the manufacturing facilities for such a product. If any such inspection or audit identifies a failure to comply with applicable regulations, or if a violation of product specifications or applicable regulations occurs independent of such an inspection or audit, the relevant regulatory authority may require remedial measures that may be costly or time-consuming to implement and that may include the temporary or permanent suspension of a clinical trial or commercial sales or the temporary or permanent closure of a manufacturing facility. Any such remedial measures imposed upon our CMO or us could harm our business, financial condition, results of operations and prospects.

If our CMOs or we fail to comply with applicable GMP regulations, AIFA, the FDA, EMA or other regulatory authorities can impose regulatory sanctions including, among other things, refusal to approve a pending application for a new product candidate or suspension or revocation of a pre-existing approval. Such an occurrence may cause our business, financial condition, results of operations and prospects to be harmed.

Additionally, if supply from any CMO or us is delayed or interrupted, there could be a significant disruption in the clinical or commercial supply of our product candidates. We have agreements in place with our CMO pursuant to which we are collaborating on GMP manufacturing processes and analytical methods for the manufacture and release of our viral vectors and certain drug products. Therefore, if we are unable to enter into an agreement with our CMO to manufacture clinical or commercial material for our product programs, or if our agreement with our CMOs were terminated, we would have to find suitable alternative manufacturers. This could delay our or our collaborators' ability to conduct clinical trials or commercialize our current and future product candidates. The regulatory authorities also may require additional clinical trials and other nonclinical and or analytical evaluations if a new manufacturer is relied upon for clinical or commercial production. Switching manufacturers may involve substantial costs, require significant comparability studies, and could result in a delay in our desired clinical and commercial timelines.

Any contamination in our manufacturing process, shortages of materials or failure of any of our key suppliers to deliver necessary components could result in interruption in the supply of our product candidates and delays in our clinical development or commercialization schedules.

Given the nature of biological manufacturing, there is a risk of contamination in our manufacturing processes. Any contamination could materially adversely affect our ability to produce product candidates on schedule and could, therefore, harm the results of operations and cause reputational damage.

Some of the materials required in our manufacturing process are derived from biologic sources. Such materials are difficult to procure and may be subject to contamination or recall. A material shortage, contamination, recall or restriction on the use of biologically derived substances in the manufacture of our product candidates could adversely impact or disrupt the commercial manufacturing or the production of clinical material, which could materially and adversely affect our development timelines and our business, financial condition, results of operations and prospects.

Patients' cellular source material must be transported from the clinical collection site to the manufacturing facility and the cryopreserved drug product must be returned to the clinical site for administration into the patient using controlled temperature shipping containers.

Once collected from the patient, the cellular source material must be transported to the manufacturing facility using a shipping container that maintains the material at a required temperature and be delivered typically within three days of collection. While we intend to use reputable couriers and agents for the transport of such materials, if the shipping container is opened or damaged such that the required temperature is not maintained, the cellular source material may be adversely impacted, and it may not be feasible to manufacture a drug product for the patient. Similarly, if a shipment is delayed due to adverse weather, misrouting, other events or held up at a customs point, the cellular source material may not be delivered within a time window that will allow for its use for the successful manufacture of a drug product. Similarly, the patient's autologous drug product must be returned to the clinical site for administration into the patient using a specialized shipping container that maintains the material at a very low temperature for a period of typically up to ten days. While we intend to use reputable couriers and agents for the transport of our drug products, if the shipping container is opened or damaged such that the very low temperature is not maintained, the drug product may be adversely impacted, and it may be unsuitable for administration to the patient or harmful. Similarly, if a shipment is delayed due to adverse weather, misrouting, held up at customs or other events, and is not delivered to the clinical site within the time period that the very low temperature is maintained, the drug product may be unsuitable for administration to the patient or harmful.

Our gene therapies are for autologous use only. Therefore, if a drug product is administered to the wrong patient, the patient could suffer harm.

Our gene therapies are autologous, so they must be administered back only to the patient from which the cellular source material was collected. While we implement specific identifiers, lot numbers and labels with cross checks for our products and operations from collection of cellular source material, through manufacture of drug product, transport of product to the clinical site up to thawing and administration of the product, it is possible that a product may be administered into the wrong patient. If an autologous gene therapies were to be administered into the wrong patient, the patient could suffer harm, including experiencing a severe adverse immune reaction and this event, should it happen, could adversely affect our business, financial condition, results of operations and prospects.

Our focus on developing our current product candidates may not yield any commercially viable products, and our failure to successfully identify and develop additional product candidates could impair our ability to grow.

As part of our growth strategy, we intend to identify, develop, and market additional product candidates beyond our existing product candidate, namely Temferon. We may spend several years completing our development of any current or future product candidates, and failure can occur at any stage. The product candidates to which we allocate our resources may not end up being successful. Because we have limited resources, we may forego or delay pursuit of opportunities with certain programs or product candidates or for indications that later prove to have greater commercial potential than Temferon or our other product candidates. Our spending on current and future research and development programs may not yield any commercially viable product candidates. If we do not accurately evaluate the commercial potential for a particular product candidate, we may relinquish valuable rights to that product candidate through collaborations, licensing arrangements, joint ventures, strategic alliances, partnerships, or other arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate. If any of these events occur, we may be forced to abandon our development efforts with respect to a particular product candidate or fail to develop a potentially successful product candidate.

In addition, certain of our current or future product candidates may not demonstrate in patients any or all the pharmacological benefits we believe they may possess or compare favorably to existing, approved therapies. We have not yet succeeded and may never succeed in demonstrating efficacy and safety of our product candidates or any future product candidates in preclinical studies, clinical trials or in obtaining marketing approval thereafter and, therefore, may not result in the discovery and development of commercially viable products.

If we are unsuccessful in our development efforts, we may not be able to advance the development of our product candidates, commercialize products, raise capital, expand our business, or continue our operations.

Risks Related to Our Reliance on Third Parties

We utilize, and expect to continue to utilize, third parties to conduct some or all aspects of our vector production and product manufacturing for the foreseeable future, and these third parties may not perform satisfactorily.

We currently rely on our CMO to produce our viral vectors and certain of our drug products for our ongoing clinical trials and preclinical studies. For future clinical trials, we intend to utilize materials manufactured by GMP-compliant CMOs. If our partners do not successfully carry out their contractual duties, meet expected deadlines or manufacture our viral vector and product candidates in accordance with regulatory requirements or if there are disagreements between us and our CMO, we will not be able to complete, or may be delayed in completing, the clinical trials required to support approval of our product candidates or AIFA, the FDA, EMA, or other regulatory agencies may refuse to accept our clinical or preclinical data. In such instances, we may need to enter an appropriate replacement third party relationship, which may not be readily available or available on acceptable terms, which would cause additional delay or increased expense prior to the approval of our product candidates and would thereby have a negative impact on our business, financial condition, results of operations and prospects.

We have partnered with a commercial GMP-compliant CMO and intend to utilize viral vectors and gene therapy products manufactured by such CMO for our future clinical trials and products for which we obtain marketing approval. There is no assurance that our CMO, or any other future third party manufacturer that we engage, will be successful in producing any or all of our viral vector or product candidates, that any such product will, if required, pass the required comparability testing, or that any materials produced by any other third-party manufacturer that we engage will have the same effect in patients that we have observed to date. We believe that our manufacturing network will have sufficient capacity to meet demand for our clinical and existing and expected initial commercial needs, but there is a risk that if supplies are interrupted or result in poor yield or quality, it would materially harm our business. Additionally, if the gene therapy industry were to grow, we may encounter increasing competition for the raw materials and consumables necessary to produce our product candidates. Furthermore, demand for CMO GMP manufacturing capabilities may grow at a faster rate than existing manufacturing capacity, which could disrupt our ability to find and retain third party manufacturers capable of producing sufficient quantities of our viral vectors or product candidates for future clinical trials or to meet expected initial commercial demand.

Under certain circumstances, our current CMO is entitled to terminate its engagements with us. If we need to enter alternative arrangements, it could delay our development activities. Our reliance on our CMO for certain manufacturing activities will reduce our control over these activities but will not relieve us of our responsibility to ensure compliance with all required regulations. In addition to our current CMO, we may rely on additional third parties to manufacture ingredients of our viral vectors and/or drug product in the future and to perform quality testing, and reliance on these third parties entails risks including:

- reduced control for certain aspects of manufacturing activities;
- termination or nonrenewal of manufacturing and service agreements with third parties in a manner or at a time that is costly or damaging to us; and
- disruptions to the operations of our third-party manufacturers and service providers caused by conditions unrelated to our business or operations, including the bankruptcy of the manufacturer or service provider.

Any of these events could lead to clinical trial delays or failure to obtain regulatory approval or impact our ability to successfully commercialize any of our product candidates. Some of these events could be the basis for AIFA, the FDA, EMA, or other regulatory authority action, including injunction, recall, seizure or total or partial suspension of product manufacture.

We rely on third parties to conduct our preclinical and clinical studies and perform other tasks for us. If these third parties do not successfully carry out their contractual duties, meet expected deadlines or comply with regulatory requirements, we may not be able to obtain regulatory approval for or commercialize our product candidates and our business could be substantially harmed.

We do not expect to independently conduct all aspects of our lentiviral vector protocol development, research, and preclinical and clinical testing. We currently rely, and plan to continue to rely, upon third party CROs to monitor and manage data for our ongoing preclinical and clinical programs. Pursuant to the amended and restated license agreement with OSR, we agreed to use OSR as the primary site in any preclinical study or clinical trial (including all phases thereof) relating to any licensed products in the field of use, subject to OSR maintaining any required quality standards and providing its services on customary and reasonable terms and consistent with then-applicable market standards. We rely on these parties, including OSR, for execution of our preclinical and clinical studies, but we can only control limited aspects of their activities. Nevertheless, we are responsible for ensuring that each of our studies is conducted in accordance with the applicable protocol, legal, regulatory, and scientific standards, and our reliance on the CROs does not relieve us of our regulatory responsibilities. We and our CROs and other vendors are required to comply with current GMP, GCP, and Good Laboratory Practices ("GLP"), which are regulations and guidelines enforced by the FDA, the Competent Authorities of the Member States of the EEA, and comparable foreign regulatory authorities for all our product candidates in clinical development. Regulatory authorities enforce these regulations through periodic inspections of study sponsors, principal investigators, study sites and other contractors. If we or any of our CROs or vendors fail to comply with applicable regulations, the clinical data generated in our clinical studies may be deemed unreliable and AIFA, the FDA, EMA, or other comparable regulatory authorities may require us to perform additional clinical studies before approving our marketing applications. We cannot assure you that upon inspection by a given regulatory authority, such regulatory authority will determine that any of our clinical studies comply with GCP regulations. In addition, our clinical studies must be conducted with product candidates which are produced under GMP regulations. Our failure to comply with these regulations may require us to repeat clinical studies, which would delay the regulatory approval process.

We and our collaborators and contract manufacturers are subject to significant regulation with respect to manufacturing our product candidates. The manufacturing facilities on which we rely may not meet regulatory requirements and have limited capacity.

Contract manufacturers and their facilities are required to comply with extensive regulatory requirements, including ensuring that quality control and manufacturing procedures conform to GMPs. These GMP regulations cover all aspects of manufacturing relating to our product candidates and components used in clinical studies. These regulations govern manufacturing processes and procedures (including record keeping) and the implementation and operation of quality systems to control and assure the quality of investigational product candidates and products approved for sale. Poor control of production processes can lead to the introduction of contaminants or to inadvertent changes in the properties or stability of our product candidates that may not be detectable in final product testing. We, our collaborators, or our contract manufacturers must supply all necessary documentation in support of a BLA or MAA on a timely basis and must adhere to GLP and GMP regulations enforced by AIFA, the FDA, EMA, and other regulatory authorities through their facilities inspection program. The facilities and quality systems of some or all our collaborators and third-party contractors must pass a pre-approval inspection for compliance with the applicable regulations as a condition of regulatory approval of our product candidates or any of our other potential product candidates. In addition, the regulatory authorities may, at any time, audit or inspect a manufacturing facility involved with the preparation of our product candidates or our other potential product candidates or the associated quality systems for compliance with the regulations applicable to the activities being conducted. We do not control the manufacturing process of, and are completely dependent on, our contract manufacturing partners for compliance with the regulatory requirements. If these facilities do not pass a pre-approval plant inspection, regulatory approval of the product candidates may not be granted or may be substantially delayed until any violations are corrected to the satisfaction of the regulatory authority, if ever. Moreover, if our contract manufacturers fail to achieve and maintain high manufacturing standards, in accordance with applicable regulatory requirements, or there are substantial manufacturing errors, this could result in patient injury or death, product shortages, product recalls or withdrawals, delays or failures in product testing or delivery, cost overruns or other problems that could seriously harm our business.

We are dependent on a limited number of suppliers and, in some instances, a sole supplier, for some of our components and materials used in our product candidates.

We currently depend on a limited number of suppliers and, in some instances, a sole supplier, for some of the components and equipment necessary to produce our viral vectors and drug product. We cannot be sure that these suppliers will remain in business, or that they will not be purchased by one of our competitors or another company that is not interested in continuing to produce these materials for our intended purpose. Our use of a sole or a limited number of suppliers of raw materials, components and finished goods exposes us to several risks, including disruptions in supply, price increases, late deliveries, and an inability to meet customer demand. There are, in general, relatively few alternative sources of supply for these components, and in some cases, no alternatives. These vendors may be unable or unwilling to meet our future demands for our clinical trials or commercial sale. Establishing additional or replacement suppliers for these components could take a substantial amount of time and it may be difficult to establish replacement suppliers who meet regulatory requirements. Any disruption in supply from any supplier or manufacturing location could lead to supply delays or interruptions which would damage our business, financial condition, results of operations and prospects.

If we are required to switch to a replacement supplier, the manufacture and delivery of our viral vectors and product candidates could be interrupted for an extended period, adversely affecting our business. Establishing additional or replacement suppliers may not be accomplished quickly. If we can find a replacement supplier, the replacement supplier would need to be qualified and may require additional regulatory authority approval, which could result in further delay. For example, AIFA, the FDA, EMA, or other regulatory authorities could require additional supplemental data, manufacturing data and comparability data up to and including clinical trial data if we rely upon a new supplier. We may be unsuccessful in demonstrating the comparability of clinical supplies which could require the conduct of additional clinical trials. While we seek to maintain adequate inventory of the components and materials used in our product candidates, any interruption or delay in the supply of components or materials, or our inability to obtain components or materials from alternate sources at acceptable prices in a timely manner, could impair our ability to conduct our clinical trials and, if our product candidates are approved, to meet the demand of our customers and cause them to cancel orders.

In addition, as part of the regulatory process for approval of our product candidates, the regulatory authorities must review and approve the individual components of our production process, which includes raw materials, the manufacturing processes, and facilities of our suppliers. Some of our current suppliers have not undergone this process nor have they had any components included in any product approved by regulatory authorities.

Our reliance on these suppliers subjects us to a number of risks that could harm our reputation, business, and financial condition, including, among other things:

- the interruption of supply resulting from modifications to or discontinuation of a supplier's operations;
- delays in product shipments resulting from uncorrected defects, reliability issues, or a supplier's variation in a component;
- a lack of long-term supply arrangements for key components with our suppliers;
- the inability to obtain adequate supply in a timely manner, or to obtain adequate supply on commercially reasonable terms;
- difficulty and cost associated with locating and qualifying alternative suppliers for our components in a timely manner;
- production delays related to the evaluation and testing of products from alternative suppliers, and corresponding regulatory qualifications;
- a delay in delivery due to our suppliers prioritizing other customer orders over ours;
- damage to our reputation caused by defective components produced by our suppliers;
- delays and/or increased costs associated with increased tariffs and the threats of additional tariffs;
- increased cost of our warranty program due to product repair or replacement based upon defects in components produced by our suppliers; and
- fluctuation in delivery by our suppliers due to changes in demand from us or their other customers.

If any of these risks materialize, costs could significantly increase and our ability to conduct our clinical trials and, if our product candidates are approved, to meet demand for our products could be impacted.

Any collaborations, licensing arrangements, joint ventures, strategic alliances, or partnerships that we may enter in the future may not be successful, which could adversely affect our ability to develop and commercialize our current and potential future product candidates.

We may seek collaborations, licensing arrangements, joint ventures, strategic alliances or partnerships with biotechnology or pharmaceutical companies or other third parties for the development or commercialization of our current and potential future product candidates. We may enter these transactions or arrangements on a selective basis depending on the merits of retaining commercialization rights for ourselves as compared to entering selective transactions or arrangements with other biotechnology or pharmaceutical companies or other third parties for each product candidate, both in the U.S. and internationally. To the extent that we decide to enter these transactions or arrangements, we will face significant competition in seeking appropriate collaborators. Moreover, collaborations or alternative transactions or arrangements are complex, and time consuming to negotiate, document and implement. We may not be successful in our efforts to establish and implement collaborations or other alternative transactions or arrangements should we choose to enter into such transactions or arrangements. The terms of any collaborations or other transactions or arrangements that we may establish may not be favorable to us.

Additionally, we may not be able to exercise sole decision-making authority regarding the transaction or arrangement, which could create the potential risk of creating impasses on decisions, and our collaborators may have economic or business interests or goals that are, or that may become, inconsistent with our business interests or goals. It is possible that conflicts may arise with our collaborators, such as conflicts concerning the achievement of performance milestones, or the interpretation of significant terms under any agreement, such as those related to financial obligations, the ownership or control of intellectual property developed during the collaboration or the scope of our or our collaborators' other rights or obligations related to development or commercialization activities. If any conflicts arise with our current or future collaborators, they may act in their self-interest, which may be averse to our best interest, and they may breach their obligations to us. In addition, we have limited control over the amount and timing of resources that our current collaborators or any future collaborators devote to our collaborators' or our future products. Disagreements between us and our collaborators can lead to delays in the development process or commercializing the applicable product candidate or product, may result in litigation or arbitration, which would increase our expenses and divert the attention of our management, and may result in termination or dissolution of the transaction or arrangement and, in such event, we may not continue to have rights to the product candidate or products relating to such transaction or arrangement or may need to purchase such rights at a premium. These disagreements can be difficult to resolve if neither of the parties has final decision-making authority.

Collaborations with biotechnology or pharmaceutical companies and other third parties often are terminated or allowed to expire by the other party. Any such termination or expiration could adversely affect us financially and could harm our business reputation.

Our reliance on third parties requires us to share our trade secrets, which increases the possibility that a competitor will discover them or that our trade secrets will be misappropriated or otherwise disclosed.

Because we rely on third parties to develop and manufacture our product candidates, we must, at times, share trade secrets with them. We seek to protect our proprietary technology in part by entering into confidentiality agreements and, if applicable, material transfer agreements, collaborative research agreements, consulting agreements or other similar agreements with our collaborators, advisors, employees, and consultants prior to beginning research or disclosing proprietary information. These agreements typically limit the rights of the third parties to use or disclose our confidential information, such as trade secrets. Despite the contractual provisions employed when working with third parties, the need to share trade secrets and other confidential information increases the risk that such trade secrets become known by our competitors, are inadvertently incorporated into the technology of others, or are disclosed or used in violation of these agreements. Given that our proprietary position is based, in part, on our know-how and trade secrets, a competitor's discovery of our trade secrets or other unauthorized use or disclosure would impair our competitive position and may have a material adverse effect on our business.

In addition, these agreements typically restrict the ability of our collaborators, advisors, employees, and consultants to publish data potentially relating to our trade secrets. Our principal investigators, physicians and academic collaborators typically have rights to publish data, if we are notified in advance and may delay publication for a specified time in order to secure our intellectual property rights arising from the collaboration. Despite our efforts to protect our trade secrets, our competitors may discover our trade secrets, either through breach of these agreements, independent development or publication of information including our trade secrets in cases where we do not have proprietary or otherwise protected rights at the time of publication. A competitor's discovery of our trade secrets would impair our competitive position and have an adverse impact on our business.

Risks Related to Intellectual Property

We depend on a license agreement with OSR to permit us to use patents and patent applications, as well as to exploit specific OSR know-how. Termination of these rights or the failure to comply with obligations under this agreement could materially harm our business and prevent us from developing or commercializing our product candidates (Temferon in particular).

We are party to an amended and restated license agreement (the "ARLA") with OSR under which we were granted rights to patents and patent applications, as well as proprietary technologies, that are important and necessary to our business, including our Temferon based product candidates. Our rights to use these patents and patent applications and employ the inventions claimed in these licensed patents, as well as the exploitation of OSR proprietary technology, are subject to the continuation of, and our compliance with, the terms of the ARLA.

The ARLA imposes upon us various diligence, payment and other obligations, including the following:

- our obligation to pay OSR various milestone payments upon the achievement of certain milestone events, such as the initiation of different phases of clinical trials of a licensed product, MAA approval by a major market country, MAA approval in the U.S., the first commercial sale of a licensed product in the U.S. and certain E.U. countries, and achievement of certain net sales levels;
- our obligation to pay OSR royalties based on net sales of each licensed product;
- our obligation to pay OSR a royalty of our net sublicensing income for each licensed product; and
- our obligation to pay costs associated with the preparation, prosecution and maintenance of the licensed patent rights.

Although we own a patent application relating to methods of treating solid cancers with Temferon in combination with a checkpoint inhibitor and a patent application relating to methods of treating renal cell carcinoma with Temferon in combination with a checkpoint inhibitor (together, the "Provisional Patents"),we are heavily reliant upon the ARLA to licensed patents that are important or necessary to the development of our technology and product candidates, including the patents relating to Temferon. Our license is exclusive only to specific fields of use, namely: the field(s) of Interferon ("IFN") gene therapy by lentiviral based-HSPC gene transfer with respect to (a) any Solid Cancer Indication (as defined in the ARLA) (including GBM and solid liver cancer) and/or (b) any Lympho-Hematopoietic Indication (as defined in the ARLA) for which we have the right to exercise an option to be included as part of the field of use, as provided in the ARLA; and (2) certain specified gene therapy products developed during the license term for use in the aforementioned field(s). Although we have exclusive option rights to license additional fields of use, or indications, upon the payment of additional fees to OSR, there is no guarantee that we will be in a position to do so within the time period specified to exercise such right.

We do not control the preparation, prosecution and maintenance of the licensed patent rights under the ARLA, or the enforcement of the licensed patent rights and know-how rights against infringement by third parties. Thus, the licensed patent rights were not drafted by us or our attorneys, and we do not control or have any input into the prosecution of these patent rights. We cannot be certain that drafting or prosecution of the licensed patent rights has been conducted in compliance with applicable laws and regulations or will result in valid and enforceable patents. OSR maintains control of the preparation, prosecution and maintenance of the licensed patent rights, and controls enforcement of the licensed patent rights and know-how rights.

Pursuant to the ARLA, OSR may terminate the agreement in the event we breach certain of our obligations or fail to make certain payments and upon our liquidation. In addition, OSR may terminate our rights as to certain fields of use for our failure to achieve certain development milestones for specified licensed products within certain time periods. In addition, OSR may terminate the agreement in the event that commercialization of a licensed product is not started within 24 months from the grant of both (i) the MAA approval and (ii) the pricing approval of such licensed product, provided that such termination will relate solely to such licensed product and to such country or region to which both such MAA approval and pricing approval were granted. If the ARLA is terminated, we may not be able to develop, manufacture, market or sell the product candidates covered by the agreement and those being tested or approved in combination with such products. Such an occurrence could materially adversely affect the value of the product candidates being developed under the ARLA.

Disputes may arise regarding intellectual property subject to, and any of our rights and obligations under, the ARLA or any other license or other strategic agreement, including:

- the scope of rights granted under the license agreement and other interpretation-related issues;
- the extent to which our technology and processes infringe, misappropriate or violate the intellectual property of the licensor that is not subject to the license agreement;
- our diligence obligations under the license agreement and what activities satisfy those diligence obligations;
- the sublicensing of patent and other rights to third parties under any such agreement or collaborative relationships;
- the inventorship and ownership of inventions and know-how resulting from the joint creation or use of intellectual property by our licensors and us and our partners; and
- the priority of invention of patented technology.

In addition, the agreements under which we license intellectual property or technology to or from third parties are complex, and certain provisions in such agreements may be susceptible to multiple interpretations. The resolution of any contract interpretation disagreement that may arise could narrow what we believe to be the scope of our rights to the relevant intellectual property or technology or increase what we believe to be our financial or other obligations under the relevant agreement, either of which could have a material adverse effect on our business, financial condition, results of operations and prospects. Moreover, if disputes over intellectual property that we have licensed prevent or impair our ability to maintain our current licensing arrangements on commercially acceptable terms, we may be unable to successfully develop and commercialize the affected product candidates.

Our business also would suffer if any current or future licensors fail to abide by the terms of the license, if the licensors fail to enforce licensed patents against infringing third parties, if the licensed patents or other rights are found to be invalid or unenforceable, or if we are unable to enter necessary licenses on acceptable terms. Moreover, our licensors may own or control intellectual property that has not been licensed to us, and as a result, we may be subject to claims, regardless of their merit, that we are infringing, misappropriating or otherwise violating the licensor's rights.

In addition, if we are unable to successfully obtain rights to required third-party intellectual property rights or maintain the existing intellectual property rights we have, we may have to seek alternative options, such as developing new product candidates with design-around technologies, which may require more time and investment, or abandon development of the relevant research programs or product candidates and our business, financial condition, results of operations and prospects could suffer.

We have filed certain patent applications and been granted licenses in certain fields of use to patent applications. There can be no assurance that any of the patent applications we have filed or for which we have licenses will result in issued patents. As a result, our ability to protect our proprietary technology in the marketplace may be limited.

We have filed certain patent applications and been granted licenses in certain fields of use to patent applications in many countries worldwide. These applications cover a range of areas including applications relating, in general terms, to methods of treating solid cancers with Temferon in combination with a checkpoint inhibitor, methods of treating renal cell carcinoma with Temferon in combination with a checkpoint inhibitor, the use of gene vectors comprising a miRNA target sequence, and the use of gene vectors comprising an interferon-alpha transgene operably linked to a miRNA-130a or miRNA-126 target sequence. Unless and until the pending patent applications are issued, their protective scope is impossible to determine. It is also impossible to predict whether or how many of the patent applications will result in issued patents. Even if pending applications are issued, they may be issued with coverage significantly narrower than what is currently sought.

Our proprietary position for our product candidates currently depends in part upon licenses to patents protecting methods of use, which may not prevent a competitor or other third party from using the same product candidate for another use.

Composition of matter patent claims on the active pharmaceutical ingredient ("API") in pharmaceutical drug products are generally considered to be the favored form of intellectual property protection for pharmaceutical products, as such patents generally provide protection without regard to any method of use, manufacture or formulation of the API used. Method of use patent claims protect the use of a product for the specified method and dosing. These types of patent claims do not prevent a competitor or other third party from making and marketing an identical API for an indication that is outside the scope of the method claims or from developing a different dosing regimen. Moreover, even if competitors or other third parties do not actively promote their product for our targeted indications or uses for which we may obtain patents, physicians may recommend that patients use these products off-label, or patients may do so themselves. Although off-label use may infringe or contribute to the infringement of method of use patents, the practice is common and such infringement is difficult to prevent or prosecute.

Even if patents are issued based on patent applications we have filed or to which we have been granted a license, because the patent positions of pharmaceutical and biotechnology products are complex and uncertain, we cannot predict the scope and extent of patent protection for our product candidates.

Any patents that may be issued based on patent applications that we have filed or been granted licenses to will not ensure sufficient protection with respect to our activities for a number of reasons, including without limitation the following:

- any issued patents may not be broad or strong enough to prevent competition from other gene therapy products including identical or similar products;
- if patents are not issued or if issued patents expire, there would be no protections against competitors making generic equivalents;
- there may be prior art of which we are not aware that may affect the validity or enforceability of a patent claim;
- there may be other patents existing, now or in the future, in the patent landscape for Temferon, or any other product candidates that we seek to commercialize or develop, if any, that will affect our freedom to operate;
- if patents that we own or have been granted licenses to are challenged, a court could determine that they are not valid or enforceable;
- a court could determine that a competitor's technology or product does not infringe patents that we own or have been granted licenses to;
- patents to which we have been granted licenses could irretrievably lapse due to failure to pay fees or otherwise comply with regulations, or could be subject to compulsory licensing; and
- if we encounter delays in our development or clinical trials, the period of time during which we could market our products under patent protection would be reduced.

Obtaining and maintaining patent protection depends on compliance with various procedural, document submission, fee payment and other requirements imposed by governmental patent agencies, and patent protection could be reduced or eliminated for noncompliance with these requirements.

Periodic maintenance fees on any issued patent are due to be paid to the U.S. Patent and Trademark Office ("USPTO") and foreign Intellectual Property Offices in several stages over the term of the patent. Maintenance fees are also due for pending patent applications in some countries. The USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment, and other similar provisions during the patent application process. While an inadvertent lapse can in many cases be cured by payment of a late fee or by other means in accordance with the applicable rules, there are situations in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. Noncompliance events that could result in abandonment or lapse of a patent or patent application include, but are not limited to, failure to respond to office actions within prescribed time limits, non-payment of fees and failure to properly legalize and submit formal documents. In such an event, our competitors might be able to enter the market, which would have a material adverse effect on our business.

The life of patent protection is limited, and third parties could develop and commercialize products and technologies similar or identical to ours and compete directly with us after the patent licensed to us expires, which could materially and adversely affect our ability to commercialize our products and technologies.

The life of a patent and the protection it affords is limited. For example, in the U.S., if all maintenance fees are timely paid, the natural expiration of a patent is generally 20 years from its earliest U.S. non-provisional filing date. In Europe, the expiration of an invention patent is 20 years from its filing date. Even if we successfully obtain patent protection for an approved drug candidate, it may face competition from generic or biosimilar medications. Manufacturers of generic or biosimilar drugs may challenge the scope, validity or enforceability of the patents underlying our technology in court or before a patent office, and the patent holder may not be successful in enforcing or defending those intellectual property rights and, as a result, we may not be able to develop or market the relevant product candidate exclusively, which would materially adversely affect any potential sales of that product.

Given the amount of time required for the development, testing and regulatory review of new drug candidates, patents protecting such drug candidates might expire before or shortly after such drug candidates are commercialized. As a result, the patent applications we have filed and the patents and patent applications licensed to us may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours. Even if we believe that the U.S. patents involved are eligible for certain (and time-limited) patent term extensions, there can be no assurance that the applicable authorities, including the FDA and the USPTO, and any equivalent regulatory authority in other countries, will agree with our assessment of whether such extensions are available, and such authorities may refuse to grant extensions to such patents, or may grant more limited extensions than requested. For example, depending upon the timing, duration, and specifics of any FDA marketing approval of any product candidates we may develop, one or more of the U.S. patents licensed to us may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Action of 1984 (the "Hatch-Waxman Amendments"). The Hatch-Waxman Amendments permit a patent extension term of up to five (5) years as compensation for patent term lost during the FDA regulatory review process. A patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, only one patent may be extended and only those claims covering the approved drug, a method for using it, or a method for manufacturing it may be extended. However, we may not be granted an extension because of, for example, failing to exercise due diligence during the testing phase or regulatory review process, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents, or otherwise failing to satisfy applicable requirements. Moreover, the applicable period or the scope of patent protection afforded could be less than requested. If we are unable to obtain patent term extension or term of any such extension is less than requested, our competitors may obtain approval of competing products following our patent expiration, and our business could be harmed. Changes in either the patent laws or interpretation of the patent laws in the U.S. and other countries may diminish the value of our patents or narrow the scope of our patent protection.

The patents licensed to us for our product candidates are expected to expire on various dates as described in "Business— Intellectual Property." Upon the expiration, we will not be able to assert such licensed patent rights against potential competitors, which would materially adversely affect our business, financial condition, results of operations and prospects.

We may need to license intellectual property from third parties, and such licenses may not be available or may not be available on commercially reasonable terms or at all.

There may be intellectual property rights existing now, or in the future, relevant to Temferon, or any other product candidates that we seek to commercialize or develop, if any, that may affect our ability to commercialize such product candidates. Although the Company is not aware of any such intellectual property rights, a third party may hold intellectual property rights, including patent rights, that are important or necessary to the development or manufacture of our product candidates. Even if all our main product candidates are covered by patents, it may be necessary for us to use the patented or proprietary technology of third parties to commercialize our product candidates, in which case we would be required to obtain a license from these third parties. Such a license may not be available on commercially reasonable terms, or at all, and we could be forced to accept unfavorable contractual terms. In that event, we may be required to expend significant time and resources to redesign our technology, product candidates, or the methods for manufacturing them or to develop or license replacement technology, all of which may not be feasible on a technical or commercial basis. If we are unable to do so, our business could be harmed.

The licensing or acquisition of third-party intellectual property rights is a competitive area, and several more established companies may pursue strategies to license or acquire third party intellectual property rights that we may consider attractive or necessary. These established companies may have a competitive advantage over us due to their size, capital resources and greater clinical development and commercialization capabilities. In addition, companies that perceive us to be a competitor may be unwilling to assign, or license rights to us. We also may be unable to license or acquire third party intellectual property rights on terms that would allow us to make an appropriate return on our investment or at all. If we are unable to successfully obtain rights to required third party intellectual property rights or maintain the existing intellectual property rights we have, we may have to abandon development of the relevant program or product candidate, which could have a material adverse effect on our business, financial condition, results of operations, and prospects.

We may become involved in lawsuits to protect or enforce our intellectual property, which could be expensive, time-consuming, and unsuccessful.

In addition to the possibility of litigation relating to infringement claims asserted against it, we may become a party to other patent litigation and other proceedings, including *inter partes* review proceedings, post-grant review proceedings, derivation proceedings declared by the USPTO and similar proceedings in foreign countries, regarding intellectual property rights with respect to our current or future technologies or product candidates or products. Pursuant to the ARLA, OSR has the right to enforce the patents at its own expense. However, if OSR fails to do so, we have the right to enforce the licensed patents in the field of use, at our expense. The cost to us of any patent litigation or other proceeding, even if resolved in our favor, could be substantial. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their substantially greater financial resources. Patent litigation and other proceedings may also absorb significant management time. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could impair our ability to compete in the marketplace.

Competitors may infringe or otherwise violate our intellectual property. As a result, we may be required to file claims to stop third-party infringement or unauthorized use. Any such claims could provoke these parties to assert counterclaims against us, including claims alleging that we infringe their patents or other intellectual property rights, and/or that any of our intellectual property ("IP"), including licensed IP, is invalid and/or unenforceable. This can be prohibitively expensive, particularly for a company of our size, and time-consuming, and even if we are successful, any award of monetary damages or other remedy we may receive may not be commercially valuable. In addition, in an infringement proceeding, a court may decide that our asserted intellectual property is not valid, or is unenforceable, or may refuse to stop the other party from using the technology at issue on the grounds that our intellectual property does not cover its technology. An adverse determination in any litigation or defense proceedings could put our intellectual property at risk of being invalidated or interpreted narrowly and could put our patent applications at risk of not being issued.

If the breadth or strength of our patent or other intellectual property rights is compromised or threatened, it could allow third parties to exploit and commercialize our technology or products or result in our inability to exploit and/or commercialize our technology and products without infringing third-party intellectual property rights. Further, third parties may be dissuaded from collaborating with us.

Interference or derivation proceedings brought by the USPTO, or its foreign counterparts may be necessary to determine the priority of inventions with respect to our patent applications, and we may also become involved in other proceedings, such as re -examination proceedings, before the USPTO or its foreign counterparts. Due to the substantial competition in the pharmaceutical space, the number of such proceedings may increase. This could delay the prosecution of our pending patent applications or impact the validity and enforceability of any future patents that we may obtain. In addition, any such litigation, submission or proceeding may be resolved adversely to us and, even if successful, may result in substantial costs and distraction to our management.

Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation, even if some jurisdictions have specific rules to maintain confidentiality during the proceedings. Moreover, intellectual property law relating to the fields in which we operate is still evolving and, consequently, patent, and other intellectual property rights in our industry, are subject to change and are often uncertain. We may not prevail in any of these suits or other efforts to protect our technology, and the damages or other remedies awarded, if any, may not be commercially valuable. During this type of litigation, there could be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, the market price for our common stock could be significantly harmed.

Intellectual property litigation could cause us to spend substantial resources and distract our personnel from their normal responsibilities.

Litigation or other legal proceedings relating to intellectual property claims, with or without merit, is unpredictable and generally expensive and time-consuming and is likely to divert significant resources from our core business, including distracting our technical and management personnel from their normal responsibilities. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock and negatively impact our ability to raise additional funds. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing, or distribution activities.

We may not have sufficient financial or other resources to adequately conduct such litigation or proceedings. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources and more mature and developed intellectual property portfolios. Accordingly, despite our efforts, we may not be able to prevent third parties from infringing upon or misappropriating or from successfully challenging our intellectual property rights. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could have a material adverse effect on our ability to compete in the marketplace.

Any trademarks we may obtain may be infringed or successfully challenged, resulting in harm to our business.

We expect to rely on trademarks, including Temferon, as one means to distinguish any of our product candidates that are approved for marketing from the products of our competitors. Other than Temferon, which we have registered in the E.U. and the U.S., we have not yet selected trademarks for our product candidates and have not yet begun the process of applying to register trademarks for any other of our product candidates. Once we select trademarks and apply to register them, our trademark applications may not be approved. Third parties may oppose our trademark applications, or otherwise challenge our use of the trademarks. If our trademarks are successfully challenged, we could be forced to rebrand our products, which could result in loss of brand recognition and could require us to devote resources to advertising and marketing new brands. Our competitors may infringe upon our trademarks and we may not have adequate resources to enforce our trademarks.

In addition, any proprietary name we propose to use with our clinical-stage product candidates or any other product candidate in the U.S. must be approved by the FDA, regardless of whether we have registered it, or applied to register it, as a trademark. The FDA typically conducts a review of proposed product names, including an evaluation of the potential for confusion with other product names. If the FDA objects to any of our proposed proprietary product names, we may be required to expend significant additional resources to identify a suitable proprietary product name that would qualify under applicable trademark laws, not infringe the existing rights of third parties and be acceptable to the FDA. The EMA may also object to our proposed proprietary product name that infringes the existing rights of third parties.

If our trademarks and trade names are not adequately protected, then we may not be able to build name recognition in our markets of interest and our business may be adversely affected. Over the long term, if we are unable to establish name recognition based on our trademarks and trade names, then we may not be able to compete effectively, and our business may be adversely affected. Our efforts to enforce or protect our proprietary rights related to trademarks, trade secrets, domain names, copyrights or other intellectual property may be ineffective and could result in substantial costs and diversion of resources and could adversely affect our business, financial condition, results of operations and growth prospects.

We may not be able to enforce intellectual property rights throughout the world.

Filing, prosecuting, and defending patent applications and issued patents on product candidates in all countries throughout the world would be prohibitively expensive, and intellectual property rights that we have been granted licenses to in some countries outside the U.S. and Italy can be less extensive than those in the U.S. and Italy. In addition, the laws of some foreign countries do not protect intellectual property to the same extent as laws in the U.S. and Italy. Consequently, we may not be able to seek to prevent third parties from practicing inventions that are the subject of patents that we have been granted licenses to in all countries outside the U.S. and Italy, or from selling or importing products made using inventions that are the subject of patents that we have been granted licenses to in and into the U.S. or other jurisdictions. Competitors, for example, may use technologies that are the subject of patents that we have been granted licenses to in jurisdictions where we have not licensed patents to develop their own products and further, may export otherwise infringing products to territories where we have been granted licenses to patents, but enforcement is not as strong as that in the U.S. and Italy.

Many companies have encountered significant problems in protecting and defending intellectual property in foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents, trade secrets and other intellectual property, particularly those relating to pharmaceutical and biotechnology products, which could make it difficult for us to stop the infringement of patents that we have been granted licenses to or marketing of competing products in violation of our proprietary rights generally. To date, we have not sought to enforce any issued patents in these foreign jurisdictions. Proceedings to enforce patent rights that we have been granted licenses to in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put patents that we have been granted licenses to at risk of being invalidated or interpreted narrowly and patent applications that we have been granted licenses to at risk of not issuing and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate, and the damages or other remedies awarded, if any, may not be commercially meaningful. The requirements for patentability may differ in certain countries, particularly developing countries. Certain countries in Europe and developing countries, including China and India, have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties. In those countries, we and our licensors may have limited remedies if patents are infringed or if we or our licensors are compelled to grant a license to a third party, which could materially diminish the value of those patents. This could limit our potential revenue opportunities. Accordingly, our efforts to enforce intellectual property rights that we have been granted licenses to around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

If we are unable to maintain effective proprietary rights for our product candidates, we may not be able to compete effectively in our markets.

In addition to the protection afforded by any issued patents to which we have been granted licenses and future patents that may be granted, our license agreement with OSR provides rights to access know-how, or trade secrets. We seek to preserve the integrity and confidentiality of our data, trade secrets and intellectual property by maintaining physical security of our premises and physical and electronic security of our information technology systems, as well as by entering into confidentiality agreements. Agreements or security measures may be breached or could expire, and we may not have adequate remedies for any breach and/or expiration. In addition, our trade secrets may otherwise become known or be independently discovered by competitors.

We cannot provide any assurances that trade secrets and other confidential proprietary information will not be disclosed in violation of confidentiality agreements or that competitors will not otherwise gain access to trade secrets or independently develop substantially equivalent information and techniques. Also, misappropriation or unauthorized and unavoidable disclosure of trade secrets could impair our competitive position and may have a material adverse effect on our business. Additionally, if the steps taken to maintain trade secrets and intellectual property are deemed inadequate, we may have insufficient recourse against third parties for misappropriating any trade secret.

Third parties may initiate legal proceedings alleging that we are infringing their intellectual property rights, the outcome of which would be uncertain and could have a material adverse effect on the success of our business.

Our commercial success depends upon our ability to develop, manufacture, market and sell our platform technology without infringing the proprietary rights of third parties. There is considerable intellectual property litigation in the biotechnology and pharmaceutical industries. While no such judicial litigation has been brought against us and we have not been held by any court to have infringed a third party's intellectual property rights, we cannot guarantee that our technology or use of our technology does not infringe third-party patents. It is also possible that we have failed to identify relevant third-party patents or applications. For example, applications filed before November 29, 2000, and certain applications filed after that date that will not be filed outside the U.S. remain confidential until patents issue. Patent applications in the U.S. and elsewhere are published approximately 18 months after the earliest filing, which is referred to as the priority date in cases where priority is claimed. Therefore, patent applications covering our technology could have been filed by others without our knowledge. Additionally, pending patent applications which have been published can, subject to certain limitations, be later amended in a manner that could cover our technology.

In March 2013, the U.S. transitioned to a 'first to file' system in which the first inventor to file a patent application will be entitled to the patent. Third parties are allowed to submit prior art prior to the issuance of a patent by the USPTO and may become involved in post-grant review or derivation proceedings for applications filed on or after March 16, 2013, interference proceedings for applications filed before March 16, 2013, *ex parte* reexamination, or *inter partes* review challenging our patent rights or the patent rights of others. An adverse determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate, our patent rights, which could adversely affect our competitive position with respect to third parties. We may become party to, or threatened with, future adversarial proceedings or litigation regarding intellectual property rights with respect to our technology, including *inter partes* review, interference, or derivation proceedings before the USPTO and similar bodies in other countries. Third parties may assert infringement claims against us based on existing intellectual property rights and intellectual property rights that may be granted in the future.

We are aware of issued patents in the U.S. that cover the lentiviral vectors used in the manufacture of our product candidates.

If we are found to infringe a third party's intellectual property rights, we could be required to obtain a license from such third party to continue developing and marketing our technology. However, we may not be able to obtain any required license on commercially reasonable terms or at all. Any inability to secure licenses or alternative technology could result in delays in the introduction of our products or lead to prohibition of the manufacture or sale of products by us. Even if we were able to obtain a license, it could be non-exclusive, thereby giving our competitors access to the same technologies licensed to us. We could be forced, including by court order, to cease commercializing the infringing technology. In addition, we could be found liable for monetary damages, including treble damages and attorneys' fees if we are found to have willfully infringed a patent. A finding of infringement could prevent us from commercializing our technology or force us to cease some of our business operations, which could materially harm our business. Claims that we have misappropriated the confidential information or trade secrets of third parties could have a similar negative impact on our business.

We may be subject to claims asserting that our employees, consultants, or advisors have wrongfully used or disclosed alleged trade secrets, inventions, or intellectual property rights of their current or former employers or claims asserting ownership of what we regard as intellectual property that we have been granted licenses to.

Certain of our employees, consultants, or advisors are currently, or were previously, employed at universities or other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although we try to ensure that our employees, consultants, and advisors do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that these individuals or we have used or disclosed intellectual property, including trade secrets or other proprietary information, of any such individual's current or former employer. Litigation may be necessary to defend against these claims. If we fail to defend any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management. Our licensors may face similar risks, which could have an adverse impact on intellectual property that is licensed to us.

In this respect, Prof. Luigi Naldini, the Chairman of our Executive Scientific Board, is an employee of OSR –- San Raffaele Hospital, and has been appointed, according to a consultancy agreement, as a director of our Executive Scientific Board for the purpose of designing and developing the preclinic research and clinic experimentation program around cancers and gene therapy. The relevant consultancy agreement sets forth any specific representation and warranty in our favor that his activities do not infringe any third party's intellectual property rights (in particular, of OSR). In this respect, Prof. Naldini has executed a statement whereby he has declared that his consultancy activities in our favor have been carried out without infringing upon the intellectual property rights of OSR. OSR is not part of this statement and, therefore, OSR could in any case address claims against us with respect to an infringement of its intellectual property right by Prof. Naldini in relation to his activity in our favor.

There may be claims challenging the inventorship of patents and other intellectual property that we have been granted licenses to.

There may be claims that former employees, collaborators, or other third parties have an interest in patents or other intellectual property that we have been granted licenses to as an inventor or co-inventor. For example, we may have inventorship disputes arise from conflicting obligations of consultants or others who are involved in developing our product candidates. Litigation may be necessary to defend against these and other claims challenging inventorship. If we fail in defending any such claims, in addition to paying monetary damages, there may be a loss of valuable intellectual property rights to us or our licensors, such as exclusive ownership of, or right to use, valuable intellectual property. Such an outcome could have a material adverse effect on our business. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees. In addition, we may receive less revenue from future products if any of our employees successfully claim compensation for their work in developing intellectual property, which in turn could have an impact on our future profitability.

Under applicable employment laws, we may not be able to prevent our employees or key consultants, after the termination of their relationship with us or –- with reference to key consultants –- during the same, to perform competitive activity in favor of other companies nor to enforce covenants not to compete and therefore may be unable to prevent our competitors from benefiting from the expertise of such employees or consultants. In addition, employees and consultants may be entitled to seek compensation for their inventions irrespective of their agreements with us.

To date, we have not entered into non-competition agreements with our current employees to prevent them, after the termination of their employment, to perform competitive activity in favor of other employers. Therefore, we cannot exclude the fact that such employers may benefit from the expertise of our current employees developed while working for us, after the termination of their employment. We sometimes enter into non-competition agreements with certain key consultants. These agreements prohibit key consultants, if they cease working for us, from competing directly with us or working for our competitors or clients for a limited period. We may be unable to enforce these agreements under the laws of the jurisdictions in which our consultants work and it may be difficult for us to restrict our competitors from benefitting from the expertise our former consultants developed while working for us. Under Italian law, a non-competition agreement could be invalidated if, for example, the geographic scope of the non-competition agreement is too broad, or, alternatively, such an agreement could be deemed by an Italian court to be an occupation ban. Such actions would make enforcing our non-competition agreements more challenging and could make it easier for our competitors to employ or benefit from the expertise of our key consultants. In addition, we cannot exclude that our current independent consultants may perform activities –during their relationship with us- which could result in competition / conflict with our activity (e.g., in case they perform their activity for the benefit of other employers or companies). Lastly, with reference to the key consultants with whom no non-competition agreement has been entered into, we cannot exclude that, after the termination of their relationship with us or during the same, other employers or companies may benefit from the expertise of such consultants developed while working for us.

In addition, under Italian law, in case of inventions developed by our employees, which were developed while performing their employment activities, but outside the performance of their contractual duties, the rights to the inventions belong to us but we are required to compensate the employees for the rights to their respective inventions. Regarding independent consultants, Italian law provides that, save for the case in which the inventive activity of the same has been set forth as the subject of the consulting agreement and compensated for this purpose, the rights to economically exploit the original contributions and inventions realized in the execution of the consulting agreement will belong to consultant.

To date, neither the employment agreements nor the consultancy agreements provide any specific compensation related to the inventive activity. Therefore, employees and independent consultants may ask for a fair compensation due to such inventions and, regarding independent consultants, the failure to pay a fair compensation could prevent us from obtaining rights on their inventions, and this could have a material adverse effect on our operations and ability to effectively compete.

Intellectual property rights do not necessarily address all potential threats.

The degree of future protection afforded by our intellectual property rights is uncertain because intellectual property rights have limitations and may not adequately protect our business or permit us to maintain our competitive advantage. For example:

- any product candidates we may develop will eventually become commercially available in generic or biosimilar product forms;
- others may be able to make products that are similar to any product candidates we may develop or utilize similar technology but that are not covered by the claims of the patents that we may own or license now or in the future;
- we, or any future license partners or collaborators, might not have been the first to make the inventions covered by the issued patent or pending patent application that we own or license now or in the future;
- we, or any future license partners or collaborators, might not have been the first to file patent applications covering certain of our or their inventions;
- others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our intellectual property rights;
- it is possible that pending patent applications currently licensed or those to which we may enter into a license regarding in the future will not lead to issued patents;
- it is possible that there are prior public disclosures that could invalidate the issued patents that have been licensed to us, or parts of such issued patents;
- it is possible that there are unpublished applications or patent applications maintained in secrecy that may later issue with claims covering our product candidates or technology similar to ours;
- issued patents to which we hold rights to may be held invalid or unenforceable, including as a result of legal challenges by our competitors;
- the claims of patent applications, if and when issued, may not cover our product candidates;
- our competitors might conduct research and development activities in countries where we do not have patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets;
- the laws of foreign countries may not protect our proprietary rights or the proprietary rights of license partners or current or future collaborators to the same extent as the laws of the U.S.;

- the inventors of our patent applications may become involved with competitors, develop products or processes that design around our patents, or become hostile to us or the patents or patent applications on which they are named as inventors;

- we engage in scientific collaborations and will continue to do so in the future, and our collaborators may develop adjacent or competing products that are outside the scope of our patents;

- any product candidates we develop may be covered by third parties' patents or other exclusive rights;

- the patents of others may harm our business;

- we may not develop additional proprietary technologies that are patentable; and

- we may choose not to file a patent to maintain certain trade secrets or know-how, and a third-party may subsequently file a patent covering such intellectual property.

Should any of these events occur, they could have a material adverse effect on our business, financial condition, results of operations, and prospects. The patent positions of biotechnology and pharmaceutical companies generally are highly uncertain, involve complex legal, technical, and factual questions and have in recent years been the subject of much litigation. As a result, the issuance, scope, validity, enforceability, and commercial value of our patents, including those patent rights licensed to us by third parties, are highly uncertain.

Risks Related to Our Business Operations

As a company currently with substantial operations outside of the U.S., our business is subject to global economic conditions, macro events, political, regulatory, pandemic, and other risks associated with international operations and macro-economic trends.

As a company with substantial operations in Italy, our business is subject to risks associated with conducting business outside the U.S. Many of our suppliers and clinical trial relationships are located outside the U.S. The global economy, including credit and financial markets, has experienced extreme volatility and disruptions, including, among other things, severely diminished liquidity, and credit availability, declines in consumer confidence, declines in economic growth, supply chain shortages, inflation, fluctuating interest rates, increased tariffs and uncertainty about economic stability. Fluctuating interest rates, coupled with reduced government spending and volatility in financial markets may increase economic uncertainty and affect investor confidence. Similarly, regional geopolitical conflicts and trade disputes have created extreme volatility in the global capital markets and are expected to have further global economic consequences, including disruptions of the global supply chain and energy markets.

Any such volatility and disruptions may adversely affect our business or the third parties on whom we rely. If the equity and credit markets deteriorate because of the political unrest or war, it may make any debt or equity financing more costly or more dilutive or more difficult to obtain in a timely manner or on favorable terms, if at all. Accordingly, our future results could be harmed by a variety of factors, including:

- economic downturns, recessions, inflation, fluctuating interest rates, supply chain shortages, rising fuel prices, tariffs or political instability in particular non-U.S. economies and markets could negatively impact our budget projections, clinical trial cost estimates, and potential clinical timeline;

- instability in the domestic and international banking systems where the Company has accounts;

- differing and changing regulatory requirements for product approvals in the U.S. and Italy;

- differing jurisdictions could present different issues for securing, maintaining or obtaining freedom to operate in such jurisdictions;
- potentially reduced protection for intellectual property rights that could impact our ability to develop and/or license our technology;
- difficulties in compliance with different, complex, and changing laws, regulations and court systems of multiple jurisdictions and compliance with a wide variety of foreign laws, treaties and regulations that could affect our need to hire subject matter experts or retain third-party experts;
- changes in non-U.S. regulations and customs, tariffs, and trade barriers;
- foreign exchange risks and currency controls due to maintaining our cash and cash equivalents both in U.S. dollars and Euros;
- changes in a specific country's or region's political or economic environment;
- trade protection measures, import or export licensing requirements or other restrictive actions by governments;
- differing reimbursement regimes and price controls in certain non-U.S. markets;
- negative consequences from changes in tax laws;
- compliance with tax, employment, immigration and labor laws for employees living or traveling abroad, including, for example, the variable tax treatment in different jurisdictions of options granted under our share incentive plans;
- workforce uncertainty in countries where labor unrest is more common than in the U.S.;
- litigation or administrative actions resulting from claims against us by current or former employees or by employees of third party contractors or consultants, individually or as part of class actions, including: (i) claims of wrongful terminations and payment of the related damages, (ii) discrimination, (iii) misclassification, (iv) claims for salary differences or for a different classification according to national collective bargaining agreement, (v) claims for the payment of social security charges or severance benefits, (vi) claims from suppliers' employees or external consultants such as, by way of example, claims for reclassification as employees, rather than independent contractors, or, as indicated above, requests for payment of salary / social security charges, (vii) any sanctions due to the above-mentioned obligations, (viii) or other violations of labor law or other alleged conduct;
- difficulties associated with staffing and managing international operations, including differing labor relations;
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad; and
- business interruptions resulting from geo-political actions, including war and terrorism, health epidemics, or natural disasters including earthquakes, typhoons, floods, and fires.

We manage our business through a small number of employees, key consultants, and third party contractors.

Our key people include our Chief Executive Officer and current Chairman, Pierluigi Paracchi, who co-founded our Company in 2014 along with Prof. Luigi Naldini, our Executive Scientific Board Chairman, and Bernhard Gentner, a member of our Executive Scientific Board. Our other key people include Carlo Russo, our Chief Medical Officer & Head of Development, Richard Slansky, our Chief Financial Officer, Barbara Regonini, our Finance Director and Stefania Mazzoleni, our Scientific Project Manager and Communications Officer. Our future growth and success depends on our ability to recruit, retain, manage, and motivate our employees and key consultants. The loss of the services of our Chief Executive Officer or any of our key personnel or the inability to hire or retain experienced management personnel could adversely affect our ability to execute our business plan and harm our operating results. Although we expect to enter into employment agreements with management, these agreements will likely be terminable at will with notice.

In addition, laws and regulations on executive compensation, including legislation in our home country, Italy, may restrict our ability to attract, motivate and retain the required level of qualified personnel.

Because of the specialized scientific and managerial nature of our business, we rely heavily on our ability to attract and retain qualified scientific and technical consultants. In particular, the loss of one or more of our key personnel could be detrimental to us if we cannot recruit suitable replacements in a timely manner. Recruiting and retaining other qualified employees, consultants, and advisors for our business, including scientific and technical personnel, will also be critical to our success. There is currently a shortage of skilled executives in our industry, which is likely to continue. As a result, competition for skilled personnel, including in gene therapy research and vector manufacturing, is intense and the turnover rate can be high. We may not be able to attract and retain personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for individuals with similar skill sets. In addition, failure to succeed in preclinical or clinical trials may make it more challenging to recruit and retain qualified personnel. The inability to recruit or the loss of the services of any executive, key employee, consultant, or advisor may impede the progress of our research, development, and commercialization objectives. We do not currently carry "key person" insurance on the lives of members of senior management. The competition for qualified personnel in the biotechnology and pharmaceutical fields is intense. Due to this intense competition, we may be unable to attract and retain qualified personnel necessary for the development of our business or to recruit suitable replacement personnel.

We rely on a single manufacturing facility, and if operations at that manufacturing facility are disrupted, we could experience delays in our clinical trials or we would need to expend additional time and capital to identify and onboard another manufacturing facility.

We face risks inherent in operating a single manufacturing facility, since any disruption, such as a fire, natural hazards or vandalism could significantly interrupt our manufacturing capability. We currently do not have alternative production plans in place or disaster-recovery facilities available. In case of a disruption, we will have to establish alternative manufacturing sources. This would require substantial capital on our part, which it may not be able to obtain on commercially acceptable terms or at all. Additionally, we would likely experience months or years of manufacturing delays as we build or locate replacement facilities and seek and obtain necessary regulatory approvals. If this occurs, we will be unable to satisfy manufacturing needs on a timely basis, if at all. Also, operating any new facilities may be more expensive than operating our current facility. Further, business interruption insurance may not adequately compensate us for any losses that may occur, and we would have to bear the additional cost of any disruption. For these reasons, a significant disruptive event at the manufacturing facility could have drastic consequences, including placing our financial stability at risk.

We will need to significantly increase the size of our organization, and we may experience difficulties in managing growth.

We currently have a very limited number of employees. If we are successful in executing our business strategy and to commercialize our products, if approved, we will need to substantially increase our operations, including expanding our employee base of managerial, operational and financial personnel. Any future growth will impose significant added responsibilities on members of management, including the need to identify, recruit, maintain and integrate additional employees. To that end, we must be able to:

- manage our clinical trials and the regulatory process effectively;
- develop our administrative, accounting and management information systems and internal controls;
- hire and train additional qualified personnel; and
- integrate current and additional management, administrative, financial and sales and marketing personnel.

Our employees, principal investigators, consultants, and commercial partners may engage in misconduct or other improper conduct or activities, including non-compliance with regulatory standards and requirements and insider trading.

We are exposed to the risk of fraud or other misconduct by our employees, principal investigators, consultants, and commercial partners. Misconduct by these parties could include intentional failures to comply with the regulations of AIFA, the FDA, EMA, or of other foreign regulatory authorities, provide accurate information to AIFA, the FDA, EMA, and other foreign regulatory authorities, comply with healthcare fraud and abuse laws and regulations in the U.S. and other countries, report financial information or data accurately or disclose unauthorized activities to us. Sales, marketing, and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Such misconduct could also involve the improper use of information obtained during clinical trials, which could result in regulatory sanctions and cause serious harm to our reputation. We have adopted a code of conduct applicable to all our employees, but it is not always possible to identify and deter employee misconduct, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to comply with these laws or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of significant fines or other sanctions.

We may be subject, directly, or indirectly, to federal and state healthcare fraud and abuse laws, false claims laws and health information privacy and security laws. If we are unable to comply, or have not fully complied, with such laws, we could face substantial penalties.

If we obtain AIFA, FDA, EMA or other regulatory authority approval for any of our product candidates and begin commercializing those products , our operations may be directly or indirectly through our customers, subject to various federal, state and/or international fraud and abuse laws, including, without limitation, the U.S. federal Anti-Kickback Statute, the U.S. federal False Claims Act and U.S. physician sunshine laws and regulations. These laws may impact, among other things, our proposed sales, marketing, and education programs. In addition, we may be subject to patient privacy regulation by both the U.S. federal government and the states and countries in which we conduct our business. The laws that may affect our ability to operate include:

- the U.S. federal Anti-Kickback Statute, which prohibits, among other things, persons from knowingly and willfully soliciting, receiving, offering or paying remuneration, directly or indirectly, to induce, or in return for, the purchase or recommendation of an item or service reimbursable under a U.S. federal healthcare program, such as the Medicare and Medicaid programs;

- U.S. federal civil and criminal false claims laws and civil monetary penalty laws, which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment from Medicare, Medicaid or other third-party payors that are false or fraudulent;

- the U.S. Health Insurance Portability and Accountability Act of 1996 (“HIPAA”), which created new federal criminal statutes that prohibit executing a scheme to defraud any healthcare benefit program and making false statements relating to healthcare matters;

- HIPAA, as amended by the Health Information Technology and Clinical Health Act, and its implementing regulations, which imposes certain requirements relating to the privacy, security and transmission of individually identifiable health information;

- the U.S. federal physician sunshine requirements under the U.S. Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act (the “PPACA”), requires manufacturers of drugs, devices and medical supplies to report annually to the U.S. Department of Health and Human Services information related to payments and other transfers of value to physicians, other healthcare providers and teaching hospitals and ownership and investment interests held by physicians and other healthcare providers and their immediate family members and applicable group purchasing organizations;

- U.S. state law equivalents of each of the above U.S. federal laws, such as anti-kickback and false claims laws that may apply to items or services reimbursed by any third-party payor, including commercial insurers; state laws that require biotechnology and pharmaceutical companies to comply with the biotechnology and pharmaceutical industries' voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government, or otherwise restrict payments that may be made to healthcare providers and other potential referral sources; state laws that require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures; and state laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts; and

- European and other foreign law equivalents of each of the laws, including reporting requirements detailing interactions with and payments to healthcare providers, and the European General Data Protection Regulation (the "GDPR"), which became effective in May 2018 and contains new provisions specifically directed at the processing of health information, higher sanctions and extra-territoriality measures intended to bring non-E.U. companies under the regulation, including companies like us that conduct clinical trials in the E.U.; we anticipate that over time we may expand our business operations to include additional operations in the E.U. and with such expansion, we would be subject to increased governmental regulation in the E.U. countries in which we might operate, including the GDPR and all relevant data protection rulings and further legislation.

The scope and enforcement of each of these laws is uncertain and subject to rapid change in the current environment of healthcare reform, especially considering the lack of applicable precedent and regulations. U.S. federal and state enforcement bodies have recently increased their scrutiny of interactions between healthcare companies and healthcare providers, which has led to several investigations, prosecutions, convictions and settlements in the healthcare industry. It is possible that U.S. and other governmental authorities will conclude that our business practices do not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other related governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, including, without limitation, damages, fines, imprisonment, disgorgement, exclusion from participation in government funded healthcare programs, such as Medicare and Medicaid, reputational harm, additional oversight and reporting obligations if we become subject to a corporate integrity agreement or similar settlement to resolve allegations of non-compliance with these laws and the curtailment or restructuring of our operations. If any of the physicians or other healthcare providers or entities with whom we expect to do business is found to be not in compliance with applicable laws, they may be subject to similar actions, penalties, and sanctions. Efforts to ensure that our business arrangements comply with applicable healthcare laws and regulations, as well as responding to possible investigations by government authorities, can be time- and resource-consuming and can divert a company's attention from the business.

Healthcare legislative and regulatory reform measures may have a material adverse effect on our business and results of operations.

Our industry is highly regulated and changes in law may adversely impact our business, operations, or financial results. The PPACA is a sweeping measure intended to, among other things, expand healthcare coverage within the U.S., primarily through the imposition of health insurance mandates on employers and individuals and expansion of the U.S. Medicaid program. Several provisions of the law may affect us and increase certain of our costs.

In addition, other legislative changes have been adopted since the PPACA was enacted. These changes include aggregate reductions in U.S. Medicare payments to providers of 2% per fiscal year, which went into effect on April 1, 2013, and, following passage of the U.S. Bipartisan Budget Act of 2018, will remain in effect through 2027 unless additional U.S. Congressional action is taken. In January 2013, President Obama signed into law the American Taxpayer Relief Act of 2012, which, among other things, further reduced Medicare payments to several types of providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These laws may result in additional reductions in Medicare and other healthcare funding, which could have a material adverse effect on our customers and, accordingly, our financial operations.

We anticipate that the PPACA, as well as other U.S. healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and an additional downward pressure on the reimbursement our customers may receive for our products. Further, there have been, and there may continue to be, judicial and Congressional challenges to certain aspects of the PPACA. For example, the U.S. Tax Cuts and Jobs Act of 2017 (the "TCJA") includes a provision repealing, effective January 1, 2019, the tax-based shared responsibility payment imposed by the PPACA on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the "individual mandate." Additional legislative and regulatory changes to the PPACA, its implementing regulations and guidance and its policies, remain possible. However, it remains unclear how any new legislation or regulation might affect the prices we may obtain for any of our product candidates for which regulatory approval is obtained. Any reduction in reimbursement from Medicare and other government programs may result in a similar reduction in payments from private payers. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability or commercialize our products.

In addition, the delivery of healthcare in the E.U., including the establishment and operation of health services and the pricing and reimbursement of medicines, is almost exclusively a matter for national, rather than E.U., law, and policy. National governments and health service providers have different priorities and approaches to the delivery of health care and the pricing and reimbursement of products in that context. In general, however, the healthcare budgetary constraints in most E.U. member states have resulted in restrictions on the pricing and reimbursement of medicines by relevant health service providers. Coupled with ever-increasing E.U. and national regulatory burdens on those wishing to develop and market products, this could prevent or delay marketing approval of our product candidates, restrict or regulate post-approval activities and affect our ability to commercialize any products for which we obtain marketing approval.

We are currently unable to predict what additional legislation or regulation, if any, relating to the health care industry may be enacted in the future or what effect recently enacted federal legislation or any such additional legislation or regulation would have on our business. The pendency or approval of such proposals or reforms could result in a decrease in the price of our securities or limit our ability to raise capital or to enter into collaboration agreements for the further development and potential commercialization of our products.

The use of any of our product candidates could result in product liability or similar claims that could be expensive, damage our reputation and harm our business.

Our business exposes us to an inherent risk of potential product liability or similar claims. Mainly in the U.S., the biotechnology and pharmaceutical industries have historically been litigious, and we face financial exposure to product liability or similar claims if the use of any of our products were to cause or contribute to injury or death. There is also the possibility that defects in the design or manufacture of any of our products might necessitate a product recall. Although we plan to maintain product liability insurance, the coverage limits of these policies may not be adequate to cover future claims. In the future, we may be unable to maintain product liability insurance on acceptable terms or at reasonable costs and such insurance may not provide us with adequate coverage against potential liabilities. A product liability claim, regardless of merit or ultimate outcome, or any product recall could result in substantial costs to us, damage to our reputation, customer dissatisfaction and frustration and a substantial diversion of management attention. A successful claim brought against us more than, or outside of, our insurance coverage, could have a material adverse effect on our business, financial condition, and results of operations.

Our internal information technology systems, or those of our third party vendors, collaborators, or other contractors or consultants, may fail or suffer cyber security breaches or other unauthorized or improper access, which could result in a significant disruption of our product development programs, give rise to significant liability, subject us to costly and protracted litigation, cause significant reputational harm, and impact our ability to operate our business effectively.

We are increasingly dependent upon information technology systems, infrastructure, and data to operate our business. In the ordinary course of business, we collect, store, and transmit confidential information (including but not limited to intellectual property, proprietary business information, and personal information). It is critical that we do so in a secure manner to maintain the confidentiality and integrity of such information. We also have outsourced elements of our operations to third parties, and as a result we manage a few third-party vendors and other contractors and consultants who have access to our confidential information.

Our internal information technology systems and those of our current and any future third party vendors, collaborators and other contractors or consultants may be vulnerable to a variety of disruptive elements, including data breaches, cyber-attacks by malicious third parties (including the deployment of computer viruses, harmful malware, ransomware, denial-of-service attacks, social engineering, and other means to affect service reliability and threaten the confidentiality, integrity, and availability of information), unauthorized access, natural disasters, terrorism, war, telecommunication and electrical failures and persons with access to systems inside our organization. In particular, the risk of a security breach or disruption, through cyber-attacks or cyber intrusion, including by computer hackers and cyber terrorists, has generally increased as the number, intensity, and sophistication of attempted attacks and intrusions from around the world have increased. We may not be able to anticipate all types of security threats, and we may not be able to implement preventive measures effective against all such security threats. Because the techniques used by cyber criminals change frequently, may not be recognized until launched, and can originate from a wide variety of sources, including outside groups such as external service providers, organized crime affiliates or terrorist organizations, we and our partners may be unable to anticipate these techniques or implement adequate preventative measures. Further, we do not have any control over the operations of the facilities or technology of third parties that collect, process and store personal data on our behalf.

While we have not experienced any significant system failure, accident, or security breach to date, if such an event were to occur and cause interruptions in our operations or a loss of, or damage to, our data or applications, or those of our third party vendors and other collaborators, contractors and consultants, it could result in a disruption of our development programs and our business operations, whether due to a loss of our trade secrets or other confidential, personal or proprietary information, significant delays or setbacks in our research, or other similar disruptions. For example, the loss of clinical trial data from completed or future clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data or applications, or inappropriate disclosure of confidential, personal, or proprietary information, we could incur significant liability, our competitive position could be harmed, our reputation could be damaged, and the further development and commercialization of our product candidates could be delayed.

Unauthorized disclosure of sensitive or confidential data, including personal information, whether through a breach of computer systems, systems failure, employee negligence, fraud or misappropriation, or otherwise, or unauthorized access to or through our information systems and networks, whether by our employees or third parties, could result in negative publicity, damage to our reputation and/or compel us to comply with federal and/or state breach notification laws and foreign law equivalents, subject us to mandatory corrective action, and otherwise subject us to liability under laws and regulations that protect the privacy and security of personal information. The costs related to significant security breaches or disruptions could be material. If the information technology systems of our third-party vendors and other collaborators, contractors and consultants become subject to disruptions or security breaches, we may be exposed to material liability and have insufficient recourse against such third parties and we may have to expend significant resources to mitigate the impact of such an event, and to develop and implement protections to prevent future events of this nature from occurring. Any of the foregoing could adversely affect our business, financial condition, results of operations or prospects.

We or the third parties upon whom we depend, may be adversely affected by earthquakes or other natural disasters and our business continuity and disaster recovery plans may not adequately protect us from a serious disaster.

Earthquakes or other natural disasters could severely disrupt our operations, and have a material adverse effect on our business, results of operations, financial condition, and prospects. If a natural disaster, power outage or other event occurred that prevented us from using all or a significant portion of our headquarters, that damaged critical infrastructure, such as the manufacturing facilities of our third-party contract manufacturers, or that otherwise disrupted operations, it may be difficult or, in certain cases, impossible for us to continue our business for a substantial period. The disaster recovery and business continuity plans that we have in place currently are limited and are unlikely to prove adequate in the event of a serious disaster or similar event. We may incur substantial expenses because of the limited nature of our disaster recovery and business continuity plans, which, particularly when taken together with our lack of earthquake insurance, could have a material adverse effect on our business, financial condition, results of operations and prospects.

Unsuccessful compliance with certain European privacy regulations could have an adverse effect on our business and reputation.

The collection and use of personal health data in the E.U. is governed, as of May 2018, by the General Data Protection Regulation 2016/679 (the "GDPR") as implemented by European Data Protection Board (the "EDPB") guidelines and E.U. Member States national legislations. General E.U. data protection rules impose several requirements relating to the consent of the individuals to whom the personal data relates, the information provided to the individuals, notification of data processing obligations to the competent national data protection authorities and the security and confidentiality of the personal data. The GDPR also extends the geographical scope of E.U. data protection law to non-E.U. entities under certain conditions, tightens existing E.U. data protection principles and creates new obligations for companies and new rights for individuals. Failure to comply with the requirements of the GDPR, the EDPB guidelines and the related national data protection laws of the E.U. Member States may result in fines and other administrative penalties. The GDPR introduces new data protection requirements in the E.U. and substantial fines for breaches of the data protection rules, including violation of articles 44 to 49 GDPR related to transfer of personal data to a recipient in a non-E.U. country. The GDPR regulations impose additional responsibility and liability in relation to personal data that we process, and we intend to put in place additional mechanisms ensuring compliance with these and/or new data protection rules. In addition, other jurisdictions, including Italy, have implemented regulations like GDPR. Regarding Italian legislation, the national Privacy and Data Protection Code has been amended according to GDPR provisions (Legislative Decree n. 196/2003 as amended and updated by Legislative Decree n. 101/2018) and imposes additional fines and administrative penalties in relation to the processing of health data and processing of data for scientific research purposes. Moreover, European data protection background is constantly changing under the drive of the EDPB on the correct interpretation and application of GDPR and the ruling activity of the Court of Justice of the E.U. (see, for instance, the recent CJEU case C-3111/18, also known as Schrems II which invalidated the E.U.-U.S. Privacy Shield Framework for transfer of data to U.S.).

The Company is compliant with most recent legislative changes in European data protection rules, adopting Data Processing Agreements containing Standard Contractual Clauses with all partners based in the U.S. and (for the transition period until June 2021) in the United Kingdom. However, changes to these European privacy regulations (and similar regulations in other jurisdictions) and unsuccessful compliance may be onerous and adversely affect our business, financial condition, prospects, results of operations and reputation.

Risks Related to Ownership of Our Securities

We cannot guarantee that we will be able to satisfy the continued listing standards of the Nasdaq going forward.

Our American Depository Shares ("ADS") are listed on the Nasdaq. However, we cannot ensure that we will be able to satisfy the continued listing standards of the Nasdaq going forward. If we cannot satisfy the continued listing standards going forward, the Nasdaq Stock Market may commence delisting procedures against us, which could result in our ADS being removed from listing on the Nasdaq. If any of our ADSs were to be delisted, the liquidity of our ADSs could be adversely affected and the market price of our ADSs could decrease. Delisting could also adversely affect the ability of the holder of our ADSs to trade or obtain quotations on our ADSs because of lower trading volumes and transaction delays. These factors could contribute to lower prices and larger spreads in the bid and ask price for our ADSs. Investors may also not be able to resell their ADSs at or above the price they paid for such securities or at all.

The trading price of the ADSs is likely to be highly volatile.

The trading price of the ADSs has been and is likely to continue to be highly volatile. The following factors, in addition to other risk factors described in this section, may have a significant impact on the market price of the ADSs:

- adverse results or delays in pre- and non-clinical studies or clinical trials;
- reports of adverse events in other gene therapy products or clinical studies of such products;
- inability to obtain additional funding;

- inability to obtain the approvals necessary to commence clinical trials;
- unsatisfactory results of clinical trials;
- announcements of regulatory approval or the failure to obtain it, or specific label indications or patient populations for its use, or changes or delays in the regulatory review process;
- announcements of therapeutic innovations or new products by us or our competitors;
- adverse actions taken by regulatory authorities with respect to our clinical trials, manufacturing supply chain or sales and marketing activities;
- changes or developments in laws or regulations applicable to the treatment of cancer tumors, or any other indication that we may seek to develop;
- any adverse changes to our relationship with manufacturers or suppliers;
- any intellectual property infringement actions in which we may become involved;
- announcements concerning our competitors or the biotechnology and pharmaceutical industries in general;
- achievement of expected product sales and profitability or our failure to meet expectations;
- our commencement of, or involvement in, litigation;
- any major changes in our board of directors or management;
- our ability to recruit and retain qualified regulatory, research and development personnel;
- legislation in the U.S. relating to the sale or pricing of biotechnology or gene therapy products;
- the depth of the trading market in the ADSs;
- economic downturns, recessions, inflation, fluctuating interest rates, supply chain shortages, rising fuel prices, tariffs or political instability in global, U.S. or particular foreign economies and markets;
- instability in the global or U.S. banking systems or the banking systems of foreign countries;
- business interruptions resulting from a local or worldwide pandemic, geopolitical actions, including war and terrorism, or natural disasters;
- the granting or exercise of employee stock options or other equity awards;
- disputes or other developments relating to proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our technologies;
- additions or departures of key scientific or management personnel;
- significant lawsuits, including patent or shareholder litigation; and
- changes in investors' and securities analysts' perception of the business risks and conditions of our business.

In addition, the stock market in general, and the Nasdaq Stock Market in particular, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of small companies. Broad market and industry factors may negatively affect the market price of the ADSs, regardless of our actual operating performance. Further, a systemic decline in the financial markets and related factors beyond our control may cause our ADS price to decline rapidly and unexpectedly.

Holders of ADSs may not receive the same distributions or dividends as those we make to the holders of our ordinary shares, and, in some limited circumstances, you may not receive dividends or other distributions on our ordinary shares and you may not receive any value for them, if it is illegal or impractical to make them available to you.

The Bank of New York Mellon, the depositary for the ADSs (the "Depositary"), has agreed to pay to you the cash dividends or other distributions it or the custodian receives on ordinary shares or other deposited securities underlying the ADSs, after deducting its fees and expenses and subject to the terms of the deposit agreement. You will receive these distributions in proportion to the number of ordinary shares the ADSs represent. However, in accordance with the limitations set forth in the deposit agreement the Depositary is not responsible if it decides that it is unlawful or impractical to make a distribution available to any holders of ADSs. For example, it would be unlawful to make a distribution to a holder of ADSs if it consists of securities that require registration under the Securities Act of 1933, as amended (the "Securities Act"), but that are not properly registered or distributed under an applicable exemption from registration. In addition, conversion into U.S. dollars from foreign currency that was part of a dividend made in respect of deposited ordinary shares may require the approval or license of, or a filing with, any government or agency thereof, which may be unobtainable. In these cases, the Depositary may determine not to distribute such property and hold it as "deposited securities" or may distribute the net cash proceeds from the sale of the dividends. We have no obligation to register under U.S. securities laws any ADSs, ordinary shares, rights or other securities received through such distributions. We also have no obligation to take any other action to permit the distribution of ADSs, ordinary shares, rights or anything else to holders of ADSs. In addition, the Depositary may withhold from such dividends or distributions its fees and an amount on account of taxes or other governmental charges to the extent the Depositary believes it is required to make such withholding. This means that you may not receive the same distributions or dividends as those we make to the holders of our ordinary shares, and, in some limited circumstances, you may not receive any value for such distributions or dividends if it is illegal or impractical for us to make them available to you. These restrictions may cause a material decline in the value of the ADSs.

Holders of ADSs must act through the Depositary to exercise voting rights relating to the ordinary shares.

Holders of the ADSs do not have the same rights as our shareholders and may only exercise the voting rights with respect to the underlying ordinary shares in accordance with the provisions of the deposit agreement. When a shareholder meeting is convened, holders of ADSs may not receive sufficient notice of a shareholder meeting to permit them to cancel their ADSs and withdraw ordinary shares to allow them to directly cast their vote with respect to any specific matter. In addition, the Depositary and its agents may not be able to send voting instructions to holders of ADSs or carry out their voting instructions in a timely manner. We will make all reasonable efforts to cause the Depositary to extend voting rights to holders of the ADSs in a timely manner, but we cannot assure holders that they will receive the voting materials in time to ensure that they can instruct the Depositary to vote the ordinary shares underlying their ADSs. Furthermore, the Depositary and its agents will not be responsible for any failure to carry out any instructions to vote, for the manner in which any vote is cast or for the effect of any such vote. As a result, holders of the ADSs may not be able to exercise their right to vote and they may lack recourse if the ordinary shares underlying their ADSs are not voted as they requested. In addition, in the capacity as a holder of ADSs, they will not be able to call a shareholder meeting.

Further, as described in more detail below, our loyalty share program is available only to holders who own their ordinary shares in registered form, and is not available to ADS holders. See "—Risks Related to Italian Law and Our Operations in Italy—Our loyalty share program could have a negative effect on the liquidity of our ADSs and may make it more difficult for investors to acquire a controlling interest, change the management or the strategy of our company or exercise influence over us, which may adversely affect the market price of the ADSs. Further, our loyalty share program is available only to holders who own their ordinary shares in registered form, and the ability of ADS holders to influence corporate decisions may therefore be limited".

ADSs holders may not be entitled to a jury trial with respect to claims arising under the deposit agreement, which could augur less favorable results to the plaintiff(s) in any such action.

The deposit agreement governing the ADSs representing our ordinary shares provides that owners and holders of ADSs, including those who purchase the ADSs in a secondary transaction, irrevocably waive the right to a trial by jury in any legal proceeding arising out of or relating to the deposit agreement, our ordinary shares or the ADSs or the transactions contemplated thereby, including claims under U.S. federal securities laws, against us or the Depositary to the fullest extent permitted by applicable law. If this jury trial waiver provision is prohibited by applicable law, an action could nevertheless proceed under the terms of the deposit agreement with a jury trial. To our knowledge, the enforceability of a jury trial waiver under the U.S. federal securities laws has not been finally adjudicated by a federal court. However, we believe that a jury trial waiver provision is generally enforceable under the laws of the State of New York, which govern the deposit agreement, by a court of the State of New York or a U.S. federal court in New York, which have non-exclusive jurisdiction over matters arising under the deposit agreement, applying such law. In determining whether to enforce a jury trial waiver provision, New York courts and U.S. federal courts will consider whether the visibility of the jury trial waiver provision within the agreement is sufficiently prominent such that a party has knowingly waived any right to trial by jury. We believe that this is the case with respect to the deposit agreement, our ordinary shares and the ADSs and the transactions contemplated thereby. In addition, New York courts will not enforce a jury trial waiver provision in order to bar a viable setoff or counterclaim sounding in fraud or one which is based upon a creditor's negligence in failing to liquidate collateral upon a guarantor's demand, or in the case of an intentional tort claim (as opposed to a contract dispute), none of which we believe are applicable in the case of the deposit agreement, our ordinary shares or the ADSs or the transactions contemplated thereby. No condition, stipulation, or provision of the deposit agreement or ADSs serves as a waiver by any owner or holder of ADSs or by us or the Depositary of compliance with any provision of the U.S. federal securities laws. If you or any other owner or holder of ADSs brings a claim against us or the Depositary in connection with matters arising under the deposit agreement, our ordinary shares or the ADSs or the transactions contemplated thereby, you or such other owner or holder may not be entitled to a jury trial with respect to such claims, which may have the effect of limiting and discouraging lawsuits against us and/or the Depositary, lead to increased costs to bring a claim, limited access to information and other imbalances of resources between such owner or holder and us, or limit such holder's ability to bring a claim in a judicial forum that such holder finds favorable. If a lawsuit is brought against us and/or the Depositary under the deposit agreement, it may be heard only by a judge or justice of the applicable trial court, which would be conducted according to different civil procedures and may augur different results than a trial by jury would have had, including results that could be less favorable to the plaintiff(s) in any such action, depending on, among other things, the nature of the claims, the judge or justice hearing such claims, and the venue of the hearing.

We may be subject to securities litigation, which is expensive and could divert management attention.

In the past, companies that have experienced volatility in the market price of their shares have been subject to securities class action litigation. We may be the target of this type of litigation in the future. Litigation of this type could result in substantial costs and diversion of management's attention and resources, which could seriously hurt our business. Any adverse determination in litigation could also subject us to significant liabilities.

Our Chief Executive Officer, directors, and shareholders who own more than 5% of our outstanding ordinary shares currently own approximately 39% of our ordinary shares and have an approximately 71% voting interest through our loyalty share program. They will therefore be able to exert significant control over matters submitted to our shareholders for approval.

Our Chief Executive Officer and directors, and shareholders who own more than 5% of our outstanding ordinary shares beneficially own approximately 39% of our ordinary shares and have an approximately 771% voting interest through our loyalty share program. This significant concentration of share ownership and voting power may adversely affect the trading price for the ADSs because investors often perceive disadvantages in owning securities in companies with controlling shareholders. As a result, these shareholders, if they acted together, could significantly influence, or even unilaterally approve matters requiring approval by our shareholders, including the election of directors and the approval of mergers or other business combination transactions. The interests of these shareholders may not always coincide with our interests or the interests of other shareholders. Also, the concentration of our beneficial ownership may have the effect of delaying, deterring, or preventing a change in our control, or may discourage bids for our shares at a premium over the market price of the shares. The significant concentration of share ownership may adversely affect the trading price of our ADSs due to investors' perception that conflicts of interest may exist or arise.

There is a substantial risk that we are or will become classified as a passive foreign investment company. If we are or become classified as a passive foreign investment company, our U.S. shareholders may suffer adverse tax consequences as a result.

In general, we will be treated as a passive foreign investment company (a "PFIC") for U.S. federal income tax purposes in any taxable year in which either:

(1) at least 75% of our gross income is "passive income;" or, (2) on average at least 50% of our assets by value produce passive income or are held for the production of passive income. Passive income for this purpose generally includes, among other things, certain dividends, interest, royalties, rents and gains from commodities and securities transactions and from the sale or exchange of property that gives rise to passive income. Passive income also includes interest income earned by reason of the temporary investment of funds, including those raised in a public offering, and the excess of certain foreign currency gains over certain foregoing currency losses.

Our status as a PFIC will depend on the nature and composition of our income and the nature, composition and value of our assets. Our status may also depend, in part, on how quickly we utilize cash proceeds received from previous offerings of our ADSs or ordinary shares in our business. Based on preliminary analysis, we believe that we were likely classified as a PFIC in 2024, and we may be classified as a PFIC for 2025 and future years. In particular, so long as we do not generate revenue from operations for any taxable year and do not receive any research and development grants, or even if we receive a research and development grant, if such grant does not constitute gross income for U.S. federal income tax purposes, we likely will be classified as a PFIC in any taxable year due to the gross income from investment of cash reserves and other passive sources that we derive.

If we are a PFIC in any taxable year during which a U.S. taxpayer holds the ADSs, such U.S. taxpayer would be subject to certain adverse U.S. federal income tax rules. In particular, if the U.S. taxpayer did not make an election to treat us as a "qualified electing fund" ("QEF") or make a "mark-to- market" election, then "excess distributions" to the U.S. taxpayer, and any gain realized on the sale or other disposition of the ADSs by the U.S. taxpayer: (1) would be allocated ratably over the U.S. taxpayer's holding period for the ADSs; (2) the amount allocated to the current taxable year and any period prior to the first day of the first taxable year in which we were a PFIC would be taxed as ordinary income; and (3) the amount allocated to each of the other taxable years would be subject to tax at the highest rate of tax in effect for the applicable class of taxpayer for that year, and an interest charge for the deemed deferral benefit would be imposed with respect to the resulting tax attributable to each such other taxable year. In addition, U.S. taxpayers that have held the ADSs during a period when we were a PFIC will be subject to the foregoing rules, even if we cease to be a PFIC in subsequent years, subject to exceptions for U.S. taxpayer who made a timely QEF or mark-to-market election. Currently, we do not expect to provide U.S. shareholders with the information necessary for a U.S. shareholder to make a QEF election. Prospective investors should assume that a QEF election will not be available. U.S. taxpayers that hold the ADSs are strongly urged to consult their tax advisors about the PFIC rules, including tax return filing requirements and the eligibility, manner, and consequences to them of making a QEF or mark-to-market election with respect to the ADSs in the event that we are a PFIC. See "Item 10. Additional Information—E. Taxation—U.S. Federal Income Tax Consequences—Passive Foreign Investment Companies" for additional information.

If securities or industry analysts do not publish or cease publishing research or reports about us, our business, or our market, or if they adversely change their recommendations or publish negative reports regarding our business or our securities, our ADS price and trading volume could decline.

The trading market for our ADSs will be influenced by the research and reports that industry or securities analysts may publish about us, our business, our market, and/or our competitors. We do not have any control over these analysts, and we cannot provide any assurance that analysts will cover us or provide favorable coverage. If any of the analysts who may cover us adversely change their recommendation regarding our securities, or provide more favorable relative recommendations about our competitors, our ADS price would likely decline. If any analyst who may cover us were to cease coverage of our company or fail to regularly publish reports on us, we could lose visibility in the financial markets, which in turn could cause our ADS price or trading volume to decline.

We have not paid, and do not intend to pay, dividends on our ordinary shares and, therefore, unless our traded securities appreciate, our investors may not benefit from holding our securities.

We have never declared or paid cash dividends on our ordinary shares. We do not anticipate paying any cash dividends on our ordinary shares in the foreseeable future. Consequently, investors may need to rely on sales of their ADSs after price appreciation, which may never occur, as the only way to realize any future gains on their investment. Investors seeking cash dividends should not purchase the ADSs. Moreover, Italian law imposes certain restrictions on our ability to declare and pay dividends. Italian law prohibits distributing dividends other than from net income or distributable reserves set forth in a company's statutory accounts approved by a meeting of shareholders and after the establishment of certain compulsory reserves. In addition, if losses from previous fiscal years have reduced a company's capital, dividends may not be paid until the capital is reconstituted or its stated amount is reduced by the amount of such losses. The application of these restrictions limits our ability to make distributions to holders of our shares See "Dividend Policy" and "Description of Share Capital and Governing Documents—Dividends and Other Distributions" for additional information.

The requirements associated with being a public company require significant company resources and management attention.

As a U.S. public company, we are subject to the reporting requirements of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), Nasdaq listing requirements and other applicable securities rules and regulations. The Exchange Act requires that we file periodic reports with respect to our business and financial condition and maintain effective disclosure controls and procedures and internal control over financial reporting. In addition, subsequent rules implemented by the SEC and the Nasdaq Stock Market may also impose various additional requirements on public companies. As a result, we have incurred and will continue to incur legal, accounting, and other expenses that we did not incur as a nonpublic company, particularly after we are no longer an "emerging growth company" as defined in the Jumpstart Our Business Startups Act ("JOBS Act"). Further, the need to establish the corporate infrastructure demanded of a public company may divert management's attention from implementing our development plans. We have made changes to our corporate governance standards, disclosure controls and financial reporting and accounting systems to meet our reporting obligations. The measures we take, however, may not be sufficient to satisfy our obligations as a public company, which could subject us to delisting of our securities, fines, sanctions, and other regulatory action and potentially civil litigation.

The JOBS Act allows us to postpone the date by which we must comply with some of the laws and regulations intended to protect investors and to reduce the amount of information we provide in our reports filed with the SEC, which could undermine investor confidence in our company and adversely affect the market price of the ADSs.

For so long as we remain an "emerging growth company" as defined in the JOBS Act, we intend to take advantage of certain exemptions from various requirements that are applicable to public companies that are not "emerging growth companies" including:

- the provisions of the Sarbanes-Oxley Act requiring that our independent registered public accounting firm provide an attestation report on the effectiveness of our internal control over financial reporting;

- Section 107 of the JOBS Act, which provides that an "emerging growth company" can take advantage of the extended transition period provided in Section 7(a)(2)(B) of the Securities Act for complying with new or revised accounting standards. This means that an "emerging growth company" can delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We are electing to delay the adoption of new or revised accounting standards. As a result of this election, our consolidated financial statements may not be comparable to companies that comply with the public company effective date; and

- any rules that may be adopted by the Public Company Accounting Oversight Board requiring mandatory audit firm rotation or a supplement to the auditor's report on the financial statements.

We intend to take advantage of these exemptions until we are no longer an "emerging growth company." We will remain an emerging growth company until the earlier of (1) the last day of the fiscal year (a) following the fifth anniversary of the date of the completion of our IPO, (b) in which we have total annual gross revenue of at least $1.235 billion, or (c) in which we are deemed to be a large accelerated filer, as defined in the rule under the Exchange Act, and (2) the date on which we have issued more than $1.0 billion in non-convertible debt during the prior three-year period.

We cannot predict if investors will find our securities less attractive because we may rely on these exemptions. If some investors find our securities less attractive as a result, there may be a less active trading market for the ADSs, and our ADS price may be more volatile and may decline.

As a foreign private issuer, we are permitted to, and we do, follow certain home country corporate governance practices instead of otherwise applicable SEC and Nasdaq requirements, which may result in less protection than is accorded to investors under rules applicable to domestic U.S. issuers.

The corporate governance rules of the Nasdaq Stock Market require listed companies to have, among other things, a majority of independent directors and independent director oversight of executive compensation, nomination of directors and corporate governance matters. As a foreign private issuer, we are permitted to, and we do, follow home country practice in lieu of these requirements. For more information, see "Item 6. Directors, Senior Management and Employees – C. Board Practices – Differences between Italian Laws and Nasdaq Requirements." As long as we rely on the foreign private issuer exemption to certain of the Nasdaq's corporate governance standards, a majority of the directors on our board of directors are not required to be independent directors. Therefore, our board of directors' approach to governance may be different from that of a board of directors consisting of a majority of independent directors, and, as a result, the management oversight of our company may be more limited than if we were subject to all of the Nasdaq Stock Market's corporate governance standards.

Accordingly, our shareholders may not have the same protection afforded to shareholders of companies that are subject to all of the corporate governance standards, and the ability of our independent directors to influence our business policies and affairs may be reduced.

We may become taxable in a jurisdiction other than Italy, and this may increase the aggregate tax burden on us.

Since incorporation, we have, on a continuous basis, had our place of effective management in Italy. We are therefore a tax resident of Italy under Italian tax law. However, we may become subject to limited income tax liability in other countries with respect to our operations in other countries, for example, the U.S., due to the existence of a permanent establishment or a permanent representative. The applicable tax laws or interpretations thereof may change. We have our place of effective management in Italy and, as such, we believe we are tax residents in Italy, although that determination is largely a matter of fact and degree based on all the circumstances, rather than a question of law, which facts and degree may also change. Changes to applicable laws or interpretations thereof and changes to applicable facts and circumstances (for example, a change of board members or the place where board meetings take place), may result in us becoming a tax resident of a jurisdiction other than Italy. Consequently, our overall effective income tax rate and income tax expense could materially increase, which could have a material adverse effect on our business, results of operations, financial condition and prospects. However, if there is a double tax treaty between Italy and the respective other country, double taxation of income may be avoided, and the detrimental tax effects mitigated by the application of the treaty.

Risks Related to Italian Law and Our Operations in Italy

We are an Italian corporation. The rights of our shareholders may be different from the rights of shareholders in companies governed by the laws of U.S. jurisdictions.

We are an Italian corporation. Our corporate affairs are governed by our articles of association and by the laws governing companies incorporated in Italy. The rights of our shareholders and the responsibilities of members of our board of directors may be different from the rights and obligations of shareholders and directors of companies governed by the laws of U.S. jurisdictions. While performing its duties, our board of directors is required by Italian law to act with the diligence required by the nature of their assignment and by their specific expertise. Italian corporate law limits the ability of our shareholders to challenge resolutions made or other actions taken by our board of directors in court. Our shareholders generally are not permitted to file a suit to reverse or void a decision or an action taken by our board of directors, except for those decisions that are detrimental to their rights. If a board resolution has not been taken in accordance with the Italian law or the Company's articles of association, only the board of statutory auditors and the absent or dissenting members of the board of directors may challenge it within 90 days of such resolution. However, the shareholders may, where they represent the thresholds provided for by Italian law, bring corporate liability action against our directors where they have acted in violation of their duties of conduct. Individual shareholders may also take action for compensation for the damage directly caused to them by the director's conduct. Under Italian law, shareholders' claims against a member of our board of directors for breach of their duties of conduct must be filed in Milan, Italy, as the place where the Company was incorporated.

Our shares are not listed in Italy, our home jurisdiction. As a result, our shareholders will not benefit from certain provisions of Italian law that are designed to protect shareholders in a public takeover offer or a change-of-control transaction and may not be protected in the same degree in a public takeover offer or a change-of-control transaction as are shareholders of certain U.S. companies or in an Italian company listed in Italy.

Because the ADSs are listed exclusively on Nasdaq and not on Italy's stock exchange, our shareholders do not benefit from the protection afforded by certain provisions of Italian law that are designed to protect shareholders in the event of a public takeover offer or a change-of-control transaction. For example, Article 120 of the Italian Financials' Consolidated Act and its implementing provisions require investors to disclose their interest in the relevant listed company if they reach, exceed, or fall below certain ownership thresholds. Similarly, the Italian takeover regime imposes a duty on any person or group of persons who acquires more than the 30% of a company's voting rights (or the 25% if such company is not a small-medium enterprise, where there is no other shareholder holding a higher stake) to make a mandatory offer for all the Company's outstanding listed equity securities. In addition, the Italian takeover regime imposes certain restrictions and obligations on bidders in a voluntary public takeover offer that are designed to protect shareholders. However, these protections are applicable only to issuers that list their equity securities in Italy and, because the ADSs are listed exclusively on Nasdaq, are not applicable to us. Furthermore, since Italian law restricts our ability to implement rights plans or U.S.-style "poison pills," our ability to resist an unsolicited takeover attempt or to protect minority shareholders in the event of a change of control transaction may be limited. Therefore, our shareholders may not be protected in the same degree in a public takeover offer or a change-of-control transaction as are shareholders in certain U.S. companies or in an Italian company listed in Italy.

The ability of shareholders to bring actions or enforce judgments against us or our directors and executive officers may be limited. Claims of U.S. civil liabilities may not be enforceable against us.

We are incorporated under the laws of Italy and our registered office and domicile is in Milan, Italy. Moreover, a majority of our directors and executive officers are not residents of the U.S., and all or a substantial portion of our assets are located outside the U.S. As a result, it may not be possible for investors to effect service of process within the U.S. upon us or upon such persons or to enforce against them judgments obtained in U.S. courts, including judgments in actions predicated upon the civil liability provisions of the federal securities laws of the U.S.

The process of seeking to raise additional funds is cumbersome, subject to the verification of an Italian notary public in compliance with our bylaws and applicable law and may require prior approval of our shareholders at an extraordinary shareholder meeting.

We are incorporated under the laws of the Republic of Italy. The principal laws and regulations that apply to our operations, those of Italy and the E.U., are different from those of the U.S. With some exceptions, to issue new equity or debt securities convertible into equity, we must increase our authorized capital. To do so, our board of directors must meet and resolve to recommend that our shareholders approve an amendment to our bylaws increasing our capital. The holders of the majority of our outstanding shares must then approve that amendment at an extraordinary shareholder meeting duly called. These meetings take time to call, and it might be very difficult to get a majority of the holders of all outstanding shares to vote in favor of the proposed resolution. In addition, an Italian notary public must verify that the capital increase follows our bylaws and with applicable Italian law. Further, under Italian law, our existing shareholders, the holders of our mandatory convertible bonds and any other holders of convertible securities have preemptive rights (except in specific cases) to acquire any such shares pro-rated on their percentage interest in our company, and on the same terms as approved for such capital increase. Alternatively, our shareholders can delegate the power to increase our capital to the board of directors, but the board's right to exercise such power, if delegated, will expire after five years. If the board does not approve a capital increase by the end of those five years, our board, and shareholders will need to meet again to re-delegate this authority.

With respect to shareholder resolutions approving a capital increase, Italian law provides that in the absence of meeting minutes, or in the event of the impossibility or illegality of the resolution, any interested person may, for a period of 180 days following the filing of the shareholder resolution with the competent Register of Companies, challenge such resolution. If a shareholder meeting was not called to approve the capital increase, the relevant resolution should be considered invalid and, any interested person may challenge the capital increase for a period of 90 days following the approval of the financial statements referring to the year during which the shareholder resolution has been, also partially, executed. In addition, once our shareholders authorize a capital increase, all those authorized shares that have been subscribed, need to be entirely paid-up before the shareholders may perform/execute a new capital increase. These restrictions could limit our ability to issue new equity or convertible debt securities on a timely basis.

Italian law places restrictions on the amount of debt securities that we may issue relative to our equity to the extent that such debt securities are not listed on regulated markets or do not otherwise provide the holder of such securities the right to purchase or convert the same into our shares.

Under Italian law, we may issue debt securities in an amount not to exceed twice the sum of our capital, our legal reserve and any other disposable reserves appearing on our latest Italian GAAP balance sheet approved by our shareholders, unless the debt securities are listed on regulated markets or provide the holder of such securities the right to purchase or convert the same into our shares, in which case such restrictions do not apply. The legal reserve is a reserve to which we allocate 5% of our Italian GAAP net income each year until it equals at least 20% of our capital. One of the other reserves that we maintain on our balance sheet is a "share premium reserve," meaning amounts paid for our ordinary shares in excess of the amount of such ordinary shares that is allocated to the capital. At December 31, 2024, the sum of our capital, legal reserves and other reserves on our unaudited Italian GAAP financial statements was €23.9 million before the Italian GAAP net loss of 8.0 million for the period. If, in the future, we issue debt securities that are not listed on regulated markets or do not provide the holder of the securities the right to purchase or convert the same into our shares, until such debt securities are repaid in full, we may not voluntarily reduce our capital or allocate our reserves (such as by declaring dividends) if it results in the aggregate of the capital and reserves being less than half of the outstanding amount of the debt. In such a case, if our equity is reduced by losses or otherwise such that the amount of the outstanding debt securities is more than twice the amount of our equity, some legal scholars are of the opinion that the ratio must be restored through a recapitalization of our company. If our equity is reduced, we could recapitalize by issuing new shares or having our shareholders contribute additional capital to us, although there can be no assurance that we would be able to find purchasers of new shares or that any of our current shareholders would be willing to contribute additional capital.

If we suffer losses that reduce our capital to less than €50,000, we will need to recapitalize, change our form of entity, or be liquidated.

Italian law requires us to reduce our shareholders' equity and, our capital, to reflect on-going losses, in certain cases of losses exceeding 1/3 of the capital of the Company. Also, as an S.p.A., we are also required to maintain a minimum capital of €50,000. If we suffer losses from operations that reduce our capital to less than €50,000, then we must either increase our capital (which we could do by issuing new shares or having our shareholders contribute additional capital to our company) to at least €50,000 (or convert the form of our company into an S.r.l. but such conversion would not be applicable, since the S.r.l. form is not consistent with being listed pursuant to Italian law). If we do not take these steps, our company could be liquidated.

We apply our operational losses against our legal reserves and capital. If our capital is reduced by more than one-third as a result of losses, our board of directors must call a shareholder meeting as soon as possible. The shareholders should take appropriate measures, which may include, inter alia, reducing the legal reserves and capital by the amount of the remaining losses, or carrying the losses forward for up to one year. If the shareholders vote to carry the losses forward up to one year, and the losses are still more than one-third of the amount of the capital at the end of the year, then we must reduce our capital by the amount of the losses.

Italian labor laws could impair our flexibility to restructure our business.

In Italy, our employees are protected by various laws which afford them consultation rights with respect to specific matters regarding their employers' business and operations, including the downsizing or closure of facilities and employee terminations. In particular, among other applicable Italian laws: (i) Laws no. 604/1966, 300/1970 and 92/2012 regulate the individual dismissals; (ii) Law no. 223/1991, concerns the collective dismissal procedure; (iii) Law no. 428/1990 as amended by legislative decree no. 18/2001, provides for the information and consultation procedure in case of a transfer of the undertaking or a part thereof; (iv) Legislative decree no. 25/2007, introduces a general right to information and consultation for employees and (v) Legislative Decree no. 23/2015 regulates the consequences of individual dismissals with specific reference to the employees hired starting from March 7, 2015.

Purchasers of our ordinary shares and ADSs may be exposed to increased transaction costs because of the Italian financial transaction tax or the proposed European financial transaction tax.

On February 14, 2013, the European Commission adopted a proposal for a directive on the financial transaction tax ("E.U. FTT") to be implemented under the enhanced cooperation procedure by eleven Member States initially (Austria, Belgium, Estonia, France, Germany, Greece, Italy, Portugal, Slovenia, Slovakia, and Spain). Following Estonia's formal withdrawal on March 16, 2016, ten Member States are currently participating in the negotiations on the proposed directive. Member States may join or leave the group of participating Member States at later stages and, subject to an agreement being reached by the participating Member States, a final directive will be enacted. The participating Member States will then implement the directive in local legislation. If the proposed directive is adopted and implemented in local legislation, investors in ordinary shares and ADSs may be exposed to increased transaction costs.

The Italian financial transaction tax (the "IFTT") applies with respect to trades entailing the transfer of (i) shares or equity-like financial instruments issued by companies resident in Italy, such as the ordinary shares; and (ii) securities representing the shares and financial instruments under (i) above (including depositary receipts such as the ADSs), regardless of the residence of the issuer. The IFTT may also apply to the transfer of ordinary shares and ADSs by a U.S. resident. The IFTT does not apply to companies having an average market capitalization lower than €500 million in the month of November of the year preceding the year in which the trade takes place. In order to benefit from this exemption, companies whose securities are listed on a foreign regulated market, such as the Company, need to be included on a list published annually by the Italian Ministry of Economy and Finance. The Company is in the process with the relevant procedures to be included in such list. For so long as the Company is not included in such list, investors in the ordinary shares and ADSs may be exposed to increased transaction costs. See "Item 10. Additional Information—E. Taxation."

It may be difficult for investors outside of Italy to enforce civil liabilities against us.

We are incorporated under the laws of Italy and our registered office and domicile is in Milan, Italy. A majority of our directors and executive officers are not residents of the U.S., and all or a substantial portion of our assets are located outside the U.S. As a result, it may not be possible for investors to effect service of process within the U.S. upon us or upon such persons.

Judgments of U.S. courts may not be directly enforceable outside of the U.S. and the enforcement of judgments of U.S. courts outside of the U.S. may be subject to limitations. Investors may also have difficulties pursuing an original action brought in a court in a jurisdiction outside the U.S. for liabilities under the securities laws of the U.S.

Our loyalty share program could have a negative effect on the liquidity of our ADSs and may make it more difficult for investors to acquire a controlling interest, change the management or the strategy of our Company or exercise influence over us, which may adversely affect the market price of the ADSs. Further, our loyalty share program is available only to holders who own their ordinary shares in registered form, and the ability of ADS holders to influence corporate decisions may therefore be limited.

At our shareholders' meeting held on May 2, 2024, our shareholders approved a loyalty share program through an amendment to our bylaws. The loyalty share program gives shareholders the opportunity to request to be included on a special list maintained by us and thereby receive increased votes for each ordinary share held in registered form after certain continuous periods of ownership of such ordinary shares. For more information regarding our loyalty share program, see "Item 10. Additional Information. B. Memorandum and Articles of Association."

Under our loyalty share program, shareholders who hold a significant quantity of ordinary shares in registered form for the continuous periods prescribed in our bylaws and who request and are included on the special list could be in a position to exercise a significant percentage of votes at meetings of shareholders and have substantial influence over our Company. A qualifying shareholder is entitled to a double vote (i.e., two votes for each ordinary share) for each ordinary share in registered form held by the same shareholder for a continuous period of not less than 24 months. An additional vote is also granted for each additional continuous 12-month period the same shareholder holds such ordinary share, for up to a total of ten votes per ordinary share. Continuous ownership prior to the registration date in the special list is taken into account. Furthermore, only shareholders who own their shares in registered form are entitled to take advantage of the loyalty share program and ADS holders are not entitled to additional voting rights. As a result, a relatively large proportion of our voting power may be concentrated in a relatively small number of registered shareholders who may have significant influence over us, and the ability of ADS holders to influence corporate decisions may therefore be limited. As a result, the loyalty share program may discourage change of control transactions that otherwise could involve payment of a premium over prevailing market prices for our ADSs or otherwise adversely impact the liquidity and market price of the ADSs.

Risks Related to the Mandatory Convertible Bond

Upon an event of default, we may not be able to make any redemption payments under the Mandatory Convertible Bond.

On March 12, 2025, the Company and Fondazione Enea Tech e Biomedical ("Enea"), a private law foundation subject to the supervision of the Ministry of Enterprises and Made in Italy, entered into a Subscription Agreement (the "Subscription Agreement") providing for the subscription of a mandatory convertible bond loan denominated "MANDATORY CONVERTIBLE LOAN GENENTA 2025-2028" (the "Mandatory Convertible Bond") by Enea, with an aggregate nominal value of up to €20 million and consisting of up to a total of 2,000 bonds (the "Convertible Bonds"), each with a nominal value of €10,000 (the "Nominal Value"), to be issued in two tranches by the Company at an issue price per unit equal to €10,000 for 100% of the Nominal Value. Upon the occurrence of certain events of default, Enea may demand the early redemption of the Convertible Bonds for a cash amount equal to 100% of the total amount thereof. We may not have sufficient assets to repay Enea and a default would also likely significantly diminish the market price of our ADSs.

Conversion of the Convertible Bonds may dilute the ownership interest of existing shareholders or may otherwise depress the price of our ADSs.

The Convertible Bonds will automatically convert into ordinary shares of the Company (the "Conversion Shares") on the earlier of (i) the occurrence of either (x) a Change of Control, which is defined as an acquisition by a person or group of persons not currently controlling the Company of more than 50% of the Company's issued share capital with voting rights or a takeover bid and/or exchange offer launched on all of the Company's outstanding ordinary shares and American depositary shares ("ADSs") or (y) the completion of an Investment Round, which is defined as any further investment transactions in the Company's share capital through the issuance of shares, convertible bonds, warrants or similar instruments for a total aggregate amount of €50,000,000 (the "Early Conversion Date" and, together with the Maturity Date, each a "Conversion Date") and (ii) three years after the First Tranche Issue Date (the "Maturity Date"). The conversion of the Convertible Bonds into Conversion Shares will dilute the ownership interests of existing shareholders to the extent we deliver shares upon conversion of the Convertible Bonds. Any sales in the public market of the Conversion Shares could adversely affect prevailing market prices of our ADSs. In addition, the existence of the Convertible Bonds may encourage short selling by market participants because the conversion of the Convertible Bonds could be used to satisfy short positions, or the anticipated conversion of the Convertible Bonds into Conversion Shares could depress the price of our ADSs.

In addition, the Convertible Bonds consist of two tranches: an initial tranche in the amount of €7,500,000 (the "First Tranche") issued on March 19, 2025 (the "First Tranche Issue Date") and a subsequent tranche in the amount of €12,500,000 (the "Second Tranche") to be issued by September 19, 2026 (the "Second Tranche Issue Date" and, together with the First Tranche Issue Date, each an "Issue Date"). The issuance of the Second Tranche on the Second Tranche Issue Date is subject to a number of conditions precedent, including but not limited to the completion of investment transactions in the Company's share capital through the issuance of shares, convertible bonds, warrants or similar instruments for a total aggregate amount of €32,500,000. If such investment transactions occur, and if the additional conditions precedent to the issuance of the Second Tranche are met, such investment transactions and the conversion of the Second Tranche into Conversion Shares may further dilute the ownership interest of existing shareholders or otherwise depress the price of our ADSs.

ITEM 4. INFORMATION ON THE COMPANY

A. History and Development of the Company

Corporate History and Operating Segment Evolution

We were founded in 2014 by San Raffaele Hospital (Ospedale San Raffaele or "OSR") in Milan, a globally recognized premier research hospital for *ex-vivo* gene therapy, with Pierluigi Paracchi (our CEO), Prof. Luigi Naldini (Chairman of our Executive Scientific Board) and Dr. Bernhard Gentner (a member of our Executive Scientific Board), to develop potential ground-breaking cell and gene cancer therapies. We leverage the vast experience in lentiviral vector ("LVV") technology of the San Raffaele Telethon Institute for Gene Therapy ("SR-Tiget"). SR-Tiget, a joint venture between OSR and Fondazione Telethon ("Telethon"), is a world-leading cell and gene therapy research institution at the forefront of developing therapies for rare diseases. SR-Tiget has a proven track record for successful collaborative clinical research programs in *ex-vivo* gene therapy. Its research has resulted in a number of approved products, including Strimvelis, an *ex-vivo* gammaretroviral vector-based gene therapy for adenosine deaminase severe combined immunodeficiency, and Libmeldy, an *ex-vivo* gene therapy for the treatment of early-onset metachromatic leukodystrophy patients, both marketed by Orchard Therapeutics. Our platform was developed in the SR-Tiget laboratories of our founders, Prof. Naldini and Dr. Gentner, and we hold exclusive rights and option rights, to certain intellectual property ("IP") originating there.

Since closing our first round of funding in May 2015, we have recruited a leading management team, established a manufacturing process for our drug product candidates, completed preclinical activities (research and Good Laboratory Practice – "GLP" – grades), engaged with Italian, European and U.S. Key Opinion Leaders to identify our clinical lead indications, and submitted our first CTA.

Our leadership team has a proven track record as biotech executives. Their expertise spans from finance and venture capital to medical affairs, from scientific research to clinical drug product development and clinical trial management. For example, members of our management team have been involved in the successful development of Ethical Oncology Science, which was acquired in 2013 for over $400 million, and Strimvelis the first ever ex-vivo approved gene therapy product that was developed under the guidance of Dr. Carlo Russo, our Chief Medical Officer and Head of Development (formerly Head of Development of R&D Biopharm and Rare Disease Units at GSK). Our management team members have played important roles in both large pharma companies such as Merck and GSK, and biotech startups, such as Adverum, Annapurna, VaxInnate Corporation, OncoSec Medical, Biological Dynamics and GenMark Diagnostics. We believe this multi-disciplinary competence provides a unique blend for the development of innovative gene and cell therapy products, and constitutes a fertile ground for alliances with industrial partners that could help us bring new therapies to patients.

Corporate Offices

Our principal executive offices are located at Via Olgettina No. 58, 20132 Milan, Italy and our telephone number is +39-02-2643-468120.

B. Business Overview

Overview

We are a clinical-stage biotechnology company engaged in the development of hematopoietic stem cell gene therapies for the treatment of solid tumors. We have developed a novel biologic platform that involves the *ex-vivo* gene transfer of a therapeutic candidate into autologous hematopoietic stem/progenitor cells ("HSPCs") to deliver immunomodulatory molecules directly to the tumor by infiltrating monocytes/macrophages (Tie2 Expressing Monocytes – "TEMs"). Our technology is designed to turn TEMs, which normally have an affinity for and travel to tumors, into a "Trojan Horse" to counteract cancer progression and to prevent tumor relapse. Our technology is not target dependent, and therefore we believe it can be used as a treatment for a broad variety of cancers.

Our technology incorporates the use of an LVV that combines a therapeutic transgene sequence, or payload, with our proprietary platform. Our proprietary platform consists of (i) the Tie-2 promoter, that drives transgene sequence transcription specifically in TEMs, and (ii) miRNA-126 target sequences to downregulate transgene expression post-transcription in those cells where the Tie-2 promoter is active and the miRNA-126 is present. We believe there are many advantages to our approach:

- *Trojan Horse Mechanism of Action ("MoA"):* We use and modify TEMs, a subpopulation of tumor-associated myeloid cells, known to be involved in tumor growth and in the inhibition of immune system response, to allow the immune system to recognize the tumor and to deliver to the cancer site a chosen therapeutic.

- *Select Regulation of Transgene Expression:* Our selected control of the chosen therapeutic gene expression is designed to avoid off-target and systemic toxicity.

- *Potential Long-Term Effect:* Through the use of hematopoietic stem cells, our therapeutic candidate is designed as a "*living therapy*" intended to break the cancer-induced immune tolerance and to establish a competent immune surveillance throughout the life of the patient.

- *Agnostic Response*: In contrast to antigen-restricted CAR-T cells, our platform is not restricted to a pre-selected tumor antigen, nor any one tumor type. As such, it may be applied to a broad range of solid tumors and cancer subtypes, which would overcome one of the central unresolved challenges of immune-oncology cancer therapies.

Our lead product candidate, Temferon, was developed using our proprietary platform and carries the interferon-alpha ("IFN-α") payload. IFN-α is a well-known therapeutic that was previously administered intravenously for treatment of various cancers, but it is currently rarely used because of its systemic toxicity. The Temferon-modified TEMs express the transgene payload, IFN-α, in the tumor microenvironment, thereby reprogramming the Tumor Micro Environment ("TME") which disrupts tumor induced immune-tolerance in blocks. Consequently, the immune system has been observed to recognize the tumor, respond, and inhibit tumor growth. Because Temferon is designed to deliver the IFN-α payload directly into the tumor, we believe it will demonstrate clinical activity without the side effect profile of systemic delivery of IFN-α. In preclinical mouse cancer models treated with Temferon both direct (anti-angiogenic, pro-apoptotic) and indirect (immune response) effects were observed.

We are currently developing Temferon for the treatment of glioblastoma multiforme ("GBM") in patients who have an unmethylated MGMT gene promoter ("uMGMT-GBM"). GBM is the most common malignant primary brain tumor, accounting for more than half of all central nervous system cancers. Patients suffering from GBM have limited, non-curative treatment options. Although these treatments may improve survival, the prognosis for GBM patients remains poor, with a median overall survival ("mOS") of approximately 13 to 15 months and only 5.5% of patients estimated to be alive five (5) years after diagnosis. With no curative treatments available and such poor prognosis for patients, there remains a large, unmet medical need. We chose uMGMT-GBM among our first targets for clinical development after considering the medical need, the active role that TEMs have in GBM pathology, and the high number of newly diagnosed uMGMT-GBM patients potentially interested in participating in our study. As a result, we believe uMGMT-GBM offers a good profile for our initial proof of concept trial in humans. The preliminary results in uMGT-GBM patients indicate that Temferon has been generally well tolerated, with no dose limiting toxicities observed to date.

We have recently started a Phase 1/2a study of Temferon in metastatic Renal Cell Carcinoma ("mRCC"),the most common form of kidney cancer accounting for close to 74,000 new cases annually in the United States. Despite treatment with curative intent, about one-third of patients experience metastatic disease recurrence. Additionally, 30% of patients present with metastatic disease at the time of diagnosis. Metastatic RCC remains a highly lethal condition with a five-year overall survival (OS) rate of approximately 14%.

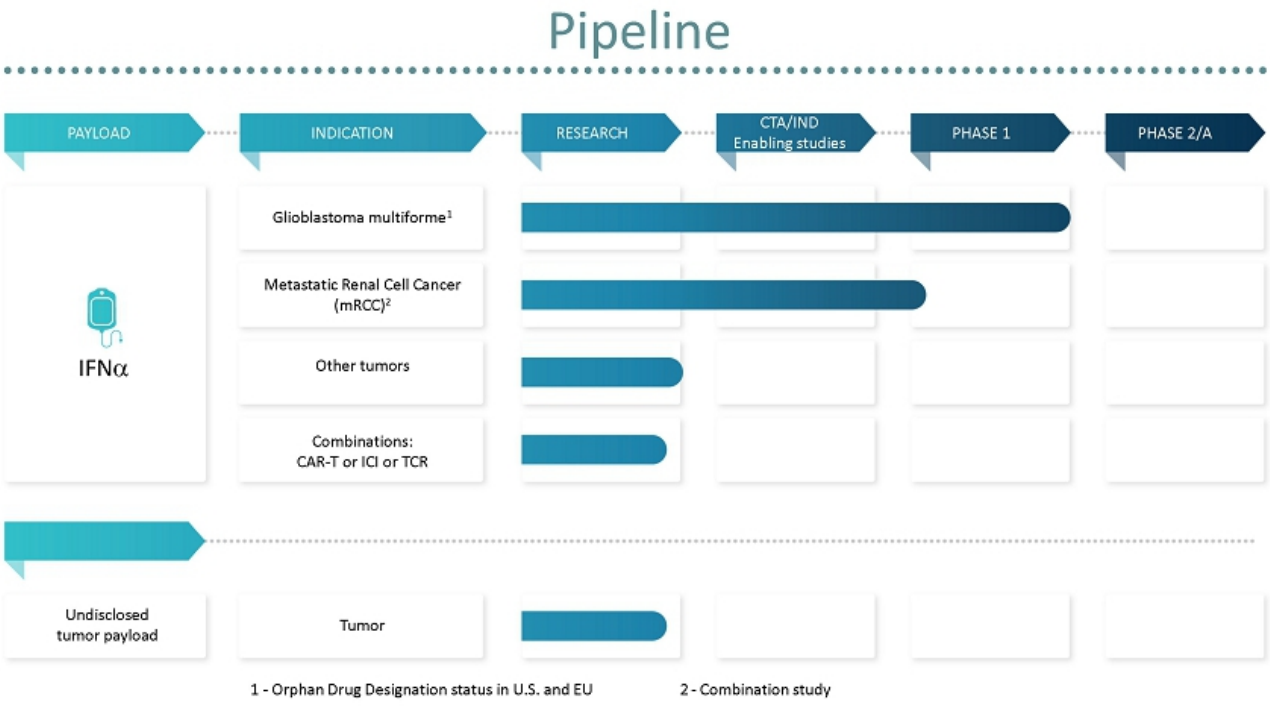
In addition to our Temferon clinical programs for uMGMT-GBM and mRCC, we have exclusive option rights to license (i) Temferon for the treatment of additional indications, and (ii) other drug candidates that are currently in the preclinical stage of development both as standalone treatments and as combination therapies.

The AGC Biologics facility in Bresso, Italy, will continue manufacturing LVV and Temferon to support Genenta's trials. For further larger studies we may use AGC's 60,000 square meter cell and gene therapy manufacturing facility located in Longmont, Colorado (U.S.), which AGC purchased from Novartis in July 2021 or another U.S.-based CMO.

Research and Development Pipeline

Our portfolio of clinical and preclinical *ex-vivo* autologous gene cancer therapies is based on our technology platform, which was originally developed in our founders' laboratories at OSR. Through our collaboration with OSR, we have worldwide commercial rights to Temferon (though our current trademark rights to Temferon are limited to the U.S. and Europe) for the treatment of GBM, mRCC, as well as exclusive option rights to license all of our other programs. Specifically, pursuant to our amended and restated license agreement with OSR, we retain exclusive option rights to license (i) any platform improvements, including our second-generation technology, which includes developments to enable the on/off regulation of the therapeutic transgene, (ii) products for additional indications that utilize our platform technology but use different transgene payloads, and (iii) combinations of our platform with therapies in the immuno-oncology ("IO") field, such as ICI, CAR-T cell therapies and TCR therapies. See "—Intellectual Property Rights— Collaboration/Licensing" for a description of our license agreements with OSR.

Our current pipeline, with clinical and preclinical stage programs, is summarized below:



**Genenta has options/rights on IP derived from preclinical data generated at SR-Tiget laboratories.*

Strategy

We are developing novel cancer therapeutics using our autologous *ex-vivo* gene therapy platform, to initially address the unmet medical needs of uMGMT-GBM patients and patients suffering from other solid cancer indications such as advanced genitourinary malignancies like metastatic renal cell carcinoma. Ultimately, we hope to broaden our platform to treat a wide variety of cancers by pursuing the following strategies:

Advance the development of our leading clinical-stage product candidate, Temferon

We are currently conducting two Phase 1/2a studies in Italy, to primarily evaluate the safety and tolerability of Temferon. We have completed the Phase 1 portion of the TEM-GBM Phase 1/2a study, which administered escalating doses of Temferon to GBM patients with an unmethylated MGMT promoter following radiotherapy. The study generated encouraging preliminary evidence of potential disease modification, including an increase in the percentage of long-term survivors (LTS) at two years compared to data reported in literature and from a registry which included matched patient population undergoing standard of care. We believe that these preliminary disease modification findings, along with the observed reprogramming of the tumor microenvironment (TME), provide a strong rationale to proceed in the clinical development of Temferon in GBM, particularly in combination with other immuno-oncology (I/O) therapies. In addition, the Phase 1/2a study in mRCC patients (TEM-GU study) offers a critical opportunity to evaluate the TME in a different solid tumor and to assess whether Temferon could restore sensitivity to TKIs or ICIs in patients who stopped responding to the TKIs or ICIs.

Extend our product pipeline across multiple indications

We intend to expand our product pipeline by:

- *Identifying additional indications suitable for Temferon.* We have selected Refractory Advanced Genitourinary Malignancies, including metastatic Renal Cell Carcinoma ("RCC"), as the second solid tumor indication for Temferon. We believe that results from ongoing clinical studies in GBM and mRCC will inform and guide future therapeutic strategies in these and other indications.

- *Using our platform with different transgene payloads*. Our platform technology is designed to enable us to use different transgene payloads to potentially achieve therapeutic outcomes in selected cancer indications. We are currently evaluating preclinical studies for two additional therapeutics using our platform with different payloads targeting solid tumors.

- *Developing a second-generation platform that enables the "on-demand" release of the transgene payload*. If we obtain convincing evidence on the ability of Temferon to slow down disease progression we intend to develop a second-generation technology platform that allows the drug products to be switched on to exert the therapeutic effects and switched off if they are no longer needed, or to mitigate toxicity. This technology may enable us to expand our treatment options to broader patient populations.

- *Exploring combination therapies*. We will seek to enter into collaborations with other companies to explore combination studies of our therapeutics with other cancer therapies, such as ICI, CAR-T cell therapies and TCR therapies. We believe our product, through its MoA, has the potential to enhance the durability and efficacy of the existing therapies, including restoring responsiveness in cases where these treatments were previously administered but lost effectiveness over time, thereby overcoming immune tolerance to the tumor and extend the durability of the response.

- *Exploiting in-licensing opportunities with OSR*. We intend to exploit in-licensing opportunities with OSR, a co-founding shareholder.

Develop and maintain efficient manufacturing processes to support anticipated growth

To meet our drug product supply needs for conducting larger trials, we intend to optimize our manufacturing processes for both lentiviral vector (LVV) and drug product (DP) production with a focus on meeting regulatory requirements for Marketing Authorization Application (MAA). This includes implementing scalable processes to enable cost-efficient production at a significantly reduced cost and exploring the potential for decentralized manufacturing approaches to further enhance flexibility, accessibility, and efficiency in delivering our product to patients. Currently, Temferon, is manufactured by the European Cell and Gene Therapy unit of AGC Biologics, a leading global contract development and manufacturing organization ("CDMO"), which is headquartered in Italy and specializes in the manufacturing of viral vectors and genetically engineered cells. AGC Biologics' facility is certified by AIFA. AGC also has a 60,000 square meter cell and gene therapy manufacturing facility located in Longmont, Colorado (U.S.), which AGC purchased from Novartis in July 2021.

Establish a patient-centered infrastructure and strong relationships with key U.S. opinion leaders working in our disease area

Since cell and gene-based therapies are relatively new approaches in oncology, we intend to implement programs to improve patient and physician education regarding the availability of gene therapy-based products for those cancers with a high unmet medical need. We have established a network of leading U.S. Key Opinion Leaders ("KOLs"), which include:Antonio Chiocca, MD, Professor Neurosurgeon-in-Chief and Chairman, Department of Neurosurgery at Brigham and Women's Hospital in Boston, MA; Frederick Lang, MD, Professor and Chairman of the Department of Neurosurgery at MD Anderson in Houston, TX; and David A. Reardon, MD, Department of Medical Oncology at Dana-Farber Cancer Institute in Boston, MA; Timothy F. Cloughesy, MD, Professor of Clinical Neurology Director of Neuro-Oncology Program at University of California Los Angeles (UCLA); Richard Everson, MD, Assistant Professor, Department of Neurosurgery at UCLA; Donald B. Kohn, MD, Distinguished Professor Depts. of MIMG, Pediatrics and MMP at UCLA; Robert Prins, PhD, Associate Professor Neurosurgery at UCLA; and Patrick Wen, MD, Professor of Neurology, Harvard Medical School, Director of the Center For Neuro-Oncology at Dana-Farber Brigham Hospital.

Develop opportunistic partnership(s) with pharmaceutical company(s)

We may choose to partner with pharmaceutical companies whose core competencies and oncology strategies are in line with ours. These partnerships could include the provision of market-approved therapies for combination testing with Temferon, enabling us to explore synergistic effects and expand potential therapeutic indications. Additionally, we are open to establishing clinical development collaborations with other biotech companies that have complementary products in development. Such partnerships would allow us to leverage combined expertise, accelerate clinical progress, and create innovative treatment options for patients with high unmet medical needs.

Our Strengths

We believe that our growing body of early clinical data evidencing the potential of our autologous *ex-vivo* gene therapy approach, coupled with our founders' expertise in the development, manufacturing and commercialization of gene and cell therapies, positions us well to provide potentially transformative therapies through a single administration to patients suffering from a broad range of cancers. We believe our key strengths include:

- ***Unique and valuable expertise.*** We are conducting our clinical trials at OSR, a leading center for *ex-vivo* gene therapy for inherited diseases. OSR has treated more than 121 patients worldwide (one of the highest number of patients treated with gene therapy for rare diseases in a research hospital), using an ex-vivo viral vector platform similar to the one we are developing for cancer treatment. Members of our executive leadership team have held senior positions at GSK, Merck, Annapurna-Adverum and other companies specializing in gene and cell therapies and rare diseases. We have partnered with academic institutions that are pioneers in autologous *ex-vivo* gene therapy and hold exclusive option rights to license additional patents and know-how to build our portfolio. Partnerships with leading academic institutions well recognized in the gene therapy field, such as SR-Tiget and OSR, are a core part of our research engine through which we are working to advance the clinical development of our product candidates and to identify new opportunities that we believe have comparably high probabilities of success in a preclinical setting. We believe our expertise, combined with our plan to leverage our relationships with leading academic institutions, will help expedite the commercialization of our lead clinical-stage product candidate and further expand our pipeline.

- ***Deep pipeline with broad utility*.** We believe that the flexibility of our technology platform combined with our exclusive option rights to in-license additional programs, gives us the ability to grow our pipeline by targeting a broad set of cancer diseases.

- ***Durable therapeutic potential*.** Preliminary data from the Phase 1 TEM-GBM study in uMGMT-GBM patients demonstrated the presence of Temferon-derived modified cells up to 24 months following a single administration of Temferon, the latest timepoint assessed within the study. Additionally, data from the long-term surveillance protocol, which tracks patients beyond two years post-treatment, further reinforces the sustained therapeutic effect observed, highlighting the potential for durable outcomes.

- ***Designed for tumor restricted therapeutic payload delivery and release.*** The design of our transgene expression cassette is intended to restrict payload expression to the tumor microenvironment. The local and tumor restricted therapeutic gene deployment approach is designed to focus the pleiotropic anti-tumor activities of the selected payload, by limiting the toxic manifestation that results from standard systemic administration of the payload.

- ***Agnostic approach.*** Our immune-gene therapy is designed as a tumor-agnostic immunotherapy, not dependent on any specific antigen target or tumor type. We believe it has the potential to be effectively applied across a broad spectrum of cancers and immune contexts, offering a versatile approach to treatment.

- ***Solid tumors targeting.*** Our platform has the potential to effectively target solid tumors, which remain challenging to treat, even by the most novel and leading-edge technologies such as ICIs and CAR-T cells. Our cellular carrier, TEMs, is naturally and actively recruited by growing tumors and has been detected in various human solid tumors, regardless of their origin or location, enhancing the versatility and reach of our therapeutic approach.

- ***Active and sustained tumor surveillance.*** Our immune-gene investigational therapy is designed to trigger the patient's own immune response and establish an active immune surveillance. Our preclinical work, which used different cancer models (B-cell acute lymphoblastic leukemia and GBM) as well as preliminary data collected from our uMGMT-GBM patients, suggests the occurrence of changes in the TME.

- ***Patient-Specific Formulation.*** Our platform offers the potential to precisely adjust the dose to be administered based on individual patient characteristics. Through the ex-vivo modification of the patient's own HSPCs and cryopreservation, we formulate the patient-specific drug product prior to therapy administration, which has the potential to enable an optimized and personalized treatment approach.

- ***Preliminary data indicate that our approach is feasible and well-tolerated.*** To date, Temferon has been well-tolerated with no dose-limiting toxicities.

- ***LVV as transgene payload delivery vehicles.*** LVVs are particularly attractive for clinical applications due to their capacity to transfer large genes/payloads and their ability to efficiently transduce non-proliferating or slowly proliferating cells, such as hematopoietic stem and progenitor cells that allow a persistent gene expression in transduced cells. Moreover, LVVs have a potentially reduced risk of genotoxicity compared to gamma-retroviral vectors. A large number of patients have been treated both with other LVV gene therapy products approved for sale and with clinical-stage LVV gene therapy product candidates for rare diseases worldwide, and generally these therapies have been well tolerated. We believe that long-term extensive follow-up across multiple diseases, with vectors expressing different genes, demonstrates the potential safety of our LVV-based autologous *ex-vivo* gene therapy approach.

- ***Applicability to a potentially large number of patients and indications***. With the advancements in the manufacturing and scaleup of cell and gene therapy products, we believe our autologous *ex-vivo* gene therapy approach has broad therapeutic potential across a large number of malignancies. The *ex-vivo* transduction of HSPCs allows for the potentially long-term production of a differentiated cellular carrier loaded with the therapeutic gene and the consequent distribution of the therapeutic payload throughout multiple organs and tissues containing solid tumors.

Status of Current IO Treatments

Despite new therapeutic approaches and new drugs having been developed or approved, substantial unmet need remains for many of the most common cancers. Immuno-oncology therapies seek to work in conjunction with the patient's own immune system to recognize and attack cancer cells selectively, without affecting normal cells, or to deliver immune system components that prevent the spread of cancer.

Immuno-oncology therapy is recognized as an important type of cancer treatment in addition to more established options such as surgery, chemotherapy, targeted therapy and radiation therapy. Indeed, the global immunotherapy drugs market size was USD 240.19 billion in 2023 and USD 284.38 billion in 2024 and is expected to reach around USD 1,300.38 billion by 2033, expanding at a compound annual growth rate of 18.4% from 2024 to 2033. The Cancer Research Institute has classified immunotherapies, which harness the body's immune system to combat cancers, into five primary categories: cell-based immunotherapy, immunomodulators, vaccines, antibody-based target therapy, and oncolytic viruses.

Class 1 - Cell-based immunotherapy	Class 2 - Immunomodulators
Cell-based immunotherapy approaches employ an immune cell transplant (***adoptive cell therapy***) to physically supplement a patient's immune system and include: • ***Tumor-Infiltrating Lymphocyte (TIL) Therapy:*** Naturally occurring T cells that have already infiltrated a patient's tumors are harvested, activated, expanded *in vitro* and finally re-infused into the patient, where they can then seek out and destroy the tumors. The antigen to which TIL are directed need to be bound by the major histocompatibility complex (MHC) in the tumor cells. • ***T Cell Receptor (TCR) Therapy***: T cells are taken from the patient, equipped with a new T cell receptor that enables them to target specific cancer antigens bound by the MHC, activated, expanded *in vitro* and finally re-infused into the patient. • ***Chimeric Antigen Receptor (CAR) T Cell Therapy:*** T cells are taken from the patient, equipped with a synthetic receptor that enables them to target specific cancer antigens, activated, expanded *in vitro* and finally re-infused into the patient. CAR-T cells may bind antigens that are not presented on the surface through MHC. The newest evolution of this approach is the use of allogeneic T cells, known as universal CAR-T. • ***Natural Killer (NK) Cell Therapy***: This recently developed cell-based immunotherapy is raising interest because NK cells have been shown to mediate graft-versus-leukemia immunity, sparing normal tissues and preventing graft-versus-host disease (GVHD). NK cells also have a natural killing mechanism recognizing MHC class I-negative targets and may be combined as well with CAR therapies. • ***Allogeneic Cell Therapy***: Allogeneic, or universal, cell therapies rely on a single source of cells to create a master cell bank, which is then used to treat multiple patients. Before introducing allogeneic cells into the body, the patient receives a conditioning regimen of chemotherapy and, sometimes, radiation therapy to weaken the patient's immune system to prevent rejection of the donated cells, which is a common complication with this therapy. As with NK cell therapy, another complication of allogeneic cell therapy is GVHD where the immune cells from the donor (the graft) may attack healthy cells in the patient's body (host). Allogeneic cell therapy is uncommon for patients who are older or have overall poor health due to their incompetent immune systems. Of these cell-based approaches, the only market approved therapy is CAR-T cell therapy.	Immunomodulators act directly on immune cells to promote anti-cancer activity and can generally be divided into four categories: • ***Immune Checkpoint Inhibitors (ICI):*** Presently, these are the most widely successful immunomodulators. They work by unlocking the "brakes" of the immune system, the so-called immune checkpoints that are activated by cancer cells to shut down immune responses and allow cancer growth. As a result, checkpoint inhibitors are able to release new immune responses against cancer as well as enhance existing responses to promote the elimination of cancer cells. Since the approval of the first ICI, ipilimumab, in 2011 for advanced melanoma, the FDA has approved seven checkpoint inhibitors to treat more than a dozen different types of cancer. • ***Cytokines:*** Cytokines are immunomodulatory molecules that are able to regulate immune cell maturation, growth and responsiveness. Currently, there are four FDA approved cytokine immunotherapies for the treatment of subsets of patients with kidney cancer, leukemia, lymphoma, melanoma and sarcoma. The first immunomodulatory approved by the FDA in 1986 for leukemia is the cytokine IFN-α. • ***Agonists:*** Agonists activate pathways that promote adaptive immune responses, either by helping to activate "killer" T cells, which directly attack cancer cells, or stimulating the activity of innate immune cells, such as dendritic cells, which coordinate overall immune responses against cancer by displaying cancer markers and enhancing T cell activity. • ***Adjuvants:*** Adjuvants activate pathways involved in the innate immune system that can stimulate general immune responses and ultimately promote adaptive immune responses. One FDA approved adjuvant immunotherapy is currently available for the treatment of subsets of patients with a type of skin cancer. The primary immunomodulators therapies target Pd-1/Pd-L1, which are immune checkpoint proteins found on the surface of T cells that cancer cells use to escape immune detection. Several large well-known pharmaceutical companies, such as Roche/Genentech and Merck, are currently pursuing this approach.

Class 3 - Vaccines	Class 4 - Antibody-based targeted therapies	Class 5 – Oncolytic viruses
Vaccines help educate, or arouse, the immune system against a potential threat. Vaccines have proven effective in preventing diseases caused by viruses and bacteria and work best as preventatives. For cancer, vaccines may be distinguished as preventive, therapeutic or personalized neoantigen vaccines. Preventive vaccines are effective for cancers clearly linked to a viral infection. Therapeutic cancer vaccines, such as Sipuleucel-T that was approved for prostate cancer patients in 2010, work to boost a patient's immune system to fight an established tumor. Personalized neoantigen vaccines aim to direct the immune responses precisely against a patient's tumor cells while sparing healthy cells from immune attack, thus possibly preventing side effects. Several types of neoantigen vaccines are currently being evaluated, both alone and in combination with other treatments, in a variety of cancer types in clinical trials.	Antibody-based targeted therapies can target either cancer cells directly or other cells/proteins that help tumors survive. There are three main categories of monoclonal antibodies: • ***"Naked" Monoclonal Antibodies*** **(mAbs)** may inhibit or block pathways that are essential to sustain cancer growth and progression or may induce other immune cells to eliminate the cancer cells. Rituximab, for the treatment of leukemia, was the first mAb approved by the FDA in 1997. • ***Antibody-Drug Conjugates (ADCs)*** are equipped with anti-cancer drugs delivered locally, after the ADC binds to its target on cancer cells. • ***Bispecific Antibodies*** may bind to two different targets at the same time. A well-known category is represented by bispecific T cell engagers, or BiTEs, that link T cells to cancer cells. Blinatumomab was the first bispecific antibody approved by the FDA in 2014 for subsets of leukemia patients.	Oncolytic viruses are natural viruses engineered to provide advantageous properties, including the decreased ability to infect healthy cells, the ability to deliver therapeutic payloads to tumor cells and the ability to induce the production of immune-boosting molecules by the infected cells. After infection, oncolytic viruses cause cancer cells to "burst," leading to the release of tumor associated antigens that can then stimulate immune responses. The oncolytic virus, T-Vec, was approved by the FDA for patients with advanced melanoma in 2015.

Current Limitations of IO Approaches

Despite significant advances, the clinical application of immunotherapy for cancer patients still faces challenges, including:

- Development of tumor resistance (positive selection of tumor cells bearing advantageous mutations);
- Dependence on specific targets and in many cases highly heterogenic tumor antigens;
- Poor response for many patients;
- Lack of a durable response;
- Side effects;
- Need for multiple dosing for most IO classes; and
- Inability to efficiently target many solid tumors.

IO for Solid Tumors

Despite the success of IO therapies for some hematological cancers, significant gaps remain in the development of efficacious IO therapies for solid tumors. There are still several challenges that IO therapies need to resolve to treat solid tumors including the ability to target delivery of a therapeutic to the solid tumor and identification of suitable prominent cell surface targets. Cell therapies have not been as successful in solid tumors in comparison to blood cancers mainly because of the absence of a suitable prominent cell surface target and the high risk of toxicity when a potential solid tumor target is expressed, even at a low level, on normal tissue. Even if targets for solid tumors with a suitable tumor-selectivity profile can be identified, other factors may limit the activity of cell therapies, including limited cell-therapy penetration and distribution, low oxygen concentration (hypoxia) barriers around cancers that may prevent T cell access to the tumor, expression by tumor cells of certain checkpoint genes and an inability to target multiple antigens at the same time.

To overcome the current limitations of IO therapies in solid tumors, a new, effective tumor therapeutic must:

1. achieve a local and tumor-targeted delivery;
2. maximize on-target effects;
3. reach the desired therapeutic index;
4. minimize the off-target side effects; and
5. potentially provide long term results.

Our Platform

Our platform technology utilizes a novel mechanism of action that we believe has the potential to address the limitations and challenges of current IO technologies. Through a single administration, our platform is designed to provide a broadly applicable treatment to deliver a tumor-targeted therapeutic, including to solid tumors. It does so by exploiting a naturally occurring cancer-induced biological process, allowing for the local delivery of the payload with a potentially durable response, in a manner that we believe will limit systemic toxicity. The ability to deliver localized and tumor-targeted payloads, by avoiding systemic or off-target toxicity, may also allow for the use of well-established immunotherapies, such as the immunomodulator IFN-α, that has shown efficacy but has had limited therapeutic applications due to side effects associated with its systemic delivery.

Specifically, we adapted an autologous *ex-vivo* gene therapy method to direct the patient's own HSPCs by loading them with an immunotherapeutic transgene sequence, or payload, that we believe can counteract cancer progression and prevent tumor relapse. We believe that by delivering a targeted therapeutic specific to cancer cells, we can reach the desired on-target anti-tumor effect while reducing off-target side effects.

Our platform technology employs the following key components:

a) use of the patient's own autologous HSPCs;

b) use of LVVs for *ex vivo* HSPCs transduction; and

c) payload delivery within the TME using specific tumor-associated myeloid cell (Tie2-expressing monocytes – "TEMs"). This "cell-confined" transgene expression is ensured by the selected promoter (Tie-2 promoter) and the imposed post-transcriptional regulation layer represented by a miRNA target sequence (miRNA-126 target sequences).

The image below illustrates the steps of our *ex-vivo* approach to transform patient's autologous HSPCs into a therapeutic product.

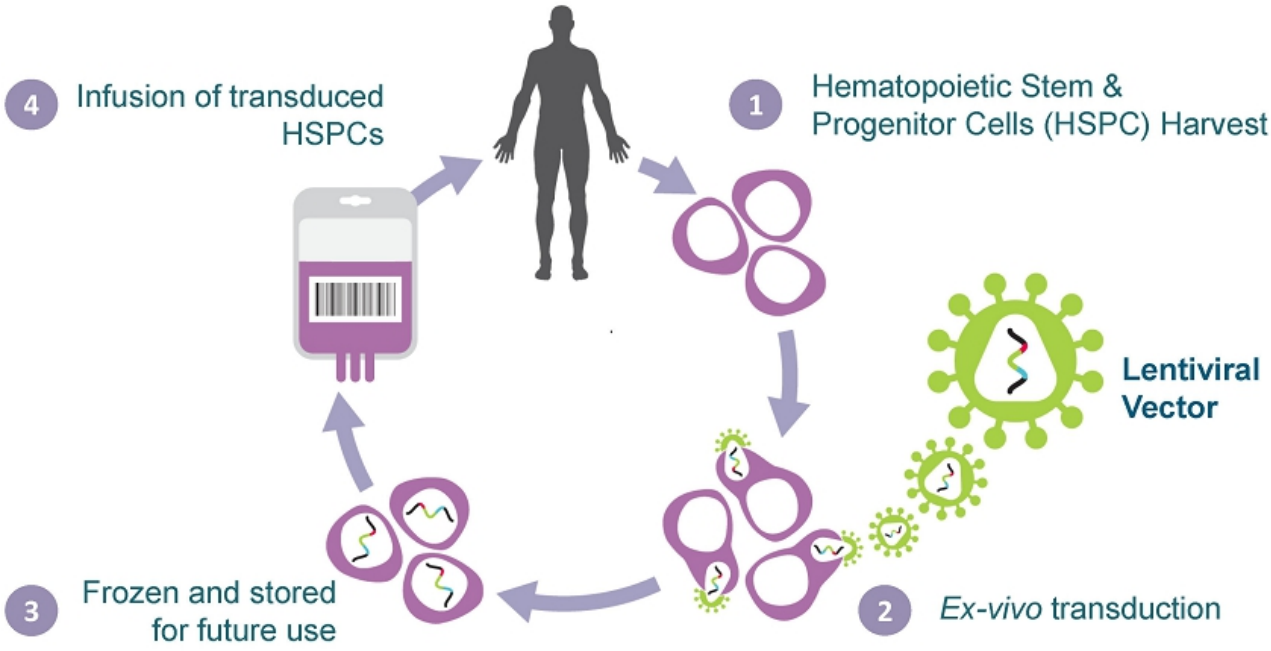


Illustration of our ex-vivo approach (steps 1-2-3) and treatment process (step 4)

(1) Patient's HSPCs are harvested by means of an apheresis process, and (2) *ex-vivo* modified by an LVV. The obtained drug product is frozen and stored for clinical use (3). When needed, the therapeutic product may be thawed and infused back in patient's blood stream (4). The engineered HSPCs will repopulate the entire hematopoietic system, giving rise to differentiated progeny bearing the introduced modification.

a) HSPCs are the Source of the Delivery Vehicle for Our Gene Therapy Approach

By re-introducing gene-modified HSPCs into the patient, we seek to take advantage of the self-renewing and multi-differentiation capability of HSPCs to enable durable and potentially long-term effects following a single treatment. HSPCs are self-renewing cells that can differentiate into all types of blood cells, including white blood cells, red blood cells and platelets. HSPCs can be obtained directly from the bone marrow or from the patient's peripheral blood with the use of a mobilizing agent that induces HSPCs to relocate from the bone marrow into the peripheral blood where they may be collected by apheresis. The advantages of using a patient's own HSPCs include the absence of graft versus host disease (GVHD) that could occur using allogeneic cells, and the potential long-term treatment durability of this approach.

b) Ex-vivo LVV based Transduction

After collection, a functional copy of the therapeutic gene is inserted into the patient's own HSPCs using a non-replicating LVV. This is an *ex-vivo* process called transduction. We believe that LVVs are the first choice for *ex-vivo* gene therapy in humans because they can (i) carry large transgenes that will allow us to expand the therapeutic options to a multitude of payloads without "size" limits and (ii) efficiently transduce non-proliferating, or slowly proliferating cells, such as hematopoietic stem and progenitor cells. Most importantly, there is already an abundance of safety data generated using these vectors to develop investigational products currently under clinical testing, including CARs, TCRs, as well as commercial products such as Kymriah® (CD-19 CAR-T, Novartis Pharma) and Zynteglo® (β-Thal, Bluebird Bio). With more than 100 clinical trials either completed or in progress using LVVs worldwide, this delivery method accounts for more than a third of *ex-vivo* modified gene therapy clinical trials.

Accordingly, extensive clinical *ex-vivo* gene therapy studies, based on LVV gene transfer, have been performed in recent years by SR-Tiget for the prevention and treatment of some severe inherited disorders, resulting in approved drugs, such as Libmeldy™. These studies have shown that LVVs constitute a valuable and safer alternative to gamma-retroviral vectors, enabling a more efficient gene transfer into HSPCs and resulting in a robust and long-term transgene expression in their progeny. The studies also have demonstrated an alleviated risk of genotoxicity because of the vector design.

Differences exist between LVVs used for *ex-vivo* transduction that could, in theory, lead to differences in the long-term safety profile of products, particularly in terms of genotoxic potential. Use of strong promoters in conditions where a high pre-existing risk for hematologic malignancies exists, such as sickle cell disease ("SCD"), could in the long-term (i.e. 5 years or more) contribute to the development of leukemia. There have been several significant adverse side effects in gene therapy treatments involving an ex-vivo transduced lentivirus vector ("LVV") gene therapy product, Bluebird Bio's elivaldogene autotemcel ("Lenti-D"), involving two SUSARs for cases of acute myeloid leukemia ("AML"), and one case involving myelodysplastic syndrome.

In February 2021, Bluebird Bio temporary suspended its gene therapy clinical trials for SCD (HGB-206 and HGB-210) and the marketing of Zynteglo® due to a suspected unexpected serious adverse reaction ("SUSAR") of acute myeloid leukemia (AML) in a SCD patient who received the product more than five years ago. In July 2021, the European Medicines Agency's ("EMA") safety committee (Pharmacovigilance Risk Assessment Committee – "PRAC") announced that there is no evidence the LVV used in both Lenti-D and the E.U.-approved gene therapy Zynteglo spurred the AML cases.

Bluebird Bio announced on August 9, 2021 that the SUSAR involving myelodysplastic syndrome occurred in one patient treated with Lenti-D over a year earlier. Bluebird Bio stated that this SUSAR "was likely mediated by Lenti-D lentiviral vector (LVV) insertion," and that "specific design features of Lenti-D LVV likely contributed to this event." As a result of this SUSAR, the FDA has placed a clinical hold on Bluebird Bio's Lenti-D phase 3 trial for cerebral adrenoleukodystrophy.

We believe that the intrinsic characteristics of the LVV we have selected as well as the properties of the promoter and control mechanisms, combined with HSPCs' ability to self-renew, allow for a stable integration of the modified gene into the HSPCs and their related differentiated progeny, potentially achieving long-term safety and protection after only a single treatment.

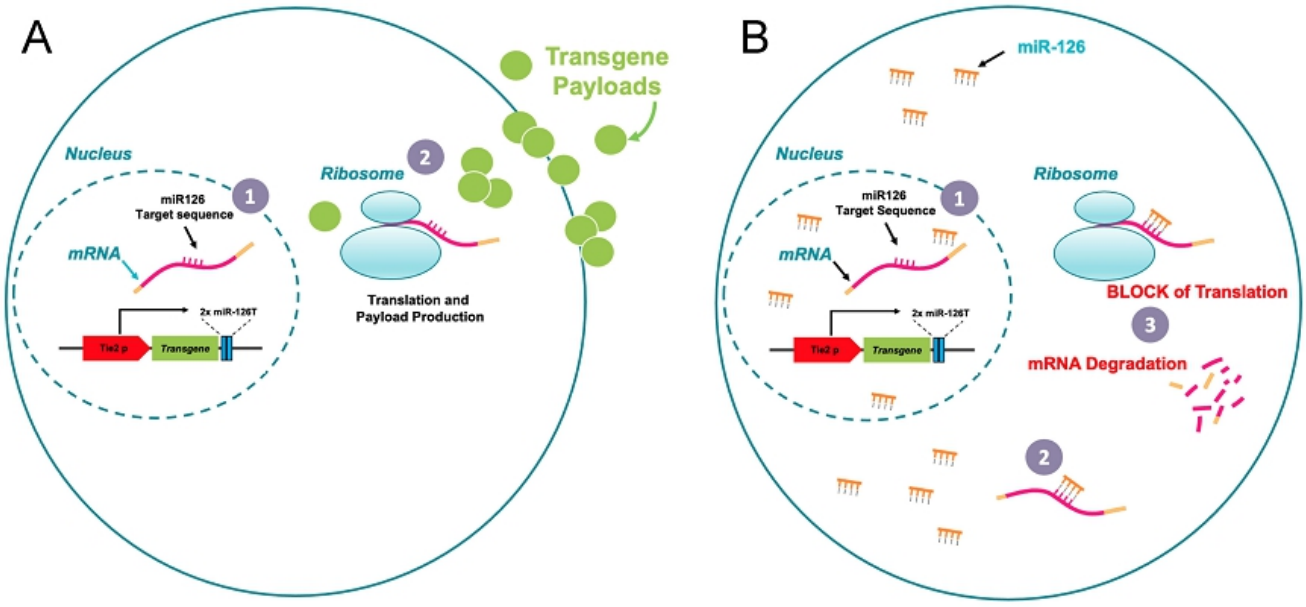
c) Tumor-Targeted Payload Delivery

Our platform technology, used by all of our product candidates including Temferon, is designed to turn TEMs, which normally have an affinity for and travel to tumors, into a "Trojan Horse" to deliver a tumor-targeted payload. The technology enables the payload to be expressed in TEMs and not in other types of cells. The following key components make up our platform technology: (i) a Tie-2 promoter that drives transgene sequence transcription specifically in TEMs, and (ii) a post-transcriptional regulation layer represented by miRNA-126 target sequences that induces the downregulation of the transgene expression in those cells where the Tie2 promoter is active and the miRNA-126 target sequence is present. This transcriptional / post-transcriptional regulatory mechanism prevents off-target effects and allows the expression of the payload by the selected cellular carrier (TEMs).

Our transgene payload expression cassette consists of two key components: the Tie-2 promoter (RED) and miRNA-126 target sequences (LIGHT BLUE)

(i) ***Tie-2 promoter.*** The Tie-2 promoter enables the transformation of TEMs into a "Trojan Horse", to deliver the therapeutic payload within the tumor microenvironment. Tumor development and progression is a multi-step process leading to cancer growth. The so called "angiogenic switch" is one of the required steps and refers to a time-restricted event during tumor progression where the balance between pro- and anti-angiogenic factors tilts towards a pro-angiogenic outcome, resulting in the transition from a "dormant" avascularized tumor to an outgrowing vascularized cancer. It is well recognized that TEMs play an active role in this regard. Indeed, TEMs are actively recruited by proliferating tumors, through signals produced by the cancer cells or stromal/endothelial components, to promote the neo-vascularization and to contribute to the establishment of an immunosuppressive tumor microenvironment that leads to the failure in tumor eradication by the immune system. Amongst chemoattractant factors of monocytes, angiopoietins (Ang) play a crucial role. These are adhesion molecules and known vascular growth factors expressed by peritumoral blood vessels. One Ang in particular, Ang-2, attracts TEMs, which binds to the Tie-2 receptor. Expression of Ang-2 is upregulated by tumor hypoxia and may function as a chemoattractant for Tie2-expressing monocytes. Moreover, TEMs' penetration into the tumor microenvironment in response to these stimuli cause Tie-2 receptor upregulation, which enhances the delivery of the payload to the tumor. Since TEMs recruitment is a naturally occurring event in the tumor development process and is a key aspect shared by several different cancers, we believe that our platform which enables the tumor targeted delivery of therapeutics represents a unique approach that may have broad applicability.

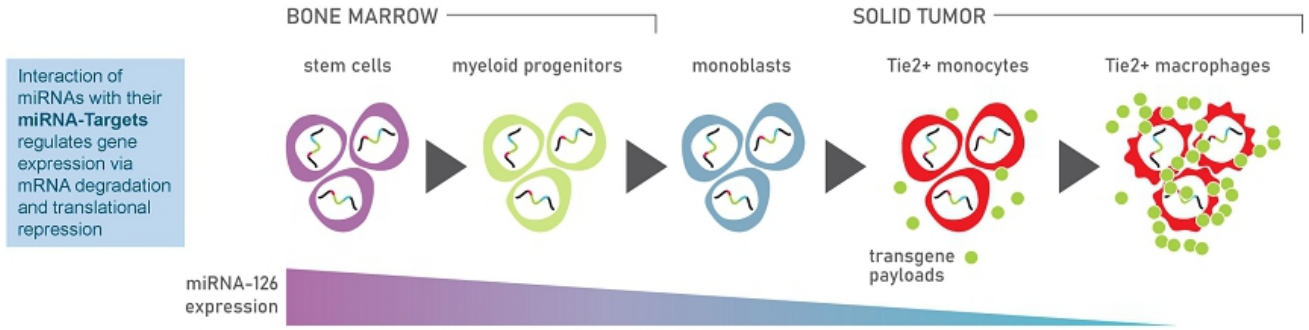
(ii) ***miRNA-126 target sequences***. The miRNA-126 target sequence serves as a post-transcriptional regulation layer that allows the expression of the transgene payload only in cells where miRNA-126 is not expressed. In our case, because miRNA-126 is highly expressed in HSPCs but down-regulated in the differentiated progeny, it switches off transgene expression in the stem and progenitor cell compartment. Indeed, Tie2 is a weak promoter expressed, in the hematopoietic compartment, by Tie2-expressing monocytes and by hematopoietic stem cells ("HSC"). In HSC, it works as a membrane-bound receptor that keeps HSC cell-to-cell interaction and adhesion with the bone marrow niche and preserves the HSC quiescent/low proliferating state.



Post-transcriptional control mechanism of transgene expression

A) Transgene expression is allowed only in cells where miRNA-126 is not expressed; (1) mRNA is transcribed into the nucleus (2) the transgene is then translated in the cytoplasm and released.

B) In those cells expressing miRNA-126 the payload production is prohibited; (1) mRNA is transcribed into the nucleus (2) miRNA-126 recognizes its target sequences on the mRNA and forms double strands of RNA (3) that are degraded or block the translation process.



De Palma et al., Cancer Cell, 2008; *Gentner et al.*, Sci Transl Med, 2010; *Escobar et al.*, Sci Transl Med, 2014; *Catarinella et al.*, EMBO Mol Med, 2016; *Escobar et al.*, Nat Commun, 2018

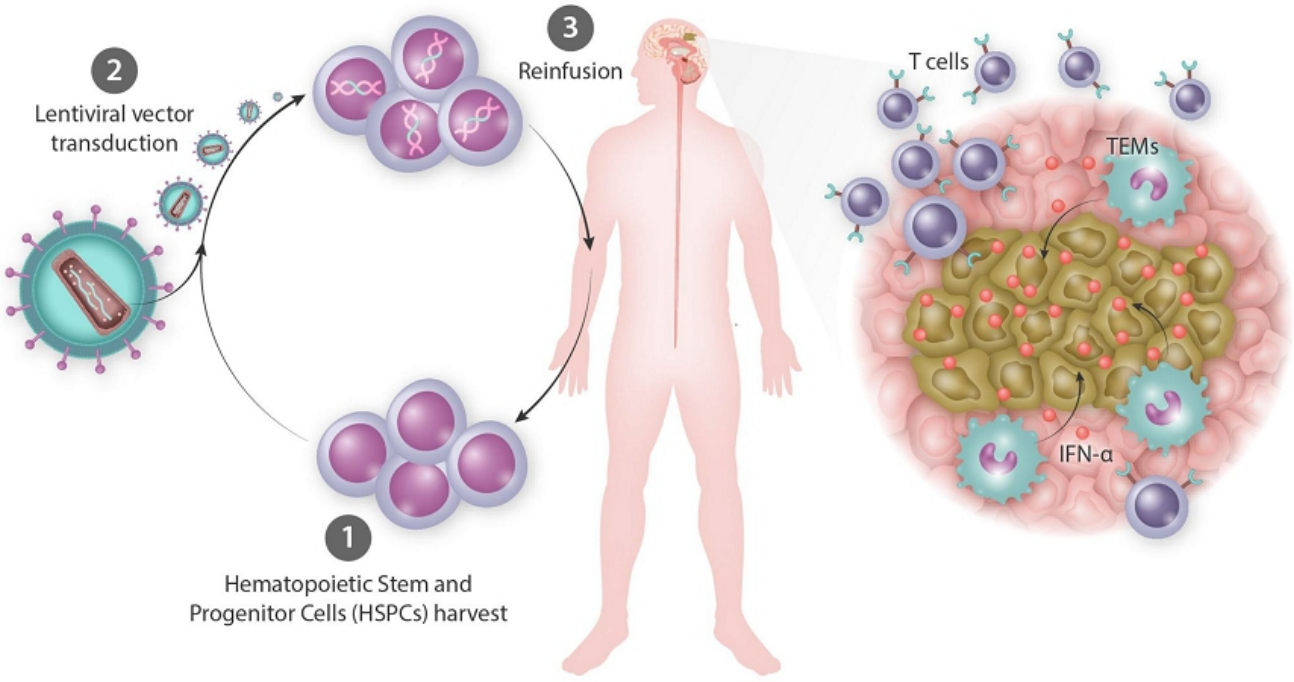
Transgene payload expression as the result of the transcriptional (promoter) and post-transcriptional regulation (miRNA-126 target sequence) imposed by our expression cassette.

We believe that combining our built-in post-transcriptional control mechanism (*miRNA-126 target sequences*), with TEMs designed as a "Trojan Horse," will allow our platform to restrict transgene expression and avoid systemic toxicity while reaching the therapeutic index to drive efficacy.

Our Leading Product Candidate: Temferon

Our lead product candidate, Temferon, consists of genetically modified HSPCs which use our platform to deliver interferon-alpha ("IFN-α"), within the tumor microenvironment via TEMs (HSPCs differentiated myeloid progeny). The IFN-α reduces angiogenesis, counteracts tumor cells proliferation and breaks the established immune-tolerance, enabling the immune system to recognize the tumor. IFN-α is a proven and known immunomodulatory molecule, or cytokine, that has limited clinical use due to the systemic toxicity associated with its intravenous administration. Our technology is designed to protect the HSPCs from IFN-α mediated activation that could negatively impact their repopulation capacity as reported in some studies of repeated systemic administration of high doses of IFN-α. We believe that this protection technology, whereby we restrict payload expression to TEMs, and the release of IFN-α within the TME, has the potential to provide efficacy without inducing systemic toxicity.

Because TEMs are associated with the growth of numerous cancer types, including solid tumors, we believe that Temferon is tumor type and tumor target agnostic and therefore may be used across a large variety of cancers. Currently, we are developing Temferon for uMGMT-GBM and mRCC.



Overview of Temferon manufacturing process and mechanism of action.

*Patient's **HSPCs** are harvested, (1) **ex-vivo** modified by **LVVs** (2) and re-introduced back in patient's blood stream (3). Once recruited within the tumor microenvironment, TEMs release IFN-α that reduces angiogenesis, counteracts tumor cells proliferation and enables the immune system to recognize the tumor.*

Temferon for uMGMT-GBM

GBM is a solid tumor affecting the brain. We have chosen this indication due to the following factors:

- ***High unmet medical need.*** The prognosis for GBM patients remains poor with few therapeutic options having limited clinical benefits.
- ***Temferon's MoA targets TEMs which have an active role in uMGMT-GBM pathology.*** GBMs are highly vascularized tumors that critically depend on the generation of tumor-associated blood vessels. Several studies demonstrate that infiltrating myeloid cells, including Tie2-expressing monocytes, contribute significantly to tumor angiogenesis, presumably by secreting pro-angiogenic factors and promoting malignant glioma growth by creating a local immunosuppressive microenvironment. Moreover, TEMs have been identified in the normal/tumor boundary from human biopsy samples of GBM patients who received treatment to reduce angiogenesis using the anti-VEGF treatment bevacizumab, and the Tie2 pathway has been implicated in the triggering of a bevacizumab-mediated VEGF-independent angiogenesis that explains the long-term refractoriness of GBMs to anti-VEGF treatment.

- ***Immunosuppressive tumor microenvironment.*** GBM is characterized by an immunosuppressive microenvironment that is mediated by tumor associated myeloid cells (including TEMs) that prevent the immune system from recognizing and rejecting the tumor. Our treatment approach is designed to exploit TEMS to deliver IFN-α to the tumor so that the immune system recognizes the tumor and halts tumor cell proliferation and recurrence.

- ***Availability of a "competent" immune system.*** Our approach relies on a patient's immune system being capable of providing an immune response upon recognition of the tumor. Therefore, we believe newly diagnosed uMGMT-GBM patients who have relatively "competent" immune systems, not yet damaged by repeated cycles of chemotherapies, are strong candidates for our candidate.

- ***Compelling preclinical data.*** Our preclinical studies, published in peer-reviewed papers, suggest that TEMs play an active role in uMGMT-GBM, and when used as a "Trojan Horse," may significantly shrink the tumor and control disease progression. In more recent unpublished studies, we have also demonstrated, in a preclinical immunocompetent GBM mouse model, that treatment by Temferon resulted in a long-lasting immune response in surviving mice, even after repeated tumor challenge intended to replicate possible tumor recurrences.

- ***Market Opportunity.*** Based on currently available treatments, the global market size for all GBM is projected to grow to over $6 billion by 2032. We believe a novel therapeutic, which demonstrates improvement over existing therapies would greatly increase the market size.

We are discussing other studies using Temferon in solid tumor indications, for which we are considering patients with unmet medical needs suffering from solid tumors which recruit TEMs in order to grow.

Disease Overview

GBM is the most common malignant primary brain tumor accounting for more than half of all central nervous system cancers and for which there is a high unmet medical need. The incidence rate is 3.20 per 100,000 persons with over 13,000 deaths per year in the U.S. This disease is lethal, and left untreated, the median survival is three (3) months. The current standard of care includes using a combination of surgery, radiation therapy, and chemotherapy for treatment. Although these treatments may improve survival, the prognosis for GBM patients remains poor with a mOS of approximately 13 to 15 months and only 5.5% of patients estimated to be alive 5 years after diagnosis. GBM may occur at any age, but 70% of cases are seen in patients between 45 and 70 years of age (median 64 years). The disease often progresses rapidly (over 2 to 3 months). Neurological signs are nonspecific as they result from intracranial hypertension and include headaches and vomiting, often associated with behavioral changes or focal neurological deficits. Variants of GBM include secondary glioblastoma (20% of total diagnosed GBM), gliosarcoma (2%) and giant cell glioblastoma (1%). We are not including these variants in our studies because they do not fully meet our selection criteria discussed above.

Current Treatment Landscape and Limitations

The current standard of care for GBM includes surgery to remove the accessible tumor followed by radiation therapy ("RTx"), chemotherapy with temozolomide ("TMZ") and/or tumor treating fields ("TTFields").

- ***Surgery*** remains the mainstay of initial treatment. If the tumor is located in a resectable region of the brain, it is used to histologically confirm the diagnosis and level of tumor burden. For many patients, removal of the tumor also results in a decrease of tumor mass-associated symptoms. Although the extent of the surgical removal of the tumor is linked to longer survival, due to the invariably infiltrative nature of the disease, even the complete removal of the accessible tumor is not curative and most people with GBM later develop recurrent tumors either near the original site or at more distant locations within the brain. Additionally, as a possible consequence of surgical procedures, permanent brain damage may occur.

- ***Radiation therapy*** improves survival and is typically started approximately three (3) to four (4) weeks after surgery. RTx is performed daily for approximately six (6) weeks. RTx induces the formation of neo-antigens and a pro-inflammatory response that are key aspects for immune system mediated disease control. However, the efficacy of RTx is impaired by hypoxia and by the negative effects of RTx on tumor infiltrating immune cells.

- ***Chemotherapy.*** Temozolomide, the current chemotherapeutic standard of care, is a DNA-alkylating agent that can cross the blood-brain barrier to reach therapeutic concentrations in the brain. The drug is administered every day during radiation therapy and then for six to 12 cycles after radiation as a maintenance therapy. Each cycle lasts 28 days, with TMZ given the first five days of each cycle, followed by 23 days of rest. TMZ adds a methyl group to DNA that, if unrepaired, leads to DNA strand breaks and cytotoxicity. More than one-third of glioblastomas are deficient in methylguanine methyltransferase ("MGMT"), a repair protein that removes the methyl group. This MGMT deficiency occurs through the methylation (silencing) of the MGMT gene promoter. Glioblastoma patients with a silenced MGMT gene who are treated with TMZ have a longer survival than those with an unmethylated MGMT. TMZ has several adverse side effects, including a cumulative bone marrow toxicity.

- ***Tumor-Treating Fields (TTFields)***. The use of TTFields to extend temozolomide maintenance chemotherapy for newly diagnosed glioblastoma patients has recently been incorporated as a new standard of care. TTFields are applied via multiple electrodes that are directly fixed to the scalp. These low-intensity, alternating electrical fields interfere with cell division ultimately leading to cell cycle arrest, aneuploidy, and apoptosis. The most common TTFields-associated adverse events (AEs) are mild-to-moderate array-associated contact dermatitis.

- ***Experimental Treatments.*** Along with the above-mentioned treatments, the addition of the antiangiogenic agent bevacizumab (BEV) to RTx and TMZ has been explored with mixed clinical results BEV was tested both a first-line treatment together with RTx and concomitant TMZ administration in newly diagnosed glioblastoma patients, as well as in combination with RTx in recurrent GBM patients. BEV was approved by the FDA as monotherapy for recurrent glioblastoma in 2009 under the name Avastin®. The EMA declined to approve BEV for recurrent glioblastoma due to the absence of a non-bevacizumab control arm, a modest overall survival increment versus historic controls, inadequate elucidation of true antitumor effect, and challenges with radiographic response assessment. More recently, an immune-checkpoint blocker nivolumab was tested in combination with TMZ and RTx in a Phase 3 trial in recurrent glioblastoma patients but showed minimal activity and no benefit in terms of mOS, resulting in failure to meet one of its primary endpoints, PFS.

Currently available GBM surgical treatments have not been able to prevent GBM recurrence because of the infiltrative nature of this disease and the absence of an effective immune system. A therapeutic able to cross the blood-brain barrier and selectively impact proliferation of cancer cells independently from the region of the brain where the tumor resides would be a significant advancement.

Our Solution

We believe that our investigational product, Temferon, has the potential to address the world unmet need of patients suffering from GBM. Through a single administration, we believe Temferon may be able to provide a long-lasting immune response, minimize systemic toxicity, counteract cancer progression and prevent tumor relapse.

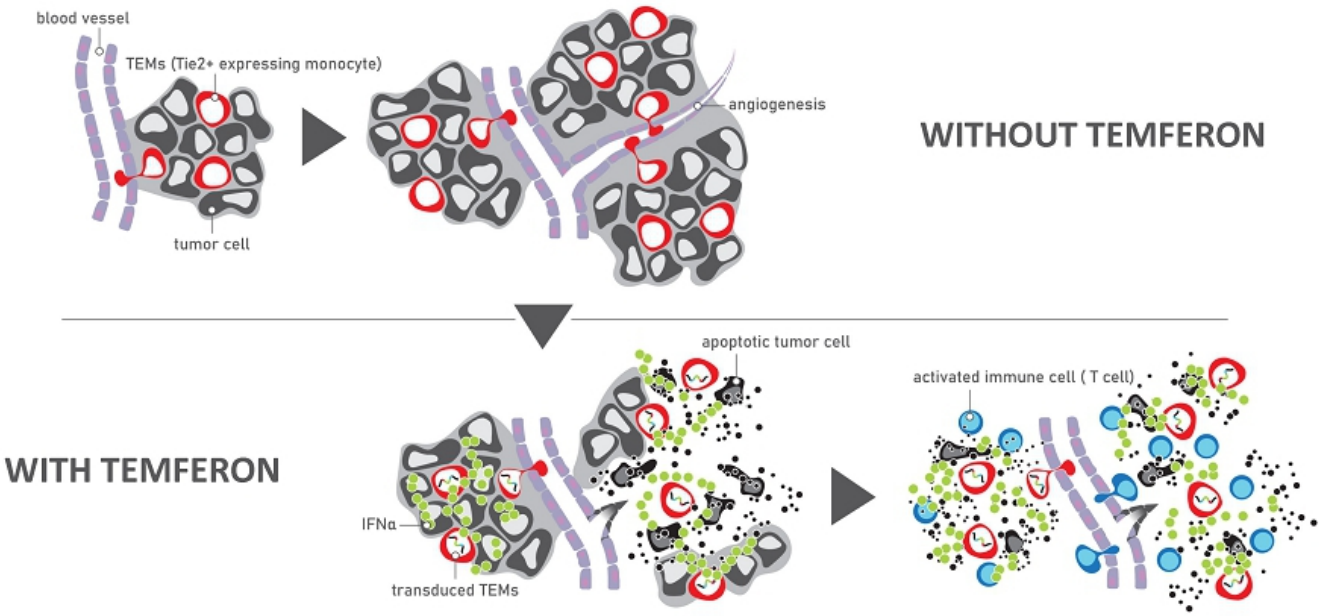
Temferon utilizes our platform and *ex-vivo* gene therapy approach to introduce a functional copy of IFN-α which is Temferon's transgene payload, into the patient's autologous HSPCs, resulting in a drug product that can then be reintroduced into the patient as outlined above (*see "Our Leading Product Candidate: Temferon" and "Our Platform"*). Temferon is designed to colonize the patient's bone marrow with the genetically modified HSPCs to continuously generate TEMs containing the IFN-α payload. Since TEMs are recruited within the tumor microenvironment, IFN-α is released solely at the targeted tumor, which may result in clinical activity without inducing systemic toxicity.

Once within the tumor microenvironment, IFN-α is expected to act both *directly* by promoting cancer cell apoptosis and inhibiting vascularization and *indirectly* by restoring the body's anti-tumor immune response, as follows:

- ***Direct Effects.*** IFN-α suppresses tumor cell proliferation and promotes the apoptosis of tumor and stromal cells by induction of proapoptotic genes or repression of anti-apoptotic genes. Moreover, IFN-α inhibits angiogenesis by downregulating the expression of proangiogenic factors.

- ***Additional Effects.*** IFN-α stimulates early innate immune responses and the subsequent adaptive immune response via multiple pathways and mechanisms, including: maturation and cross-priming capacity of dendritic cells ("DCs"); upregulation of the expression of tumor-associated surface antigens and MHC class I molecules on tumor cells and of MHC class I and II molecules on DCs; enhanced priming and survival of T cells; enhanced humoral immunity; increased cytotoxic activity of NK cells and macrophages; control of helper T cell population balance (Th1=Th2); immunoglobulin class switching of B cells; and the regulation of CD8+ cytotoxic T-lymphocyte responses.

We believe that through these immunomodulatory functions and based on our preclinical data, IFN-α increases tumor immunogenicity, recruits and activates immune cells within the tumor milieu, breaks established tumor-induced immunotolerance and may induce tumor rejection.



De Palma et al., Cancer Cell, 2008; *Gentner et al.*, Sci Transl Med, 2010; *Escobar et al.*, Sci Transl Med, 2014; *Cataninella et al.*, EMBO Mol Med, 2016; *Escobar et al.*, Nat Commun, 2018

Overview of Temferon antitumor activity

Once recruited at the tumor site, instead of fostering tumor growth and inhibiting the immune systems, TEMs start to release IFN-α that triggers cancer cell apoptosis and arms the immune cells to fight the cancer.

Clinical Development of Temferon in uMGMT-GBM

Preclinical Data

In 2008, a study conducted by De Palma et. al., demonstrated the potential of Tie2-expressing monocytes (TEMs) as vehicles for targeted interferon-alpha (IFN-α) delivery in cancer therapy. By exploiting the tumor-homing properties of TEMs, researchers achieved localized IFN-α delivery, resulting in significant inhibition of tumor growth and metastasis across various tumor models, including glioblastoma multiforme (GBM). Specifically, in the GBM model, treatment with TEM-mediated IFN-α delivery led to a substantial reduction in tumor burden and prolonged survival in treated animals, showcasing the potential for TEMs to modulate the tumor microenvironment effectively (PubMed PMID 18835032). Building upon this approach, a 2022 study conducted by Birocchi et. al., further highlighted the therapeutic potential of IFN-α in GBM treatment. Using a platform for inducible and localized cytokine delivery, researchers achieved controlled IFN-α release within the tumor microenvironment, demonstrating robust anti-tumor effects. This approach was observed to not only inhibit tumor growth but also reprogram the GBM microenvironment toward a pro-inflammatory and anti-tumor state. Notably, localized delivery mitigated the systemic toxicity typically associated with recombinant IFN-α administration, underscoring the importance of spatial and temporal control in enhancing efficacy and safety (PubMed PMID 35857642). Collectively, these studies underscore the therapeutic potential of utilizing TEMs and controlled cytokine delivery for targeted GBM treatment, offering promising avenues for enhancing anti-tumor immunity and controlling tumor progression.

Phase 1/2a Clinical Trial

The TEM-GBM study is a single-arm, open label, dose escalation, Phase 1/2a clinical trial, designed to evaluate the feasibility, safety, tolerability, biological activity (Phase 1) and efficacy (Phase 2) of Temferon in glioblastoma patients with an unmethylated MGMT gene ("uMGMT-GBM"). The trial is being conducted at two clinical centers of excellence located in Milan, Italy:

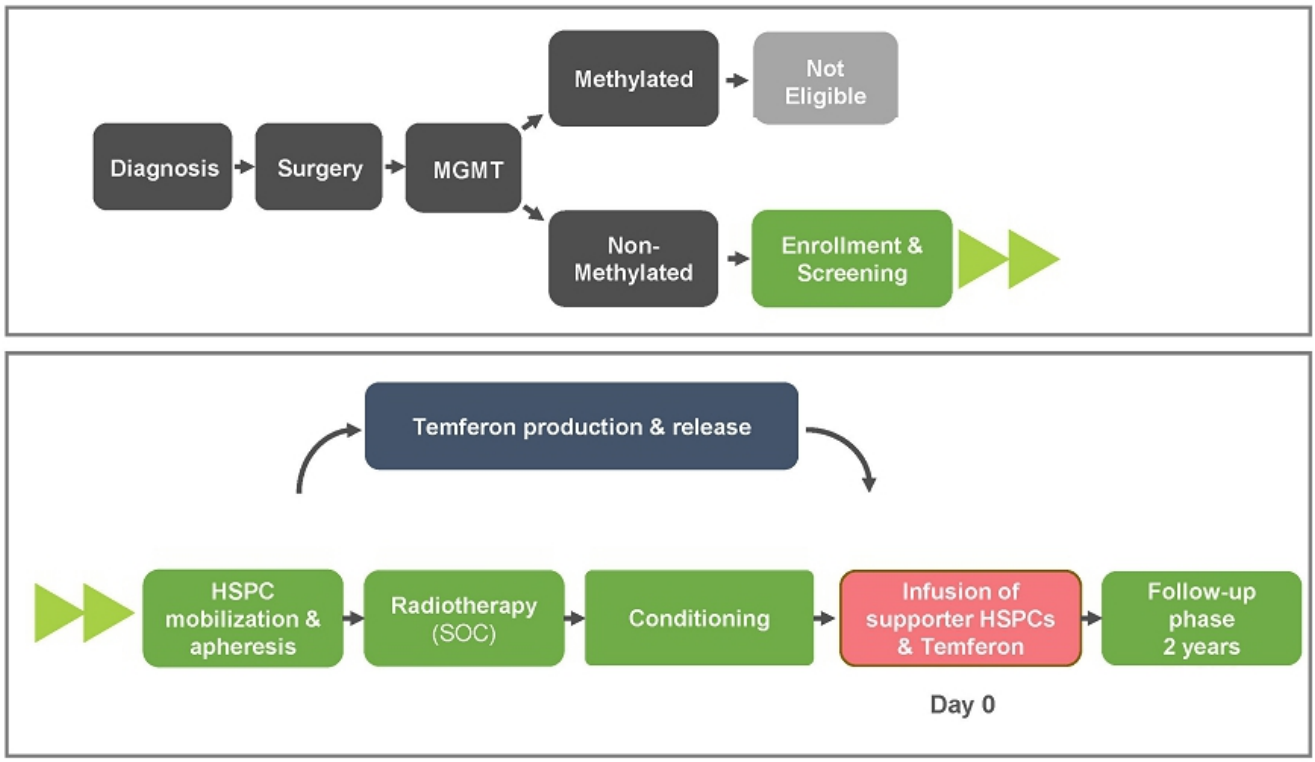
(i) Istituto Nazionale Neurologico "*Carlo Besta*", an internationally recognized leading center in neuroscience, specializing in the diagnosis and treatment of neurological diseases in adults and children, and (ii) OSR, which has a recognized expertise in complex and innovative diagnostic and therapeutic approaches in onco-hematological patients and in gene therapy treatments.

Study Design

The investigational treatment involves the use of autologous CD34+-enriched hematopoietic progenitor cells genetically modified with a lentiviral vector encoding human interferon-α2. This therapy is specifically targeted at adult patients aged 18 to 70 years with GBM characterized by an unmethylated O-6-methylguanine-DNA methyltransferase (MGMT) gene promoter, a subgroup known for poorer response to standard therapies. We believe this trial represents an innovative strategy for modulating the tumor microenvironment and enhancing anti-tumor immunity in GBM patients.

uMGMT-GBM patients are identified immediately after surgery, upon confirmation of the diagnosis and MGMT methylation status. After enrollment, each patient is screened for eligibility, and if eligible is subjected to the mobilization procedure to induce HSPCs to exit from the bone marrow niche and to migrate into the peripheral blood where they are collected by leukapheresis. Immediately after collection, each patient's HSPCs are sent to our CMO to be genetically modified and become Temferon. Escalating doses of Temferon (0.5-4 x 106 cells/kg) are administered via autologous stem cell transplant (ASCT) following the conditioning regimen, and after the administration of unmodified supporter stem cells. The study has been designed to test different ASCT conditioning regimens (BCNU+tiothepa, busulfan+tiothepa, busulfan monotherapy) as well as administering varying quantities of supporter cells (2-3 x 106 cells/kg) to identify the optimal setting for ensuring engraftment and durability of the drug product and as an effort to optimizing the benefit/risk ratio. We believe that this design enables the study not only to identify the most effective approach for enhancing the engraftment and persistence of Temferon cells but will also allow for optimization of the therapeutic outcome. After Temferon administration, each patient will be followed for two years.

The figure below depicts the different stages of TEM-GBM study enrollment and treatment.



The primary objectives of the dose-escalation phase (Phase 1) of the study are focused on determining the maximum tolerated dose (MTD) of the genetically modified cells and identifying the recommended dose to be carried forward into Phase 2. These objectives are pursued by closely monitoring dose-limiting toxicities (DLTs) and assessing treatment-related adverse events (AEs). Additionally, the study aims to assess the overall safety profile of the therapy, which includes evaluating any significant toxicities linked to both the harvesting of hematopoietic stem/progenitor cells (HSPCs) and the administration of the genetically modified cells. The secondary objectives include assessing the engraftment of the genetically modified cells in patients, monitoring the pharmacokinetics and pharmacodynamics, and evaluating early indicators of anti-tumor activity. These include important clinical endpoints such as progression-free survival (PFS) and overall survival (OS). The study also seeks to explore biomarkers related to the modulation of immune responses and potential changes in the tumor microenvironment that may indicate therapeutic efficacy. Moreover, the study will assess clinical responses using standard iRANO criteria, which includes tracking responses such as complete response (CR), partial response (PR), stable disease (SD), and progressive disease (PD). Survival metrics will be evaluated at various timepoints, and quality of life (QoL) will be measured using scales such as the Eastern Cooperative Oncology Group Performance Status (ECOG) and Karnofsky Performance Status (KPS). These tools will help monitor changes over time, enabling to gauge both the physical well-being and the functional capacity of patients as the study progresses. Through these comprehensive objectives, we believe the study will allow not only to assess the safety and tolerability of the therapy but also to identify promising biomarkers and early signs of efficacy that may guide future treatment strategies in GBM and potentially other cancers. The study EudraCT Number is 2023-510299-29-00 and can be found at EMA and FDA clinical trial registries here:

- https://euclinicaltrials.eu/search-for-clinical-trials/?lang=en&EUCT=2023-510299-29-00; and
- https://clinicaltrials.gov/study/NCT03866109?intr=Temferon&rank=3.

The information contained on, or that can be accessed through, these websites is not part of, and is not incorporated by reference into, this report. We have included these website addresses in this report solely as an inactive textual reference. Investors should not rely on any such information in deciding whether to purchase our securities.

Preliminary Interim Results.

In the dose-escalation phase (Phase 1), each cohort tested varying doses of Temferon, of unmodified supporter cells and a different conditioning regimen (see the "Study Design" section above). The study revealed that transduced cells engrafted and persisted across all cohorts as a function of the Temferon administered dose.

Phase 1 safety data highlighted a quick hematologic recovery (median 14 days). Only one serious adverse reaction, attributed to Temferon (elevated liver enzymes) was recorded. This occurred early in the treatment of a patient who subsequently achieved survival beyond three years. Most of the adverse events observed in the trial were attributed to autologous stem cell transplant procedures, including conditioning chemotherapy, concomitant medications, or disease progression, and most resolved over time. Three patients with GBM died within 122 days of Temferon administration, which were determined to be due to complications associated with conditioning chemotherapy and potentially concomitant steroid use. Busulfan monotherapy, as a conditioning regimen, demonstrated a better safety profile compared to combination therapies, with fewer adverse events, especially during the first 90 days, making it the preferred regimen moving forward into Phase 2.

Regarding efficacy, while no complete responses were observed, the data suggested tumor stabilization for up to 6 months post-Temferon infusion in several patients. The median progression-free survival (PFS) and overall survival (OS) following Temferon infusion were promising, aligning with existing data from GBM patients. The study also highlighted an increase in the percentage of long-term survivors (LTS) at two years compared to data reported in literature. However, given the small sample size in dose-escalation setting, definitive conclusions on survival benefits cannot be made at this stage.

The biological activity of Temferon was assessed in patients requiring a second surgery due to disease progression, providing the only source of post-treatment GBM specimens for analysis. While these samples offer valuable insights into Temferon's mechanism of action, we believe their limitation lies in being derived from patients in the treatment escape phase, potentially underestimating the therapy's full biological effects. Preliminary analysis of the tumor microenvironment (TME) using single-cell RNA (scRNA) analysis, comparing Temferon-treated patients (RTx+Temferon) with those treated according to the standard of care (Stupp protocol: TMZ+RTx), revealed a widespread induction of an interferon-response in Temferon-treated patients. This response was evident both within the tumor and the immune TME, including tumor-associated myeloid cells and T-cells, and demonstrated significant reprogramming of the myeloid compartment toward a pro-inflammatory (M1-like) state. This reprogramming was accompanied by a consistent increase in CD8 lymphocytes with effector phenotypes, including a subset of putatively tumor-reactive T cells, which were more prominently observed in Temferon-treated patients. Moreover, Temferon treatment was observed to induce the expansion of T-cell clones and promote T-cell recruitment within the TME, distinguishing it from the effects seen in patients treated with the SOC. However, the prolonged presence of tumor-reactive T-cell clones in Temferon-treated patients was associated with PD-1 upregulation, a marker of immune exhaustion caused by sustained tumor-antigen stimulation. We believe this upregulation of PD-1 may have interfered with the long-term maintenance of the anti-tumor response, partially limiting its efficacy over time. Despite this limitation, Temferon successfully primed the immune TME toward a robust and durable inflammatory phenotype, setting the stage for a potentially long-lasting immune response, even in GBM.

We believe these results align with our preclinical data, supporting the immune activation effects mediated by Temferon in uMGMT-GBM patients. In conclusion, Phase 1 data suggest that Temferon is well-tolerated at doses up to $4x10^6$ CD34+ cells/kg, particularly when combined with busulfan monotherapy. Moving forward, Phase 2 will aim to confirm these results while further investigating long-term efficacy and safety.

TEM-GBM Clinical Development Plan

Considering the encouraging changes observed in the tumor microenvironment (TME) of patients treated with Temferon, we are actively exploring the potential to combine Temferon with immune-oncology (I/O) therapies. In particular, we are highly interested in immune checkpoint inhibitors (ICIs) due to their established role in reactivating exhausted T cells, enhancing and extend anti-tumor immune responses.

This strategy is further supported by recent evidence demonstrating the potential of activating anti-tumor immunity in GBM when ICI are used as neoadjuvant early treatment.

This paradigm shift aligns closely with our ongoing efforts to reprogram the TME. The robust immune activation observed in Temferon-treated patients—including the reprogramming of the myeloid compartment toward a pro-inflammatory (M1-like) state and the expansion of effector CD8+ T cells—creates an ideal foundation for synergistic combinations with ICIs. We believe that the primed inflammatory phenotype induced by Temferon may enhance the efficacy of ICIs by overcoming key barriers to anti-tumor immunity in GBM, as highlighted in the referenced study.

Our future clinical plan aims to evaluate these combination approaches in GBM patients, leveraging the unique mechanism of Temferon to establish a robust immune contexture within the TME, potentially enhancing response rates and extending survival outcomes.

Furthermore, in 2023 the U.S. Food and Drug Administration (FDA) and the European Commission each granted Orphan Drug Designation ("ODD") to Temferon for the treatment of glioblastoma multiforme, underscoring its therapeutic potential in this critical area of unmet need.

Second Solid Tumor Indication

We selected metastatic renal cell carcinoma ("mRCC") as the second solid tumor to investigate. Renal cell carcinoma ("RCC") is a type of cancer that affects the genito-urinary system. The rationale for focusing on mRCC is based on the same considerations to those underlying the uMGMT-GBM indication, specifically:

- ***High unmet medical need and market opportunity*.** The prognosis for patients with mRCC remains poor.
- ***Suitable tumor microenvironment.*** mRCC is distinguished by an immunotherapy-responsive tumor microenvironment in which TEMs play a critical role.
- ***IFN-α and advanced genitourinary malignancies.*** mRCC has shown remarkable sensitivity to IFN-α treatment. Nearly 15 years ago, immunotherapy with IFN-α or interleukin-2 revolutionized the systemic treatment of RCC, establishing a foundation for immunotherapy in this field. More recently, the targeted delivery of IFN-α through an innovative in vivo gene therapy approach for genitourinary cancers has demonstrated significant clinical benefit, culminating in and leading to the FDA approval of Adstiladrin®. This reinforces the critical role of IFN-α in genitourinary malignancies and highlights the exceptional responsiveness of these tumors to immune-oncology (I/O) approaches.
- ***Market Opportunity.*** Based on currently available treatments, the RCC market for therapeutics is projected to grow 5.1% annually, reaching $12.7 billion in 2032. We believe a novel therapeutic which demonstrates improvement over existing therapies would have the potential to meaningfully grow the market size.

Disease Overview

Renal Cell Carcinoma ("RCC"):

Renal cell carcinoma accounts for over 80% of primary renal malignancies, with clear cell RCC being the most common (75% of all parenchymal renal malignancies).

Combination therapy (dual IO or an IO plus VEGF-TKI) is now recommended as first-line therapy. The treatment choice in the second and subsequent lines depends on the regimens received in prior lines, usually avoiding rechallenging a patient with the same agents. The second-line setting is dominated by the use of single-agent TKIs, (cabozantinib or pazopanib) and lenvatinib combined with the everolimus (mTOR inhibitor). Other treatments include the TKIs sunitinib and sorafenib, and the mTOR inhibitor temsirolimus. Single-agent nivolumab is approved for second-line treatment, but is used mainly for patients who did not receive an ICI in the first line. A hypoxia-inducible factor 2α (HIF2α) inhibitor, belzutifan, is approved for treating patients with RCC with VHL disease (3–6% of RCCs) who do not require immediate surgery. Multiple Phase 3 trials are ongoing to expand its label in RCC, including in late-line advanced or metastatic settings and in combination with other approved targeted therapies in the adjuvant and first-line settings.

Our Solution

Similar to the results we have observed to date for Temferon for the treatment of GBM, we believe that Temferon may have the ability overcome certain of the limitations of the current standard of care for the treatment of RCC that are not curative/resolutive by stopping/delaying disease progression.

Clinical Development of Temferon in advanced genitourinary malignancies

TEM-GU Phase 1/2a Clinical Trial

The TEM-GU study is an open-label, single-center, Phase 1/2 therapeutic-exploratory clinical trial designed to evaluate the safety, tolerability, biological activity, and efficacy of Temferon in patients with metastatic renal cell carcinoma ("mRCC"). The study aims to evaluate the combination of Temferon with either immune checkpoint inhibitors ("ICI") or tyrosine kinase inhibitor (TKI), to determine the most effective treatment for patients who have shown disease progression after standard treatments. The study is being conducted at the Genitourinary Oncology Unit at San Raffaele Hospital, Milan, Italy. This site is renowned for its expertise in the management of urological cancers and will offer cutting-edge care to the enrolled patients. Hematological follow-up and the administration of Temferon will take place at the specialist hematology and bone marrow transplant unit within the same hospital, ensuring coordinated and comprehensive patient care.

Study Design

The investigational treatment utilizes autologous CD34+-enriched hematopoietic progenitor cells genetically modified with a lentiviral vector encoding human interferon-α2. Eligible patients, who must have progressed after standard treatments, will undergo screening, followed by HSPC harvest and genetic modification. A conditioning regimen precedes Temferon infusion, after which patients are monitored closely until hematologic recovery. Tumor biopsies will be performed pre- and post Temferon administration. After Temferon administration, patients will receive also either ICI or TKI depending on their prior treatment lines. Patients will then continue with regular follow-ups for up to one year.

The primary endpoints of the study focus on assessing the safety and tolerability of both the conditioning regimen and Temferon through clinical and laboratory surveillance, autoimmune assessments, and adverse event monitoring. Secondary endpoints aim to explore the long-term safety of Temferon, the incidence of specific adverse events, hematological recovery, presence of transduced myeloid cells, functional status, response rates, progression-free survival, and overall survival. Additionally, the biological activity of Temferon, tumor microenvironment changes and biomarkers will be evaluated via biopsy analysis.

The study EudraCT Number is 2024-512898-27-00 and can be found at EMA and FDA clinical trial registries here:

- https://euclinicaltrials.eu/search-for-clinical-trials/?lang=en&EUCT=2024-512898-27-00 and
- https://clinicaltrials.gov/study/NCT06716853?intr=Temferon&rank=1

The information contained on, or that can be accessed through, these websites is not part of, and is not incorporated by reference into, this report. We have included these website addresses in this report solely as an inactive textual reference. Investors should not rely on any such information in deciding whether to purchase our securities.

TEM-GU Clinical Development Plan

The Phase 1/2a study in metastatic RCC (TEM-GU) represents a key opportunity to investigate whether Temferon can restore sensitivity to TKIs or ICIs in patients who previously failed to respond. By combining Temferon with these agents, the study aims to enhance therapeutic efficacy in difficult-to-treat populations. This approach will help assess the potential of Temferon as a viable treatment option to overcome resistance to standard therapies. We believe that positive clinical results not only will support the expansion of Temferon's exploration in combination therapies for RCC patients but also will pave the way for testing Temferon in other related indications. This could significantly broaden Temferon potential application in immune-oncology, especially in cancers with similar tumor microenvironment characteristics.

Additional Pipeline Pre-Clinical Programs

Our platform technology was designed to be flexible so that it can be adapted to potentially treat a variety of cancers. We believe that Temferon, in combination with a variety of current existing therapeutics, has the potential to enhance overall efficacy because its mechanism of action is intended to abrogate tumor induced tolerance. Additionally, we are developing a second-generation platform which is designed to release our therapeutic payload "on demand". Finally, our proprietary platform is designed to control the expression of a potentially wide variety of therapeutic payloads we may choose for different targets.

Combination Treatment

While therapies to treat several types of cancers, such as ICI, CAR-T and TCR, are rapidly transforming the practice of oncology, clinical data point to the risk of late relapses after treatment with these therapeutics. Thus, the data suggest that the durability of the response to these therapies remains a significant challenge. We believe that the potentially agnostic nature of Temferon, its activity observed in our clinical trials to date, which includes the abrogation of tumor induced tolerance, and its potentially synergistic mechanism of action, makes it a suitable candidate to be considered for combination treatments. Specifically, Temferon may be a good candidate to be used in combination with other immune-oncology drugs, such as CAR-T and ICI, to extend the durability of the response in very aggressive tumors. We believe that this additional Temferon application is supported by the promising results coming from the combination studies performed using Temferon with CAR-T, TCR and ICI in our pre-clinical programs as discussed below.

In preclinical studies conducted in the laboratories of our founders, Prof. Luigi Naldini and Dr. Bernhard Gentner, Temferon was evaluated in combination with CAR T, TCR-edited T cells directed against tumor-associated antigens and immune checkpoint blockers. The results showed promising additive-to-synergistic anti-tumor activity in leukemia experimental models (Escobar et al., Nature Communication 2018), glioblastoma models, and multiple myeloma mouse models. Specifically, a CD19 CAR-T approach in a leukemia mouse model had a detectable, but not significant, effect on the tumor burden. However, when used in combination with Temferon, the combination treatment resulted in a significant inhibition of the hematological malignancy, with a significant fraction of CAR-T/Temferon treated mice surviving to the latest timepoint of analysis. Similarly, the combination of IFN gene therapy to α-CTLA4, an immune check point blocker, or adoptive T cell therapy, significantly improved the survival of the mice (Escobar et al., Nature Communication 2018). Further, in a multiple myeloma mouse model, Temferon was administered in combination with human TCR-edited T cells directed against NY-ESO1 and anti-myeloma drugs. The combination approach showed promising additive-to-synergistic effects without exacerbating hematologic or systemic toxicities. These results lead us to believe that IFN gene therapy might also boost the efficacy of other immunotherapies.

Switchable Platform

Our founders are developing a second-generation platform designed to release the therapeutic payload “on demand” to potentially allow in vivo control of its efficacy. Potential advantages of this application include (i) broadening the clinical application to patient populations with more favorable pre-treatment prognoses; (ii) control of long-term side effects that may arise from the chronic exposure to immunostimulatory molecules and (iii) the ability to activate the immune system on demand to recognize tumors based on clinical need.

An inducible version of the IFN-α payload has been generated by fusing the protein with a destabilizing domain (DD), which targets the protein to proteasomal degradation, unless a small molecule ligand binding to the DD and stabilizing it, is administered. The optimized fusion construct is delivered by the TEM platform and the exogenous administration of the ligand switches on its secretion within the tumor. The results from experiments performed in the laboratory of Prof. Naldini with a glioblastoma mouse model showed similar anti-tumor activity of the inducible and wild-type IFN payload. Moreover, the inducible construct allows switching of IFN release upon tumor clearance (Birocchi et al., Sci Transl Med 2022). We plan to use our second-generation platform carrying an IFN-α payload in combination with CAR T cells to target glioblastoma-associated antigens or immune checkpoint blockers in an experimental tumor model in mice.

Other Payloads

Our platform is designed to allow the control of the expression of any payload we use. Similar to IFN-α, there are several alternative payloads with immunotherapeutic properties that were previously systemically delivered to patients but were discontinued due to significant toxicity that prevented the drug from reaching therapeutic dosages (e.g. TNF-Alpha). Because we believe that our first- and second-generation platforms may have the ability to overcome certain limitations associated with systemic administration, we are testing them with additional payloads such as IFN- g, IL-12 and TNF-α. Because each payload triggers a unique biological response, we believe our platform may enable a personalized treatment approach.

Additional immune activating cytokines have been tested for TEM-mediated gene-based delivery to tumor models in mice. Current pre-clinical results suggest the feasibility and specificity of tumor-targeted delivery of IFN-g and TNF-α and further support our hypothesis that the specific transcriptional and microRNA regulated expression of the payload prevents toxicity. Data generated in the laboratory of our founders in a leukemia model showed that IFN-g but not TNF-α mediates anti-tumor activity when delivered *ex vivo*. Further *ex vivo* studies showed enhanced anti-tumor activity upon combined delivery of two cytokines by the TEM-based platform.

Moreover, experiments conducted with our second-generation inducible platform expressing IL-12 support the hypothesis that our proprietary transcriptional and microRNA regulated expression of the payload may prevent or limit toxicity. Indeed, IL-12 is a potent cytokine that must be kept within a therapeutic dose range to prevent toxicity. Targeted delivery and anti-tumor activity of the new inducible payload are being investigated (Mucci et al., EMBO Mol Med 2021). The laboratory of Prof. Naldini plans to test the combination of TEM-mediated gene-based delivery of inducible Il-12 or additional inducible payloads with CAR-T, TCR and ICI in experimental murine tumor models.

Competition

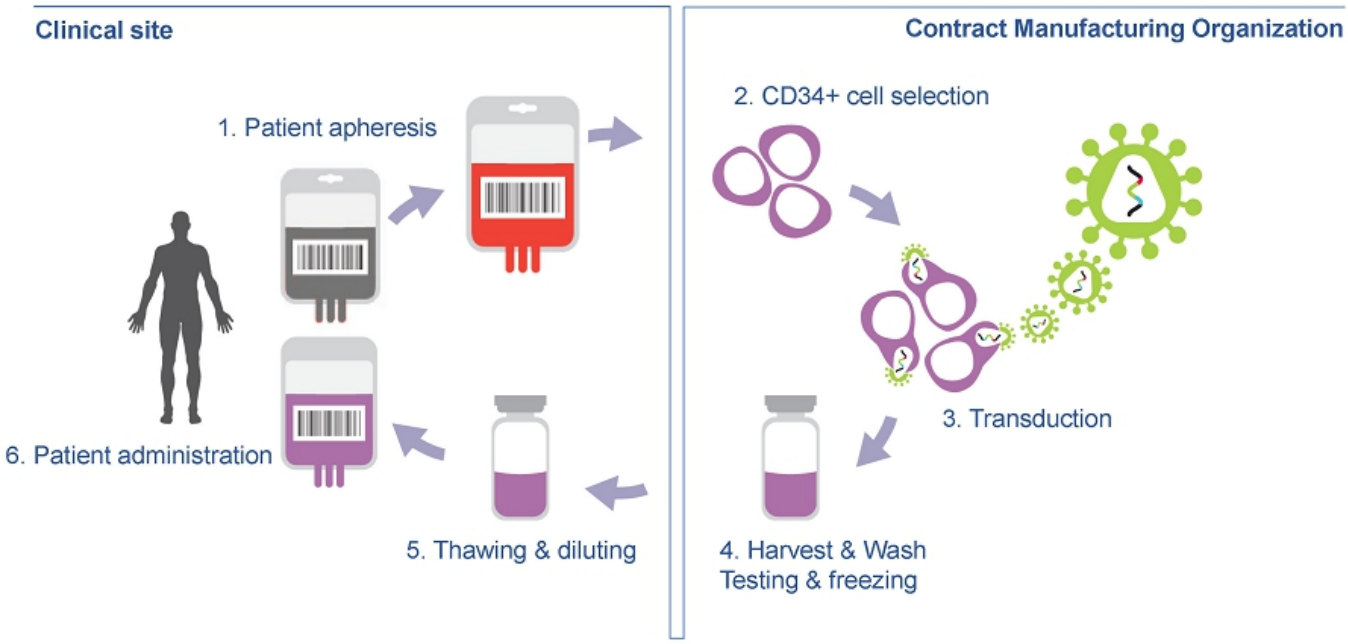
Biotechnology and pharmaceutical industries put significant resources in developing novel and proprietary therapies for the treatment of cancer. For the cell therapy field in particular, this results in rapidly advancing and changing technologies, intense competition and a strong emphasis on intellectual property. While we believe that our leading product candidate, Temferon and our scientific expertise in the field of cell and gene therapy provide us with competitive advantages, we face potential competition from various sources, including larger and better-funded pharmaceutical, specialty pharmaceutical and biotechnology companies, as well as from academic institutions, governmental agencies and public and private research institutions.

Manufacturing

The manufacturing process for our autologous cell and gene therapy approach requires the following steps:

1. HSPCs harvesting in a specialized clinical center (leukapheresis)
2. Shipping of apheresis bag/s to the selected contract manufacturing organization (CMO)
3. CD34+ cells enrichment
4. *Ex-vivo* transduction of CD34+ cells with our LVV,
5. Cryopreservation, characterization and release by a Qualified Person of the obtained drug product.

The LVV manufacturing needed for the *ex-vivo* transduction process, as well as steps from 3 to 5, are conducted by the CMO. The figure below delineates the steps and the timeline for manufacturing Temferon.



Overview of Temferon Manufacturing Process

We have entered into agreements with AGC Biologics to manufacture our LVV and certain drug products for our ongoing clinical programs in Italy. AGC Biologics is a leading global contract development and manufacturing organization ("CDMO"), providing world-class development and manufacture of mammalian and microbial-based therapeutic proteins of plasmid DNA and, with the acquisition of Molecular Medicine S.p.A. ("MolMed"), of viral vectors and genetically engineered cells. AGC Biologics is recognized as the leading cell and gene therapy CDMO focused on research, development, production and clinical validation of cell and gene therapies for the treatment of cancer and rare diseases. Indeed, Strimvelis, the first ever market approved *ex-vivo* gene therapy for children, was developed and is still currently manufactured by AGC Biologics (formerly MolMed). Accordingly, Orchard Therapeutics (NasdaqGS: ORTX) in July 2020 renewed their collaboration agreement with AGC which will continue to support activities related to the development and manufacturing of vectors and drug products for several of Orchard's investigational *ex-vivo* hematopoietic stem cell (HSC) gene therapies in the upcoming years, including the recent E.U. market authorized gene therapy drug *Libmeldy.*

AGC Biologics Capabilities

Our agreements with AGC establish agreed-upon timelines for purchase order submissions and manufacturing date changes/cancellation. The agreements also set milestones both during the clinical phase and any future commercial phase of our product candidates and for technology transfer if required, as well as customary termination provisions, allowing for termination by a party upon the other party's uncured material breach or upon the other party's insolvency. We have recently strengthened our collaboration with AGC Biologics to enhance cell therapy manufacturing. On January 9, 2025, we announced the introduction of an exclusive GMP suite at AGC Biologics's facility in Italy, dedicated to the production of Temferon batches. We believe this enhancement will improve the efficiency and reliability of our manufacturing processes. AGC Biologics facility in Bresso, Italy, will also continue manufacturing LVV to support Genenta's trials.

First and Second Amendment to Development and Master Services Agreement

On September 19, 2024, we entered into an amendment to the Master Services Agreement with AGC Biologics to extend the term of the Master Services Agreement to June 30, 2025 (the "First Amendment"). The First Amendment was considered effective retroactive from March 5, 2024, the day on which the Master Service Agreement expired, to cover the preceding period during which the same Master Service Agreement continued to be operating. Additionally, on October 14, 2024, we entered into an Agreement for the Conduct of Clinical Trials on Medical Products with OSR) to conduct an open-label 1/2 clinical trial in Renal Cell Cancer.

Effective December 24, 2024, we and AGC Biologics entered into the Second Amendment (the "Second Amendment") to the Development and Master Services Agreement, effective as of March 6, 2019 and as amended as of March 5, 2024 (the "MSA"), pursuant to which AGC Biologics manufactures our LVV) and certain drug products for our ongoing clinical programs in Italy.

In conjunction with entry into the Second Amendment, we also entered into work statement No. 1 to manufacture, test and release certain of our cell therapy products.

The Second Amendment provides that AGC Biologics will reserve an exclusive GMP suite (the "EGS") for our exclusive benefit in connection with manufacturing services for cell therapy and commit a specified number of full-time equivalent employees to us. In addition, AGC Biologics will make the EGS available for a specified number of weeks per a recurring 12-month period commencing in the first quarter of 2025. In the event this specified number of weeks is not reached, AGC will issue certain credit notes to us equal to the lost volume of activity. Further, if AGC is unable to offer EGC availability for this specified number of weeks over a 12 month period, AGC Biologics will issue certain credit notes to us as a penalty based on formulas specified in the Second Amendment.

The Second Amendment also provides that AGC Biologics will charge us monthly fees during the ramp-up phase, which begins on such specified date in the first quarter of 2025 and is estimated to end in the third quarter of 2025, and annual fees, payable quarterly, once the ramp-up phase is completed, as specified in the work statement.

Government Regulation

Government authorities in the U.S., at the federal, state and local levels, and in other countries and jurisdictions, including the E.U., extensively regulate, among other things, the research, development, testing, manufacture, sales, pricing, reimbursement, quality control, approval, packaging, storage, recordkeeping, labeling, advertising, promotion, distribution, marketing, post-approval monitoring and reporting, and import and export of biopharmaceutical products. The processes for obtaining marketing approvals in the U.S. and in foreign countries and jurisdictions, along with compliance with applicable statutes and regulations and other regulatory authorities, require the expenditure of substantial time and financial resources.

Approval and Regulation of Drugs in the United States

In the U.S., drug products are regulated by the FDA under the Federal Food, Drug, and Cosmetic Act and other laws, including, in the case of biologics, the Public Health Service Act ("PHSA"). Drug products are also subject to other federal, state and local statutes and regulations. A failure to comply with any applicable requirements during the product development, approval, or post-approval periods may lead to administrative or judicial sanctions, including, among other things, the imposition by the FDA or an institutional review board ("IRB") of a hold on clinical trials, refusal to approve pending marketing applications or supplements, withdrawal oDRf approval, warning letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, or administrative, civil and/or criminal investigation, penalties or prosecution.

In the U.S., all cell therapy product candidates are regulated by the FDA as biologics. Biologics require the submission of a BLA and approval by the FDA prior to being marketed in the U.S. Manufacturers of biologics may also be subject to state and local regulation.

The steps required before a biologic may be marketed in the U.S. generally include:

- completion of preclinical studies, animal studies and formulation studies, performed in accordance with the FDA's good laboratory practices ("GLP") requirements, and applicable requirements for the humane use of laboratory animals or other applicable regulations;
- submission to the FDA of an application for an investigational new drug application ("IND"), which must become effective before human clinical trials may commence;

- approval of the protocol and related documentation by an independent IRB or ethics committee at each clinical trial site before each trial may be initiated;
- performance of adequate and well-controlled clinical trials under protocols submitted to the FDA and reviewed and approved by each IRB, conducted in accordance with the FDA's good clinical practices ("GCPs") requirements and any additional requirements for the protection of human research subjects and their health information to establish the safety, purity and potency of the biologic for each targeted indication;
- preparation of and submission to FDA of a biologics license application ("BLA") for marketing approval that includes sufficient evidence of establishing the safety, purity, and potency of the proposed biological product for its intended indication, including from results of nonclinical testing and clinical trials;
- a determination by the FDA within 60 days of its receipt of a BLA to accept and file the application;
- satisfactory completion of an FDA pre-license inspection of the manufacturing facility or facilities where the biological product is produced to assess compliance with current good manufacturing practices ("cGMPs") to assure that the facilities, methods and controls are adequate to preserve the biological product's identity, strength, quality and purity;
- satisfactory completion of an FDA Advisory Committee review, if applicable;
- potential FDA audit of the preclinical study and clinical trial sites that generated the data in support of the BLA in accordance with any applicable expedited programs or designations;
- payment of user fees for FDA review of the BLA (unless a fee waiver applies);
- FDA review and approval, or licensure, of the BLA to permit commercial marketing of the product for particular indications for use in the U.S.;
- satisfactory completion of an FDA inspection of the manufacturing facilities at which the biologic is produced to assess compliance with current Good Manufacturing Practices ("cGMP") and to assure that the facilities, methods and controls are adequate; and
- FDA review and approval of the BLA.

Preclinical Studies and the IND Process

Before testing any biological product candidate in humans, the product candidate enters the preclinical testing stage. Preclinical studies include laboratory evaluation of a product's biological characteristics, chemistry, formulation and toxicity, as well as animal studies to assess the characteristics and potential safety and efficacy of the product candidate. The conduct of the preclinical studies must comply with federal regulations and requirements, including, as applicable, GLP and the Animal Welfare Act.

Prior to commencing an initial clinical trial in humans with a product candidate in the U.S., an IND must be submitted to the FDA and the FDA must allow the IND to proceed. An IND is an exemption from the FD&C Act that allows an unapproved product candidate to be shipped in interstate commerce for use in an investigational clinical trial and a request for FDA allowance that such investigational product may be administered to humans in connection with such trial. Such authorization must be secured prior to interstate shipment and administration. In support of a request for an IND, the clinical trial sponsor must submit the results of the preclinical tests, together with manufacturing information, analytical data, any available clinical data or literature and a proposed clinical protocol, to the FDA as part of the IND. An IND must become effective before human clinical trials may begin. Once submitted, the IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA places the IND on a full or partial clinical hold within that 30-day time period. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial or part of the study can begin. Submission of an IND therefore may or may not result in FDA authorization to begin a clinical trial. The FDA also may impose clinical holds on a sponsor's IND at any time before or during clinical trials due to, among other considerations, unreasonable or significant safety concerns, inability to assess safety concerns, lack of qualified investigators, a misleading or materially incomplete investigator brochure, study design deficiencies, interference with the conduct or completion of a study designed to be adequate and well-controlled for the same or another investigational product, insufficient quantities of investigational product, lack of effectiveness, or non-compliance. If the FDA imposes a clinical hold, studies may not recommence without FDA authorization and then only under terms authorized by the FDA.

Clinical Trials

Clinical trials involve the administration of the product candidate to healthy volunteers or patients under the supervision of qualified investigators. Clinical trials are subject to extensive regulation and must be conducted in compliance with (i) federal regulations, (ii) GCP standards, which set safeguards to protect the rights and health of patients and establish standards for conducting, recording data from, and reporting results of clinical trials, and (iii) protocols detailing, among other things, the objectives of the trial, subject selection and exclusion criteria, the parameters and criteria to be used in monitoring safety, and the effectiveness criteria to be evaluated, if any. Foreign studies conducted under an IND generally must meet the same requirements that apply to studies being conducted in the U.S. The informed written consent of each study patient must be obtained before the patient may begin participation in the clinical trial. The study protocol, study plan, and informed consent forms for each clinical trial must be reviewed and approved by an IRB for each clinical site, and the study must be conducted under the auspices of an IRB for each trial site. Investigators and IRBs must also comply with FDA regulations and guidelines, including those regarding oversight of study patient informed consent, complying with the study protocol and investigational plan, adequately monitoring the clinical trial, and timely reporting of adverse events. An IRB can suspend or terminate approval of a clinical trial at its institution, or an institution it represents, if the clinical trial is not being conducted in accordance with the IRB's requirements or if the product candidate has been associated with unexpected serious harm to patients.

The clinical trial program for a product candidate is generally divided into three phases. Although the phases are usually conducted sequentially, they may overlap or be combined. The three phases are as follows:

- *Phase 1*. Phase 1 involves the initial introduction of a product candidate into humans. Phase 1 clinical trials are typically conducted in healthy human subjects, but in some situations are conducted in patients with the target disease or condition. These clinical trials are generally designed to evaluate the safety, metabolism, pharmacokinetic ("PK") properties and pharmacologic actions of the product candidate in humans, the side effects associated with increasing doses and, if possible, to gain early evidence of effectiveness. During Phase 1 clinical trials, sufficient information about the product candidate's PK properties and pharmacological effects may be obtained to inform and support the design of Phase 2 clinical trials.

- *Phase 2*. Phase 2 includes the controlled clinical trials conducted to obtain initial evidence of effectiveness of the product candidate for a particular indication(s) in patients with the target disease or condition, to determine dosage tolerance and optimal dosage, and to gather additional information on possible adverse side effects and safety risks associated with the product candidate. Phase 2 clinical trials are typically well-controlled, closely monitored, and conducted in a limited patient population; and

- *Phase 3*. Phase 3 clinical trials are clinical trials conducted in an expanded patient population at geographically dispersed clinical trial sites. They are performed after preliminary evidence suggesting effectiveness of the product candidate has been obtained and are intended to further evaluate dosage, clinical effectiveness and safety, to establish the overall benefit-risk relationship of the product candidate and to provide an adequate basis for regulatory approval. In most cases, the FDA requires two adequate and well controlled Phase 3 clinical trials to demonstrate the efficacy of the product candidate, although a single Phase 3 clinical trial with other confirmatory evidence may be sufficient in certain instances.

In August 2018, the FDA released a draft guidance entitled "Expansion Cohorts: Use in First-In-Human Clinical Trials to Expedite Development of Oncology Drugs and Biologics," which outlines how developers can utilize an adaptive trial design commonly referred to as a seamless trial design in early stages of oncology biological product development (i.e., the first-in-human clinical trial) to compress the traditional three phases of trials into one continuous trial called an expansion cohort trial. Information to support the design of individual expansion cohorts are included in IND applications and assessed by FDA. Expansion cohort trials can potentially bring efficiency to biological product development and reduce developmental costs and time.

In some cases, the FDA may require, or companies may voluntarily pursue, additional clinical trials after a product is approved to gain more information about the product. These post-approval clinical trials, sometimes referred to as Phase 4 clinical trials, may also be made a condition to approval of the BLA. Failure to exhibit due diligence regarding conducting required Phase 4 clinical trials could result in withdrawal of approval for products.

Concurrent with clinical trials, companies usually complete additional animal studies and also must develop additional information about the chemistry and physical characteristics of the biological product as well as finalize a process for manufacturing the product in commercial quantities in accordance with cGMP requirements. To help reduce the risk of the introduction of adventitious agents with use of biological products, the PHSA, emphasizes the importance of manufacturing control for products whose attributes cannot be precisely defined. The manufacturing process must be capable of consistently producing quality batches of the product candidate and, among other things, the sponsor must develop methods for testing the identity, strength, quality, potency and purity of the final biological product. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the biological product candidate does not undergo unacceptable deterioration over its shelf life.

During all phases of clinical development, regulatory agencies require extensive monitoring and auditing of all clinical activities, clinical data, and clinical trial investigators. Annual progress reports detailing the results of the clinical trials must be submitted to the FDA. Written IND safety reports must be promptly submitted to the FDA and the investigators for serious and unexpected adverse events, any findings from other studies, tests in laboratory animals or in vitro testing that suggest a significant risk for human subjects, or any clinically important increase in the rate of a serious suspected adverse reaction over that listed in the protocol or investigator brochure. The sponsor must submit an IND safety report within 15 calendar days after the sponsor determines that the information qualifies for reporting. The sponsor also must notify the FDA of any unexpected fatal or life-threatening suspected adverse reaction within seven calendar days after the sponsor's initial receipt of the information.

The decision to suspend or terminate development of a product candidate may be made by either a health authority body, such as the FDA, by an IRB, or by a company for various reasons and during any phase of clinical trials. The FDA may order the temporary or permanent discontinuation of a clinical trial at any time or impose other sanctions if it believes that the clinical trial either is not being conducted in accordance with FDA requirements or presents an unacceptable risk to the clinical trial patients. In some cases, clinical trials are overseen by a data safety monitoring board, which is an independent group of qualified experts organized by the trial sponsor to evaluate at designated points in time whether or not a trial may move forward and/or should be modified. These decisions are based on unblinded access to data from the ongoing trial and generally involve determinations regarding the benefit-risk ratio for study patients and the scientific integrity and validity of the clinical trial.

In addition, there are requirements for the registration of certain clinical trials of product candidates on public registries, such as www.clinicaltrials.gov, and the submission of certain information pertaining to these trials, including clinical trial results, after trial completion.

Assuming successful completion of all required testing in accordance with all applicable regulatory requirements, a sponsor submits extensive information about the product candidate to the FDA in the form of a BLA to request marketing approval for the product candidate in specified indications.

Biologics License Applications

In order to obtain approval to market a biologic in the U.S., a BLA must be submitted to the FDA that provides data establishing the safety and effectiveness of the product candidate for the proposed indication. The BLA includes all relevant data available from pertinent preclinical studies and clinical trials, including negative or ambiguous results as well as positive findings, together with detailed information relating to the product's chemistry, manufacturing, controls and proposed labeling, among other things. Data can come from company-sponsored clinical trials intended to test the safety and effectiveness of a product candidate, or from a number of alternative sources, including studies initiated by investigators. To support marketing approval, the data submitted must be sufficient in quality and quantity to establish the safety and effectiveness of the product candidate to the satisfaction of the FDA.

Under the Prescription Drug User Fee Act ("PDUFA"), as amended, the fees payable to the FDA for reviewing an original BLA, as well as annual program fees for approved products, can be substantial, subject to certain limited deferrals, waivers and reductions that may be available. The FDA has 60 days from receipt of a BLA to determine whether the application will be accepted for filing based on the agency's threshold determination that it is sufficiently complete to permit substantive review. The FDA may refuse to accept for filing any BLA that it deems incomplete or not properly reviewable at the time of submission, in which case the BLA will have to be updated and resubmitted. The FDA's PDUFA review goal (which is not a legal requirement) is to review 90% of priority BLA applications within six months of filing and 90% of standard applications within 10 months of filing, but the FDA can and frequently does extend this review timeline to consider certain later-submitted information or information intended to clarify or supplement information provided in the initial submission. The FDA may not complete its review or approve a BLA within these established goal review times. The FDA reviews the BLA to determine, among other things, whether the proposed product is safe, pure, and potent for its intended use, and whether the product is being manufactured in compliance with cGMP to ensure its continued safety, purity and potency. The FDA may also refer applications for novel product candidates which present difficult questions of safety or efficacy to an advisory committee, typically a panel that includes clinicians and other experts, for review, evaluation and a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions.

Before approving a BLA, the FDA will inspect the facilities at which the product is manufactured or the facilities that are significantly involved in the product development and distribution process and will not approve the product candidate unless cGMP compliance is satisfactory and the manufacturing processes and facilities are adequate to assure consistent production of the product within required specifications. Additionally, before approving a BLA, the FDA will typically inspect one or more clinical sites to assure compliance with GCP requirements.

Under the Pediatric Research Equity Act, certain BLAs must include an assessment, generally based on clinical trial data, of the safety and effectiveness of the biological product in relevant pediatric populations. The FDA may waive or defer the requirement for a pediatric assessment, either at a company's request or by its own initiative, including waivers for certain products not likely to be used in a substantial number of pediatric patients. Unless otherwise required by regulation, products with orphan drug designation are exempt from these requirements for orphan-designated indications with no formal waiver process required.

After the FDA evaluates the BLA and the manufacturing facilities, the FDA may issue either an approval letter or a complete response letter. A complete response letter generally outlines the deficiencies in the submission and may require substantial additional testing or information in order for the FDA to reconsider the application. If and when those deficiencies have been addressed to the FDA's satisfaction in a resubmission of the BLA, the FDA may issue an approval letter. The FDA's PDUFA review goal is to review such resubmissions within two or six months of receipt, depending on the type of information included. Notwithstanding the submission of any requested additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval and deny approval of a resubmitted BLA. FDA approval of any application may include many delays or never be granted. An approval letter authorizes commercial marketing of the product candidate with specific prescribing information for specific indications. As a condition of BLA approval, the FDA may require a risk evaluation and mitigation strategy ("REMS") to help ensure that the benefits of the product outweigh the potential risks. REMS can include Medication Guides, communication plans for healthcare professionals, and also may include elements to assure safe use ("ETASU"). ETASU can include, but are not limited to, special training or certification for prescribing or dispensing, dispensing only under certain circumstances, special monitoring, and the use of patient registries. The requirement for a REMS can materially affect the potential market and profitability of the biologic. Moreover, product approval may require substantial post-approval testing and surveillance to monitor the biologic's safety, purity, or potency, which can be costly.

Changes to some of the conditions established in an approved application, including changes in indications, labeling, or manufacturing processes or facilities, require submission and FDA approval of a new BLA or a supplemental BLA before the change can be implemented. A supplemental BLA for a new indication typically requires clinical data similar to that in the original application, and the FDA generally uses the same procedures and actions in reviewing a supplemental BLA as it does in reviewing a new BLA.

Product approvals may be withdrawn if compliance with regulatory standards is not maintained or if safety or manufacturing problems occur following initial marketing. For example, quality control and manufacturing procedures must conform, on an ongoing basis, to cGMP requirements, and the FDA periodically inspects manufacturing facilities to assess compliance with cGMP. Accordingly, manufacturers must continue to spend time, money and effort to maintain cGMP compliance. In addition, new or modified government requirements, including from new legislation, may be established that could delay or prevent regulatory approval of our product candidates under development or affect our ability to maintain product approvals we have obtained.

Regulation of Companion Diagnostics.

For drugs and therapeutic biologics where the use of a specific diagnostic test is essential for the safe and effective use of the therapeutic product, such as when the use of a product is limited to a specific patient subpopulation that can be identified by using the test, regulatory authorities may require, as a condition of approval, that a relevant "companion diagnostic" test also be approved or cleared for the appropriate indication. This general policy approach may be inapplicable in cases where the drug or therapeutic biologic is intended to treat a serious or life-threatening condition for which no satisfactory alternative treatment exists and the benefits from the use of a product with an unapproved companion diagnostic device are so pronounced as to outweigh the risks from the lack of an approved companion diagnostic. Companion diagnostics are generally regulated as medical devices by regulatory authorities and relevant statutes and regulations govern, among other things, medical device design and development, preclinical and clinical testing, premarket regulatory review, manufacturing, labeling, storage, advertising and promotion, sales and distribution, export and import, and post-market surveillance.

Orphan Drug Designation

The FDA may grant orphan drug designation to biologics intended to treat a rare disease or condition that affects fewer than 200,000 individuals in the U.S. or a disease or condition that affects 200,000 or more individuals in the U.S. but there is no reasonable expectation that the cost of developing and making the biologic would be recovered from sales in the U.S. Orphan drug designation must be requested before submitting a BLA. After the FDA grants orphan drug designation, the identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA. Orphan drug designation does not convey any advantage in or shorten the duration of the regulatory review and approval process.

In the U.S., orphan drug designation entitles a party to financial incentives, such as opportunities for grant funding towards clinical trial costs, tax credits for certain research and user fee waivers under certain circumstances. In addition, if a company receives the first FDA approval of a drug or biologic for the indication for which it has orphan drug designation, the product is entitled to seven years of orphan exclusivity, which means the FDA may not approve any other application for the "same" drug or biologic for the same indication for a period of seven years, except in limited circumstances, such as a showing of clinical superiority over the product with orphan exclusivity. The FDA can revoke a product's orphan drug exclusivity under certain circumstances, including when the product sponsor is unable to assure the availability of sufficient quantities of the product to meet patient needs. Orphan drug exclusivity does not prevent the FDA from approving a different drug or biologic for the same disease or condition, or the same drug or biologic for a different disease or condition.

In the EEA, the criteria for designating an "orphan medicinal product" are similar in principle to those in the U.S. Under Article 3 of Regulation (EC) 141/2000, a medicinal product may be designated as an orphan medicinal product if it meets the following criteria: (a) it is intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating conditions; (b) either such condition that affects no more than five in 10,000 people in the E.U.; or without the benefits derived from orphan status, it must be unlikely that the marketing of the medicine would generate sufficient return in the E.U. to justify the investment needed for its development; and (c) there exists no satisfactory method of diagnosis, prevention or treatment of the condition concerned, or, if such a method exists, the medicinal product would be of significant benefit to those affected by the condition. The application for orphan designation must be submitted to the EMA and approved by the European Commission before an application is made for marketing authorization for the product. Once designated, orphan medicinal product designation also entitles a party to financial incentives such as reduction of fees or fee waivers. Moreover, ten years of market exclusivity is granted, if the product continues to be designated as an orphan medicinal product upon grant of the marketing authorization. During this ten-year period, with a limited number of exceptions, neither the competent authorities of the E.U. Member States, the EMA, or the European Commission are permitted to accept applications or grant marketing authorization for other similar medicinal products with the same therapeutic indication. A "similar medicinal product" is defined as a medicinal product containing a similar active substance or substances as contained in an authorized orphan medicinal product, and which is intended for the same therapeutic indication. However, marketing authorization may be granted to a similar medicinal product with the same orphan indication during the ten-year period with the consent of the marketing authorization holder for the original orphan medicinal product or if the manufacturer of the original orphan medicinal product is unable to supply sufficient quantities. Marketing authorization may also be granted to a similar medicinal product with the same orphan indication if this latter product is demonstrated to be safer, more effective or otherwise clinically superior to the original orphan medicinal product. This period of market exclusivity may be reduced to six years if, at the end of the fifth year, it is established that the orphan designation criteria are no longer met, including where it can be demonstrated on the basis of available evidence that the product is sufficiently profitable not to justify maintenance of market exclusivity.

Expedited Programs in the United States and Other Jurisdictions

In the U.S., the FDA has various programs, including fast track designation, breakthrough therapy designation, accelerated approval and priority review, that are intended to expedite or simplify the process for the development and FDA review of drugs and biologics that are intended for the treatment of serious or life-threatening diseases or conditions. A product may be granted fast track designation if it is intended for the treatment of a serious or life-threatening condition and demonstrates the potential to address unmet medical needs for such condition. Fast track designation applies to the combination of the product and the specific indication for which it is being studied. The sponsor of a new drug or biologic may request the FDA to designate the drug or biologic as a fast-track product at any time during the clinical development of the product. With fast-track designation, the sponsor may be eligible for more frequent opportunities to obtain the FDA's feedback. Another benefit of fast-track designation, for example, is that the FDA may consider for review sections of the marketing application on a rolling basis before the complete application is submitted if certain conditions are satisfied, including an agreement with the FDA on the proposed schedule for submission of portions of the application and the payment of applicable user fees before the FDA may initiate a review. Even if a product candidate receives fast track designation, the designation can be rescinded and provides no assurance that a product will be reviewed or approved more expeditiously than would otherwise have been the case, or that the product will be approved at all.

Under the FDA's breakthrough therapy program, a sponsor may seek FDA designation of its product candidate as a breakthrough therapy if the product candidate is intended, alone or in combination with one or more other drugs or biologics, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that it may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. Breakthrough therapy designation comes with all of the benefits of fast-track designation. The FDA may take other actions appropriate to expedite the development and review of the product candidate, including holding meetings with the sponsor and providing timely advice to, and interactive communication with, the sponsor regarding the development program. Even if one or more of our product candidates receives breakthrough therapy designation, the designation can be rescinded and provides no assurance that a product will be reviewed or approved more expeditiously than would otherwise have been the case, or that the product will be approved at all.

A product candidate may be eligible for accelerated approval. Drug or biological products studied for their safety and effectiveness in treating serious or life-threatening illnesses and that provide meaningful therapeutic benefit over existing treatments may receive accelerated approval, which means that they may be approved on the basis of adequate and well-controlled clinical trials establishing that the product has an effect on a surrogate endpoint that is reasonably likely to predict a clinical benefit, or on the basis of an effect on an intermediate clinical endpoint other than survival or irreversible morbidity or mortality, that is reasonably likely to predict irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments. As a condition of approval, the FDA generally requires that a sponsor of a drug or biological product receiving accelerated approval perform adequate and well-controlled post-marketing clinical trials to verify the clinical benefit in relationship to the surrogate endpoint or ultimate outcome in relationship to the clinical benefit. In addition, the FDA currently requires as a condition for accelerated approval pre-approval of promotional materials, which could adversely impact the timing of the commercial launch of the product. The FDA may withdraw approval of a drug or indication approved under accelerated approval if, for example, the confirmatory trial fails to verify the predicted clinical benefit of the product.

The FDA may grant priority review designation to a product candidate, which sets the user fee target date for FDA action on the application at six months from FDA filing. Priority review may be granted where a product is intended to treat a serious or life-threatening disease or condition and, if approved, has the potential to provide a safe and effective therapy where no satisfactory alternative therapy exists or a significant improvement in safety or efficacy compared to available therapy. If criteria are not met for priority review, the standard FDA review period is ten months from FDA filing. Priority review designation does not change the scientific/medical standard for approval or the quality of evidence necessary to support approval.

Under the 21st Century Cures Act, a drug is eligible for regenerative medicine advanced therapy ("RMAT") designation if (i) the drug is a regenerative medicine therapy, which is defined by FDA to include cell therapy, therapeutic tissue engineering product, human cell and tissue product, any combination product using such therapies or products, and certain human gene therapies and xenogeneic cell products, except for human cells, tissues, and cellular and tissue-based products that are regulated solely under Section 361 of the Public Health Service Act and part 1271 of Title 21, Code of Federal Regulations; (ii) the drug is intended to treat, modify, reverse, or cure a serious or life-threatening disease or condition; and (iii) preliminary clinical evidence indicates that the drug has the potential to address unmet medical needs for such disease or condition. An RMAT designation include all the benefits of the fast track and breakthrough therapy designation programs, including early interactions with FDA, and the potential to support accelerated approval and address post-approval requirements. An RMAT designation request should be submitted with the IND or after and, ideally, no later than the end-of-phase 2 meeting. Even if a product candidate receives RMAT designation, the designation can be rescinded and provides no assurance that a product will be reviewed or approved more expeditiously than would otherwise have been the case, or that the product will be approved at all.

Under the centralized procedure in the EEA, the maximum timeframe for the evaluation of a marketing authorization application is 210 days (excluding "clock stops," when additional written or oral information is to be provided by the applicant in response to questions asked by the CHMP). Clock stops may extend the timeframe of evaluation of a marketing authorization application considerably beyond 210 days.

Accelerated evaluation might be granted by CHMP in exceptional cases, when a medicinal product is expected to be of a major public health interest, which should be justified and assessed on a case-by-case basis. In this circumstance, EMA ensures that the opinion of CHMP is given within 150 days (excluding clock stops).

Expanded Access to an Investigational Drug for Treatment Use

Expanded access, also called "compassionate use," is the use of investigational new drug products outside of clinical trials to treat patients with serious or immediately life-threatening diseases or conditions when there are no comparable or satisfactory alternative treatment options. The FDA regulations allow access to investigational drugs under an IND by the sponsor or the treating physician for treatment purposes on a case -by-case basis for individual patients, intermediate-size patient populations, and larger populations for use of the drug under a treatment protocol or Treatment IND Application.

The suitability of treating a patient or a group of patients under expanded access is determined by the following: if patient(s) have a serious or immediately life-threatening disease or condition, there is no comparable or satisfactory alternative therapy to diagnose, monitor, or treat the disease or condition, the potential patient benefit justifies the potential risks of the treatment and the potential risks are not unreasonable in the context or condition to be treated, and the expanded use of the investigational drug for the requested treatment will not interfere with the initiation, conduct or completion of clinical investigations that could support marketing approval of the product candidate or otherwise compromise the potential development of the product candidate.

Sponsors of one or more investigational drugs for the treatment of a serious disease(s) or condition(s) make publicly available their policies for evaluating and responding to requests for expanded access for individual patients. This provision requires drug companies to make publicly available their policies for expanded access for individual patient access to products intended for serious diseases. Sponsors are required to make such policies publicly available upon the earlier of initiation of a Phase 2 or Phase 3 study or 15 days after the drug receives breakthrough therapy, fast track, or regenerative medicine advanced therapy designation. Additionally, in 2018 the Right to Try Act, was signed into law. The law, among other things, provides a federal framework for certain patients to access certain investigational new drug products that have completed a Phase 1 clinical trial and that are undergoing investigation for FDA approval. Under certain circumstances, eligible patients can seek treatment without enrolling in clinical trials and without obtaining FDA permission under the FDA expanded access program. There is no obligation for a drug manufacturer to make its drug products available to eligible patients as a result of the Right to Try Act.

U.S. market exclusivity

A biological product can obtain pediatric market exclusivity in the U.S. Pediatric exclusivity, if granted, adds six months to existing exclusivity periods, including some regulatory exclusivity periods tied to patent terms. This six-month exclusivity, which runs from the end of other exclusivity protection or patent term, may be granted based on the voluntary completion of a pediatric study in accordance with an FDA-issued "Written Request" for such a study.

The Biologics Price Competition and Innovation Act of 2009 ("BPCIA"), created an abbreviated approval pathway for biological products shown to be biosimilar to, or interchangeable with, an FDA-licensed reference biological product. This amendment to the PHSA attempts to minimize duplicative testing. Biosimilarity, which requires that there be no clinically meaningful differences between the biological product and the reference product in terms of safety, purity, and potency, can be shown through analytical studies, animal studies, and a clinical trial or trials. Interchangeability requires that a product is biosimilar to the reference product and the product must demonstrate that it can be expected to produce the same clinical results as the reference product and, for products administered multiple times, the biologic and the reference biologic may be switched after one has been previously administered without increasing safety risks or risks of diminished efficacy relative to exclusive use of the reference biologic. However, complexities associated with the larger, and often more complex, structure of biological products, as well as the process by which such products are manufactured, pose significant hurdles to implementation that are still being worked out by the FDA.

FDA will not accept an application for a biosimilar or interchangeable product based on the reference biological product until four years after the date of first licensure of the reference product, and FDA will not approve an application for a biosimilar or interchangeable product based on the reference biological product until 12 years after the date of first licensure of the reference product. "First licensure" typically means the initial date the particular product at issue was licensed in the U.S. Date of first licensure does not include the date of licensure of (and a new period of exclusivity is not available for) a biological product if the licensure is for a supplement for the biological product or for a subsequent application by the same sponsor or manufacturer of the biological product (or licensor, predecessor in interest, or other related entity) for a change (not including a modification to the structure of the biological product) that results in a new indication, route of administration, dosing schedule, dosage form, delivery system, delivery device or strength, or for a modification to the structure of the biological product that does not result in a change in safety, purity, or potency. The BPCIA is complex and continues to be interpreted and implemented by the FDA. In addition, government proposals have sought to reduce the 12-year reference product exclusivity period. Other aspects of the BPCIA, some of which may impact the BPCIA exclusivity provisions, have also been the subject of recent litigation. As a result, the ultimate implementation and impact of the BPCIA is subject to significant uncertainty.

Post-approval requirements

Rigorous and extensive FDA regulation of biological products continues after approval, particularly with respect to cGMP requirements, as well as requirements relating to record keeping, reporting of adverse experiences, periodic reporting, product sampling and distribution, and advertising and promotion of the product. Manufacturers of products are required to comply with applicable requirements in the cGMP regulations, including quality control and quality assurance and maintenance of records and documentation. Other post-approval requirements applicable to biological products, include reporting of cGMP deviations that may affect the identity, potency, purity and overall safety of a distributed product, record keeping requirements, reporting of adverse effects, reporting updated safety and efficacy information, and complying with electronic record and signature requirements. After a BLA is approved, the product also may be subject to official lot release. As part of the manufacturing process, the manufacturer is required to perform certain tests on each lot of the product before it is released for distribution. If the product is subject to official release by the FDA, the manufacturer submits samples of each lot of product to the FDA together with a release protocol showing a summary of the history of manufacture of the lot and the results of all of the manufacturer's tests performed on the lot. The FDA also may perform certain confirmatory tests on lots of some products before releasing the lots for distribution by the manufacturer. In addition, the FDA conducts laboratory research related to the regulatory standards on the safety, purity, potency, and effectiveness of biological products.

As a condition of BLA approval, the FDA may require post-marketing testing, including Phase 4 clinical trials, and surveillance to further assess and monitor the product's safety and effectiveness after commercialization. Regulatory approval of oncology products often requires that patients in clinical trials be followed for long periods to determine the overall survival benefit of the product. In addition, as a holder of an approved BLA, a company would be required to report adverse reactions and production problems to the FDA, to provide updated safety and efficacy information, and to comply with requirements concerning advertising and promotional labeling for any of its products.

Manufacturers must comply with the FDA's advertising and promotion requirements, such as those related to direct-to-consumer advertising, the prohibition on promoting products for uses or in patient populations that are not described in the product's approved labeling (known as "off-label use"), industry-sponsored scientific and educational activities, and promotional activities involving the internet. Discovery of previously unknown problems with a product or failure to comply with applicable regulatory requirements after approval may result in serious and extensive restrictions on a product or the manufacturer or holder of an approved BLA, as well as lead to potential market disruptions. These restrictions may include suspension of product manufacturing until the FDA is assured that quality standards can be met, continuing oversight of manufacturing by the FDA under a "consent decree," which frequently includes the imposition of costs and continuing inspections over a period of many years, as well as possible withdrawal of the product from the market. Other potential consequences include interruption of production, issuance of warning letters or other enforcement letters, refusal to approve pending BLAs or supplements to approved BLAs, product seizure or detention, product recalls, fines, and injunctions or imposition of civil and/or criminal penalties.

In addition, changes to the manufacturing process are strictly regulated, and, depending on the significance of the change, may require prior FDA approval before being implemented. FDA regulations also require investigation, correction, and reporting of any deviations from cGMP and impose reporting and documentation requirements upon a company and any third-party manufacturers that a company may decide to use. Accordingly, manufacturers must continue to expend time, money and effort in the area of production and quality control to maintain compliance with cGMP and other aspects of regulatory compliance.

Biological product manufacturers and other entities involved in the manufacture and distribution of approved biological products are required to register their establishments with the FDA and certain state agencies and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with cGMP and other laws. Accordingly, manufacturers must continue to expend time, money, and effort in the area of production and quality control to maintain cGMP compliance.

Newly discovered or developed safety or effectiveness data may require changes to a product's approved labeling, including the addition of new warnings and contraindications, and also may require the implementation of other risk management measures, such as additional post-market clinical trials to assess new safety risks or distribution-related or other restrictions under a REMS. In addition, changes to the manufacturing process or facility generally require prior FDA approval before being implemented and other types of changes to the approved product, such as adding new indications and additional labeling claims, are also subject to further FDA review and approval.

Patent Term Restoration and Extension

Depending upon the timing, duration and specifics of the FDA approval of our product candidates, some of our U.S. patents may be eligible for limited patent term extension. The provisions of the Drug Price Competition and Patent Term Restoration Act, informally known as the Hatch-Waxman Act, permit a patent restoration term of up to five years as compensation for patent term lost during product development and the FDA regulatory review process. However, patent term restoration cannot extend the remaining term of a patent beyond a total of 14 years from the product's approval date. The patent term restoration period is generally one-half the time between the effective date of an IND and the submission date of a BLA plus the time between the submission date of a BLA and the approval of that application. Only one patent applicable to an approved product is eligible for the extension and the application for the extension must be submitted prior to the expiration of the patent. The U.S. Patent and Trademark Office, in consultation with the FDA, reviews and approves the application for any patent term extension or restoration. In the future, we may apply for restoration of patent term for one of our currently owned or licensed patents to add patent life beyond its current expiration date, depending on the expected length of the clinical trials and other factors involved in the filing of the relevant BLA.

Many other countries also provide for patent term extensions or similar extensions of patent protection for biologic products. For example, in Japan, it may be possible to extend the patent term for up to five years and in Europe, it may be possible to obtain a supplementary patent certificate that would effectively extend patent protection for up to five years.

Health Care Laws and Regulations

Health care providers and third-party payors play a primary role in the recommendation and prescription of drug products that are granted marketing approval. Arrangements with providers, consultants, third-party payors and customers are subject to broadly applicable fraud and abuse, anti-kickback, false claims laws, patient privacy laws and regulations and other health care laws and regulations that may constrain business and/or financial arrangements. Restrictions under applicable federal and state health care laws and regulations include the following:

- the federal Anti-Kickback Statute, which prohibits, among other things, persons and entities from knowingly and willfully soliciting, offering, paying, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made, in whole or in part, under a federal health care program such as Medicare and Medicaid;

- the federal civil and criminal false claims laws, including the civil False Claims Act, and civil monetary penalties laws, which prohibit individuals or entities from, among other things, knowingly presenting, or causing to be presented, directly or indirectly, to the federal government, claims for payment that are false, fictitious or fraudulent or knowingly making, using or causing to made or used a false record or statement to avoid, decrease or conceal an obligation to pay money to the federal government;

- the federal Health Insurance Portability and Accountability Act of 1996 ("HIPAA"), which created additional federal criminal laws that prohibit, among other things, knowingly and willfully executing, or attempting to execute, a scheme to defraud any health care benefit program or making false statements relating to health care matters;

- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, and their respective implementing regulations, including the Final Omnibus Rule published in January 2013, which impose obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information;

- the federal false statements statute, which prohibits knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement in connection with the delivery of or payment for health care benefits, items or services;

- the FCPA which prohibits companies and their intermediaries from making, or offering or promising to make improper payments to non-U.S. officials for the purpose of obtaining or retaining business or otherwise seeking favorable treatment;

- the federal transparency requirements known as the federal Physician Payments Sunshine Act, under the PPACA, which requires certain manufacturers of drugs, devices, biologics and medical supplies to report annually to the Centers for Medicare & Medicaid Services within the U.S. Department of Health and Human Services, information related to payments and other transfers of value made by that entity to physicians and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members; and

- analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws, which may apply to health care items or services that are reimbursed by non-government third-party payors, including private insurers.

Further, some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government in addition to requiring manufacturers to report information related to payments to physicians and other health care providers or marketing expenditures. Additionally, some state and local laws require the registration of pharmaceutical sales representatives in the jurisdiction. State and foreign laws also govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

Pharmaceutical Insurance Coverage and Health Care Reform

In the U.S. and markets in other countries, patients who are prescribed treatments for their conditions and providers performing the prescribed services generally rely on third-party payors to reimburse all or part of the associated health care costs. Significant uncertainty exists as to the coverage and reimbursement status of drug products approved by the FDA and other government authorities. Thus, even if a product candidate is approved, sales of such product will depend, in part, on the extent to which third-party payors, including government health programs in the U.S. such as Medicare and Medicaid, commercial health insurers and managed care organizations, provide coverage and establish adequate reimbursement levels for, the product. The process for determining whether a payor will provide coverage for a drug product may be separate from the process for setting the price or reimbursement rate that the payor will pay for the drug product once coverage is approved. Third-party payors are increasingly challenging the prices charged, examining the medical necessity and reviewing the cost-effectiveness of medical products and services and imposing controls to manage costs. Third-party payors may limit coverage to specific products on an approved list, also known as a formulary, which might not include all of the approved products for a particular indication.

In order to secure coverage and reimbursement for any product candidate that might be approved for sale, a company may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of the product, in addition to the costs required to obtain FDA or other comparable marketing approvals. Nonetheless, product candidates may not be considered medically necessary or cost effective. A decision by a third-party payor not to cover a product candidate could reduce physician utilization once the product candidate is approved. Additionally, a payor's decision to provide coverage for a drug product does not imply that an adequate reimbursement rate will be approved. Further, one payor's determination to provide coverage for a product does not assure that other payors will also provide coverage and reimbursement for the product, and the level of coverage and reimbursement can differ significantly from payor to payor.

The containment of health care costs also has become a priority of federal, state and foreign governments and the prices of products have been a focus in this effort. Governments have shown significant interest in implementing cost-containment programs, including price controls, restrictions on reimbursement and requirements for substitution of generic drug products. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit a company's revenue generated from the sale of any approved drug products. Coverage policies and third-party reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more drug products for which a company or its collaborators receive marketing approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

There have been a number of federal and state proposals during the last few years regarding the pricing of pharmaceutical and biopharmaceutical products, limiting coverage and reimbursement for drugs and biologics and other medical products, government control and other changes to the health care system in the U.S.

In March 2010, the U.S. Congress enacted the PPACA, which, among other things, included changes to the coverage and payment for drug products under government health care programs. The PPACA effected the following changes of importance to our potential product candidates:

- established an annual, nondeductible fee on any entity that manufactures or imports specified branded prescription drugs and biologic agents, apportioned among these entities according to their market share in certain government healthcare programs;
- expanded eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to certain individuals with income at or below 133% of the federal poverty level, thereby potentially increasing a manufacturer's Medicaid rebate liability;
- expanded manufacturers' rebate liability under the Medicaid Drug Rebate Program by increasing the minimum rebate for both branded and generic drugs and revising the definition of "average manufacturer price" for calculating and reporting Medicaid drug rebates on outpatient prescription drug prices;
- addressed a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected;
- expanded the types of entities eligible for the 340B drug discount program;
- established the Medicare Part D coverage gap discount program by requiring manufacturers to provide a 70% point-of-sale discount off of the negotiated price of applicable brand drugs to eligible beneficiaries during their coverage gap period as a condition for the manufacturers' outpatient drugs to be covered under Medicare Part D; and
- established a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research.

Other legislative changes have been proposed and adopted in the U.S. since the PPACA was enacted. In August 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. This included aggregate reductions of Medicare payments to providers up to 2% per fiscal year, which went into effect in April 2013 and, due to subsequent legislative amendments, will remain in effect through 2027 unless additional congressional action is taken. In January 2013, President Obama signed into law the American Taxpayer Relief Act of 2012, which, among other things, further reduced Medicare payments to several providers, including hospitals, imaging centers and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

Since enactment of the PPACA, there have been numerous legal challenges and congressional actions to repeal and replace provisions of the law. For example, with enactment of the TCJA, which was signed by the President on December 22, 2017, Congress repealed the "individual mandate." The repeal of this provision, which requires most Americans to carry a minimal level of health insurance, will become effective in 2019. According to the Congressional Budget Office, the repeal of the individual mandate will cause 13 million fewer Americans to be insured in 2027 and premiums in insurance markets may rise. Additionally, on January 22, 2018, the President signed a continuing resolution on appropriations for fiscal year 2018 that delayed the implementation of certain PPACA-mandated fees, including the so-called "Cadillac" tax on certain high cost employer-sponsored insurance plans, the annual fee imposed on certain health insurance providers based on market share, and the medical device excise tax on non-exempt medical devices. Further, the Bipartisan Budget Act of 2018, among other things, amended the PPACA, effective January 1, 2019, to increase from 50% to 70% the point-of-sale discount that is owed by pharmaceutical manufacturers who participate in Medicare Part D and to close the coverage gap in most Medicare drug plans, commonly referred to as the "donut hole". Congress will likely consider other legislation to replace elements of the PPACA during the next congressional session.

The presidential administration has also taken executive actions to undermine or delay implementation of the PPACA. In January 2017, the President signed an Executive Order directing federal agencies with authorities and responsibilities under the PPACA to waive, defer, grant exemptions from, or delay the implementation of any provision of the PPACA that would impose a fiscal or regulatory burden on states, individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. In October 2017, the President signed a second Executive Order allowing for the use of association health plans and short-term health insurance, which may provide fewer health benefits than the plans sold through the PPACA exchanges. At the same time, the presidential administration announced that it will discontinue the payment of cost-sharing reduction ("CSR") payments to insurance companies until Congress approves the appropriation of funds for such CSR payments. The loss of CSR payments is expected to increase premiums on certain policies issued by qualified health plans under the PPACA. A bipartisan bill to appropriate funds for CSR payments was introduced in the Senate, but the future of that bill is uncertain. In addition, the Centers for Medicare & Medicaid Services has recently proposed regulations that would give states greater flexibility in setting benchmarks for insurers in the individual and small group marketplaces, which may have the effect of relaxing the essential health benefits required under the PPACA for plans sold through such marketplaces.

Further, there have been several recent U.S. congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the costs of drugs under Medicare and reform government program reimbursement methodologies for drug products. At the federal level, the presidential administration's budget proposal for fiscal year 2019 contained further drug price control measures that could be enacted during the 2019 budget process or in other future legislation, including, for example, measures to permit Medicare Part D plans to negotiate the price of certain drugs under Medicare Part B, to allow some states to negotiate drug prices under Medicaid, and to eliminate cost sharing for generic drugs for low-income patients. While any proposed measures will require authorization through additional legislation to become effective, Congress and the presidential administration have each indicated that it will continue to seek new legislative and/or administrative measures to control drug costs.

At the state level, individual states are increasingly aggressive in passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. In addition, regional health care authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products, and which suppliers will be included in their prescription drug and other health care programs.

Review and Approval of Medicinal Products in Europe

In order to market any medicinal product outside of the U.S., a company must also comply with numerous and varying regulatory requirements of other countries and jurisdictions regarding quality, safety and efficacy and governing, among other things, clinical trials, marketing authorization, commercial sales and distribution of medicinal products. Whether or not it obtains FDA approval for a product candidate, an applicant will need to obtain the necessary approvals by the comparable non-U.S. regulatory authorities before it can commence clinical trials or marketing of the product in those countries or jurisdictions. Some countries outside of the U.S. have a similar process that requires the submission of a CTA much like the IND prior to the commencement of human clinical trials. In the E.U., for example, a CTA must be submitted to the national competent authorities of the E.U. Member States where the clinical trial is conducted and to an independent ethics committee, much like the FDA and IRB, respectively. Once the CTA is approved in accordance with a country's requirements, clinical trial development may proceed.

In April 2014, the E.U. adopted a new Clinical Trials Regulation (E.U.) No 536/2014, which is set to replace the current Clinical Trials Directive 2001/20/EC. It will overhaul the current system of approvals for clinical trials in the E.U. Specifically, the new regulation, which will be directly applicable in all Member States (meaning that no national implementing legislation in each E.U.. Member State is required), aims at simplifying and streamlining the approval of clinical trials in the E.U.. For instance, the new Clinical Trials Regulation provides for a streamlined application procedure via a single-entry point and strictly defined deadlines for the assessment of clinical trial applications. It is expected that the new Clinical Trials Regulation will come into effect following confirmation of full functionality of the Clinical Trials Information System, the centralized E.U. portal and database for clinical trials foreseen by the new Clinical Trials regulation, through an independent audit. In January 2022, the Clinical Trials Regulation entered into application harmonizing the submission, assessment and supervision processes for clinical trials in the E.U.

Clinical Trial Regulations in Italy

Under the E.U. and E.U.-member country legislation, any application for marketing authorization must be accompanied by the results of clinical trials conducted in accordance with applicable regulations. A unified regulation on clinical trial procedures has been approved (E.U. Reg. 536/2014), but is not yet effective. The currently applicable rule is E.U. Directive 2001/20, as implemented in the various E.U. member countries from time to time through national laws and regulations.

We are currently conducting or planning Phase 1/2a clinical trials on Temferon in Italy, in accordance with the specific regulations applicable to such early-phase trials. As discussed elsewhere in this report, we are currently conducting our TEM-GBM 001 study on UMGMT-GBM patients .

The applicable Italian regulation is the Decree of April 27, 2015 of the Ministry of Health, providing a precise sequence of approvals for the start of Phase I studies and subsequent amendments to the related protocols. According to such Decree, an initial request must be submitted to AIFA seeking a technical-scientific opinion of Istituto Superiore di Sanità (ISS), acting on behalf of AIFA, on the admissibility of the request. Upon the favorable opinion of ISS, Italian Regulatory Authority ("AIFA") issues an authorization to proceed with the planned study, and the rules generally governing the conduct of clinical trials (Legislative Decree 211 of June 24, 2003, implementing in Italy E.U. Directive 2001/20, Decree of December 17, 2004 of the Ministry of Health for non-profit studies, plus procedural rules such as the Decree of December 21, 2007, so called "CTA decree", for the prescribed formats), are of application.

Based on the AIFA approval, the Independent Ethics Committees ("IECs") of the research centers participating in the trial issue their opinions on the conduct of the study, having evaluated the study protocol and all other relevant documentation such as the informed consent form ("ICF"), the insurance policy underwritten by the sponsor, the information and consent form for data protection purposes. The IEC of the Coordinating Center issues first its opinion – the so-called *Parere Unico*, lit. "sole opinion" ("PU") - and then the IECs of the other participating centers accept or refuse the PU in its entirety (they may seek amendment to the ICF on the basis of local operating circumstances).

All documents pertaining to each specific step of the procedure, in the right sequence, must be loaded on the online database of AIFA ("Osservatorio sulle Sperimentazioni Cliniche", or "OsSC"); the OsSC system provides certain controls to make sure that e.g. no IEC opinion can be loaded before the pertinent AIFA approval, or that the opinions of the participating sites cannot be loaded before the PU is loaded. It may occur however that, due to calendar mismatches in the calendars of IEC meeting (usually held on a monthly basis), an approval may precede by a few days a "prior" one (typically, the PU or the AIFA approval): in such cases the IEC approval is issued under reservation ("*con riserva*") and can be loaded in advance accordingly, under the assumption that the documents subjected to evaluation - protocol (updated) version, ICF and the rest – coincide exactly.

Marketing Authorization Application for Biologic Medicinal Products

To obtain regulatory approval to commercialize a new drug in the EEA (comprising the E.U. Member States plus Iceland, Liechtenstein and Norway, we must submit a marketing authorization application.

In the E.U., a marketing authorization for a medicinal product can be obtained through a centralized, mutual recognition, decentralized procedure, or national procedure (single country). The centralized procedure is mandatory for certain medicinal products, including orphan medicinal products, those produced by biotechnology, advanced therapy medicinal products (gene therapy, somatic cell therapy and tissue-engineered products) and those with a new active substance indicated for the treatment of HIV, AIDS, cancer, neurodegenerative disorders, autoimmune and other immune dysfunctions, viral diseases or diabetes, and is optional for certain other products, including medicinal products with a new active substance for other indications, and products that are a significant therapeutic, scientific or technical innovation, or whose authorization would be in the interest of public health.

Under the centralized procedure, the applicant can submit a single application for marketing authorization to the EMA which will provide a positive opinion regarding the application if it meets certain quality, safety, and efficacy requirements. Based on the opinion of the EMA, the European Commission takes a final decision to grant a centralized marketing authorization which permits the marketing of a product throughout the EEA. Under the centralized procedure, the maximum timeframe for the evaluation of a marketing authorization application is 210 days (excluding clock stops, when additional written or oral information is to be provided by the applicant in response to questions asked by the EMA Committee for Medicinal Products for Human Use ("CHMP")). Clock stops may extend the timeframe of evaluation of a marketing authorization application considerably beyond 210 days. Where the CHMP gives a positive opinion, it provides the opinion together with supporting documentation to the European Commission, who make the final decision to grant a marketing authorization, which is issued within 67 days of receipt of the EMA's recommendation. Accelerated assessment might be granted by the CHMP in exceptional cases, when a medicinal product is expected to be of major public health interest, particularly from the point of view of therapeutic innovation. The timeframe for the evaluation of a marketing authorization application under the accelerated assessment procedure is 150 days, excluding clock stops, but it is possible that the CHMP may revert to the standard time limit for the centralized procedure if it determines that it is no longer appropriate to conduct an accelerated assessment.

Now that the United Kingdom (which comprises Great Britain and Northern Ireland) has left the E.U., Great Britain will no longer be covered by centralized marketing authorizations (under the Northern Irish Protocol, centralized marketing authorizations will continue to be recognized in Northern Ireland). All medicinal products with a current centralized marketing authorization were automatically converted to Great Britain marketing authorizations on January 1, 2021. For a period of two years from January 1, 2021, the Medicines and Healthcare products Regulatory Agency ("MHRA"), the United Kingdom medicines regulator, may rely on a decision taken by the European Commission on the approval of a new marketing authorization in the centralized procedure, in order to more quickly grant a new Great Britain marketing authorization. A separate application will, however, still be required.

For other countries outside of the E.U., such as the United Kingdom and countries in Eastern Europe, Latin America or Asia, the requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement vary from country to country. Internationally, clinical trials are generally required to be conducted in accordance with cGCPs, applicable regulatory requirements of each jurisdiction and the medical ethics principles that have their origin in the Declaration of Helsinki. If we fail to comply with applicable foreign regulatory requirements, we may be subject to, among other things, fines, suspension or withdrawal of regulatory approvals, product recalls, seizure of products, operating restrictions and criminal prosecution.

Advertising, Promotion and Compliance

In the E.U., the advertising and promotion of our products will also be subject to E.U. laws and E.U. Member States' national laws governing promotion of medicinal products, interactions with physicians, misleading and comparative advertising and unfair commercial practices. These laws require that promotional materials and advertising in relation to medicinal products comply with the product's Summary of Product Characteristics ("SmPC"), as approved by the competent authorities. The SmPC is the document that provides information to physicians concerning the safe and effective use of the medicinal product. The SmPC forms an intrinsic and integral part of the marketing authorization granted for the medicinal product. Promotion of a medicinal product that does not comply with the SmPC is considered to constitute off -label promotion and is prohibited in the E.U. The applicable laws at the E.U. level and in the individual E.U. Member States also prohibit the direct-to-consumer advertising of prescription-only medicinal products. Violations of the rules governing the promotion of medicinal products in the E.U. could be penalized by administrative measures, fines and imprisonment. As the United Kingdom medicinal products legislation is still largely based on E.U. legislation, the promotion of prescription-only medicines to the public and promotion of medicinal products not in compliance with the SmPC are both also prohibited under United Kingdom law.

During all phases of development (pre- and post-marketing), failure to comply with applicable regulatory requirements may result in administrative or judicial sanctions. These penalties could include the imposition of a clinical hold on trials, refusal to approve pending applications, withdrawal of an approval, warning letters, product recalls, product seizures, total or partial suspension of production or distribution, product detention or refusal to permit the import or export of products, injunctions, fines, civil penalties, or criminal prosecution. Any agency or judicial enforcement action could have a material adverse effect on us.

Regulatory Data Protection in the EEA

In the EEA, innovative medicinal products approved on the basis of a complete independent data package qualify for eight years of data exclusivity upon marketing authorization and an additional two years of market exclusivity pursuant to Directive 2001/83/EC. Regulation (EC) No 726/2004 repeats this entitlement for medicinal products authorized in accordance the centralized authorization procedure. Data exclusivity prevents applicants for authorization of generics or biosimilars of these innovative products from referencing the innovator's data when applying for a generic or biosimilar marketing authorization for a period of eight years from the date on which the innovator's product was first authorized in the EEA. During an additional two-year period of market exclusivity, a generic or biosimilar marketing authorization can be submitted and authorized, and the innovator's data may be referenced, but no generic or biosimilar medicinal product can be placed on the E.U. market until the expiration of the market exclusivity. The overall 10-year period will be extended to a maximum of 11 years if, during the first eight years of those 10 years, the marketing authorization holder obtains an authorization for one or more new therapeutic indications which, during the scientific evaluation prior to their authorization, are held to bring a significant clinical benefit in comparison with existing therapies. Even if an innovative medicinal product gains the prescribed period of data exclusivity, another company may market another version of the product if such company obtained a marketing authorization based on a marketing authorization application with a complete independent data package of pharmaceutical tests, preclinical tests and clinical trials.

Periods of Authorization and Renewals

A marketing authorization has an initial validity for five years in principle. The marketing authorization may be renewed after five years on the basis of a re-evaluation of the risk-benefit balance by the EMA or by the competent authority of the relevant Member State. To this end, the marketing authorization holder must provide the EMA or the competent authority with a consolidated version of the file in respect of quality, safety, and efficacy, including all variations introduced since the marketing authorization was granted, at least six months before the marketing authorization ceases to be valid. The European Commission or the competent authorities of the EEA Member States may decide on justified grounds relating to pharmacovigilance, to proceed with one further five-year period of marketing authorization. Once subsequently definitively renewed, the marketing authorization shall be valid for an unlimited period. Any authorization which is not followed by the actual placing of the medicinal product on the EEA market (in case of centralized procedure) or on the market of the authorizing EEA Member State within three years after authorization ceases to be valid (the so-called sunset clause).

Pediatric Studies and Exclusivity

Prior to obtaining a marketing authorization in the EEA, applicants must demonstrate compliance with all measures included in an EMA-approved PIP covering all subsets of the pediatric population, unless the EMA has granted a product-specific waiver, a class waiver, or a deferral for one or more of the measures included in the PIP. The respective requirements for all marketing authorization procedures are laid down in Regulation (EC) No 1901/2006, commonly referred to as the Pediatric Regulation. This requirement also applies when a company wants to add a new indication, pharmaceutical form or route of administration for a medicine that is already authorized. The Pediatric Committee of the EMA ("PDCO") may grant deferrals for some medicines, allowing a company to delay development of the medicine for children until there is enough information to demonstrate its effectiveness and safety in adults. The PDCO may also grant waivers when development of a medicine for children is not needed or is not appropriate, such as for diseases that only affect an adult population. Before a marketing authorization application can be filed, or an existing marketing authorization can be amended, the EMA must determine that a company actually complied with the agreed studies and measures listed in each relevant PIP, unless the EMA has granted: (i) a product-specific waiver, (ii) a class waiver or (iii) a deferral for one or more of the measures included in the PIP. If an applicant obtains a marketing authorization in all EEA Member States, or a marketing authorization granted in the centralized procedure by the European Commission, and the study results of the pediatric clinical trials conducted in accordance with the PIP are included in the drug product information, even when negative, the medicine is then eligible for an additional six-month period of qualifying patent protection through extension of the term of the Supplementary Protection Certificate. In the case of orphan medicinal products, a two-year extension of the orphan market exclusivity may be available. This pediatric reward is subject to specific conditions and is not automatically available when data in compliance with the PIP are developed and submitted.

Regulatory Requirements after a Marketing Authorization has been Obtained

In case an authorization for a medicinal product in the EEA is obtained, the holder of the marketing authorization is required to comply with a range of requirements applicable to the manufacturing, marketing, promotion and sale of medicinal products. These include:

- Compliance with the E.U.'s stringent pharmacovigilance or safety reporting rules must be ensured. These rules can impose post-authorization studies and additional monitoring obligations.

- The manufacturing of authorized medicinal products, for which a separate manufacturer's license is mandatory, must also be conducted in strict compliance with the applicable E.U. laws, regulations and guidance, including Directive 2001/83/EC, Directive 2003/94/EC, Regulation (EC) No 726/2004 and the European Commission Guidelines for Good Manufacturing Practice ("E.U. cGMP"). These requirements include compliance with E.U. cGMP standards when manufacturing medicinal products and APIs, including the manufacture of API outside of the E.U. with the intention to import the API into the E.U..

- The marketing and promotion of authorized drugs, including industry-sponsored continuing medical education and advertising directed toward the prescribers of drugs and/or the general public, are strictly regulated in the E.U. notably under Directive 2001/83EC, as amended, and E. Member State laws. Direct-to-consumer advertising of prescription medicines is prohibited across the E.U..

General Data Protection Regulation

The collection, use, disclosure, transfer or other processing of personal data of individuals (natural persons) in the E.U., including personal health data, is governed by the GDPR, which became effective and applicable on May 25, 2018. Since the application of the GDPR, the European data protection law background has been constantly implemented through the activity of the European Data Protection Board (EDPB) and the respective, national Supervisory Authorities, concerning the correct interpretation and application of the GDPR, as well as through the ruling of the Court of Justice of the E.U. (CJEU). The GDPR and E.U. Member States national data protection legislation, including Italy, are wide-ranging in scope and impose numerous requirements on companies that process personal data, including requirements relating to the processing of health and other sensitive data. For example, it is essential to obtain consent of the individuals to whom the personal data relates, providing notice to individuals regarding data processing activities, implementing suitable safeguards to protect the security and confidentiality of personal data, providing notification of data breaches, and taking certain measures when engaging third party processors. The GDPR also imposes strict rules on the transfer of personal data to countries outside the E.U., including the U.S. and the United Kingdom, and allows data protection authorities to impose large penalties for violations of the GDPR, including potential fines of up to € 20 million or 4% of annual global revenues, whichever is greater. As regards the transfer of (pseudonymized) personal data to the U.S., the CJEU case C-3111/18, also known as Schrems II, invalidated the European Commission's adequacy decision for the E.U.-U.S. Privacy Shield Framework, which the majority of U.S. companies relied on to conduct trans-Atlantic trade in compliance with E.U. data protection rules. The decision reinforced the importance of data protection to global commerce and imposed E.U. companies trading with U.S. companies or organizations to rely the transfer of personal data on other legal basis or appropriate safeguards provided for in the GDPR, such as Standard Contractual Clauses (SCC), Binding Corporate Rules (BCR) or derogations for specific situations. The Privacy Shield Framework has now been replaced by the so-called "Data Privacy Framework E.U.-U.S. (DPF)", an agreement that entered into force after the adoption of the EU Commission's adequacy decision of 10 July 2023. US companies that adhere to the DPF are considered compliant with the GDPR requirements and data transfer from the E.U. to the U.S. within this framework is thus considered compliant. In June 2021, the E.U. Commission adopted decisions on the United Kingdom's adequacy under the E.U.'s GDPR and Law Enforcement Directive (LED). In both cases, the European Commission found the United Kingdom to be adequate. This means that most data can continue to flow from the E.U. and the EEA without the need for additional safeguards. The GDPR also confers a private right of action on data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies and obtain compensation for damages. Compliance with the GDPR and all relevant E.U. data protection rules will be a rigorous and time-intensive process that may increase our cost of doing business.

The GDPR also confers a private right of action on data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies and obtain compensation for damages.

Compliance with the GDPR and all relevant E.U. data protection rules will be a rigorous and time-intensive process that may increase our cost of doing business.

Pricing Decisions for Approved Drug Products

In the E.U., pricing and reimbursement schemes vary widely from country to country. Some countries provide that drug products may be marketed only after a reimbursement price has been agreed. Some countries may require the completion of additional studies that compare the cost-effectiveness of a particular product candidate to currently available therapies or so-called health technology assessments, in order to obtain reimbursement or pricing approval. For example, the E.U. provides options for the E.U. Member States to restrict the range of drug products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. E.U. Member States may approve a specific price for a product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the product on the market. Other E.U. Member States allow companies to fix their own prices for drug products, but monitor and control prescription volumes and issue guidance to physicians to limit prescriptions. Recently, many countries in the E.U. have increased the amount of discounts required on pharmaceuticals and these efforts could continue as countries attempt to manage health care expenditures, especially in light of the severe fiscal and debt crises experienced by many countries in the E.U. The downward pressure on health care costs in general, particularly with respect to prescription products, has become intense. As a result, increasingly high barriers are being erected to the entry of new drug products. Political, economic and regulatory developments may further complicate pricing negotiations, and pricing negotiations may continue after reimbursement has been obtained. Reference pricing used by various E.U. Member States, and parallel trade, i.e., arbitrage between low-priced and high-priced E.U. Member States, can further reduce prices. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any drug products, if approved in those countries.

Intellectual Property Rights

Our goal is to obtain, maintain and enforce patent protection for our product candidates, formulations, processes, methods and any other proprietary technologies, preserve our trade secrets, and operate without infringing on the proprietary rights of other parties, both in the U.S. and in other countries. Our policy is to actively seek to obtain, where appropriate, the broadest intellectual property protection possible for our current product candidates and any future product candidates, proprietary information and proprietary technology through a combination of contractual arrangements and patents, both in the U.S. and abroad. However, patent protection may not afford us with complete protection against competitors who seek to circumvent our patents.

We also depend upon the skills, knowledge, experience and know-how of our management and research and development personnel, as well as that of our advisors, consultants and other contractors. To help protect our proprietary know-how, which is not patentable, and for inventions for which patents may be difficult to enforce, we currently rely and will in the future rely on trade secret protection and confidentiality agreements to protect our interests. To this end, we require all of our employees, consultants, advisors and other contractors to enter into confidentiality agreements that prohibit the disclosure of confidential information and, where applicable, require disclosure and assignment to us of the ideas, developments, discoveries and inventions important to our business.

Temferon

Temferon is protected by the following patents families that contain both issued and/or pending patent applications.

In April 2024, we filed a patent application relating to methods of treating solid cancers with Temferon in combination with a checkpoint inhibitor and, in September 2024, we filed a patent application relating to methods of treating renal cell carcinoma with Temferon in combination with a checkpoint inhibitor. These provisional patents are wholly owned by us.

In addition, while the following patent families are jointly owned by OSR and Fondazione Telethon (Telethon), as set forth in our December 15, 2014 license agreement with OSR (described below), Telethon granted OSR a worldwide exclusive license, with the right to sublicense, its rights in the patent families pursuant to a separate cooperation agreement between OSR and Telethon. As described below, we have a worldwide exclusive license, from OSR, to the following patent families (including the U.S. and European family members indicated) in the fields of: GBM, solid liver cancer (LC) and any lympho-hematopoietic indication:

Focus / Family	U.S.	E.U.	Expiration
Gene Vector comprising mi-RNA (composition and method of treatment claims) PCT/IB2006/002266 (WO 2007/000668).	USP 10,000,757* USP 9,556,438 USP 11,753,643 USSN 18/191,611 (pending)	EP 2002003 B1	5/26/2026*
Gene Vector comprising mi-RNA (composition and method of treatment claims) PCT/IB2010/001166 (WO / 2010/125471)	USP 10,287,579 USP 9,951,328 USP 11,407,996 USSN 17/855,135 (pending)	EP 2424571 B1 EP 20167404.1 (pending)	4/30/2030
Type 1 Interferon Gene Therapy (method of treatment claims) PCT/EP2018/060238 (WO 2018/193119)	USSN 16/604,484 (pending)	EP 3612624 B1 EP 24202037.8 (pending)	4/20/2038**
Type 1 Interferon Gene Therapy (composition and method of treatment claims) PCT/EP2024/057093 (WO2024194223)	WO2024194223 (pending)	WO2024194223 (pending)	3/15/2044

* Later expiration for certain U.S. patents pursuant to patent term adjustment (35 U.S.C. §154(b)).

** Application pending, anticipated expiration based on 20-year patent term.

Our technology incorporates the use of a lentiviral vector (“LVV”) that combines a therapeutic transgene sequence, or payload, with our proprietary platform. Our proprietary platform consists of (i) the Tie-2 promoter, that drives transgene sequence transcription specifically in TEMs, and (ii) miRNA-126 target sequences to downregulate transgene expression post-transcription in those cells where the Tie-2 promoter is active and the miRNA-126 is present. Intellectual property protection for our proprietary platform includes an exclusive license to all issued patents and pending applications (if any) in the PCT/IB2006/002266 (WO 2007/000668) and PCT/IB2010/001166 (WO / 2010/125471) families, as well as trade secrets. [We retain the option to exclusively license the PCT/EP2018/060238 and PCT/EP2024/057093 patent families (which we have not yet exercised), along with any improvements, for additional indications (fields of use) and other product candidates.]

In addition to patents and patent applications that we own or have been granted licenses to, we may also rely on unpatented trade secrets, know-how, and continuing technological innovation to develop and maintain our competitive position. We seek to protect know-how and trade secrets through an active program of legal mechanism including invention assignments, confidentiality agreements, material transfer agreements, research collaborations and licenses to protect our product candidates. These agreements may be breached, and we may not have adequate remedies for any breach. In addition, trade secrets may otherwise become known or be independently discovered by competitors. To the extent that our employees, consultants, scientific advisors or other contractors use intellectual property owned by others in their work for us, disputes may arise as to the rights in related or resulting know-how and inventions. For a more comprehensive discussion of the risks related to our intellectual property, please see “Risk Factors — Risks Related to Our Intellectual Property.”

Collaboration / Licensing

Amended and Restated License Agreement with Ospedale San Raffaele

We entered into an amended and restated license agreement (the "ARLA") with OSR in March 2023. The ARLA replaced the Company's original license agreement originally entered into with OSR on December 15, 2014, as subsequently amended on March 16, 2017, February 1, 2019, December 23, 2020, September 28, 2021, January 22, 2022, September 29, 2022 and December 22, 2022 (the "Original OSR License Agreement").

The effectiveness of the ARLA was subject to Italy's Law Decree No. 21 of March 15, 2012 (i.e., the Italian *Golden Power* regulations), as subsequently amended and supplemented, and would not become effective until the applicable Italian governmental authority consented to the ARLA. On April 20, 2023, such consent was received and the ARLA became effective.

Pursuant to the terms of the ARLA, OSR has granted us an exclusive, royalty-bearing, non-transferrable (except with the prior written consent of OSR), sublicensable, worldwide license, subject to certain retained rights, to: (1) certain patents, patent applications and existing know-how for the use in the field(s) of Interferon ("IFN") gene therapy by lentiviral based- HSPC gene transfer with respect to (a) any solid cancer indication (including glioblastoma and solid liver cancer) and/or (b) any lympho-hematopoietic indication for which we exercise an option (described below); and (2) certain gene therapy products (subject to certain specified exceptions related to replication competent viruses) developed during the license term for use in the aforementioned field(s) consisting of any lentivirals or other viral vectors regulated by miR126 and/or miR130 and/or other miRs with the same expression pattern as miR126 and miR130 in hematopoietic cells for the expression of IFN under the control of a Tie2 promoter. Lympho-hematopoietic indication means any indication related to lympho-hematopoietic malignancies and solid cancer indication means any solid cancer indication (e.g., without limitation, breast, pancreas, colon cancer), with each affected human organ counting as a specific solid cancer indication.

The rights retained by OSR, and extending to its affiliates, include the right to use the licensed technology for internal research within the field(s) of use, the right to use the licensed technology within the field(s) of use other than in relation to the licensed products, and the right to use the licensed technology for any use outside the field(s) of use, but subject to the options described below. In addition, we granted OSR a perpetual, worldwide, royalty-free, non-exclusive license to any improvement generated by us with respect to the licensed technology, to conduct internal research within the field(s) of use directly, or in or with the collaboration third parties; and for any use outside the field(s) of use, in which case the license is sublicensable by OSR. Finally, the world-wide rights for the field(s) of use granted to us regarding the Lentigen know-how are non-exclusive and cannot be sublicensed due to a pre-existing nonexclusive sublicense to these rights between OSR and GlaxoSmithKline Intellectual Property Development Limited.

Pursuant to the ARLA, we have an exclusive option exercisable until April 20, 2026 to any OSR product improvements at no additional cost, which could be useful for the development and/or commercialization of licensed products in the field of use. We also have an exclusive option exercisable until April 20, 2026 (the "LHI Option Period") to any lympho-hematopoietic indication(s) to be included as part of the field of use, on an indication-by-indication basis, subject to the payment of specified option fees and milestone payments:

- €1.0 million for the first lympho-hematopoietic indication;
- €0.5 million for the second lympho-hematopoietic indication; and
- €0.3 million for the third lympho-hematopoietic indication.

No option fee is due for the fourth lympho-hematopoietic indication and any subsequent lympho-hematopoietic indications.

We have the right to extend the LHI Option Period twice for additional 12-month periods, subject to the payment of specified extension fees.

Prior to the effective date of the ARLA, we paid OSR an upfront fee in amount equal to €250,000 pursuant to the Original OSR License Agreement.

Pursuant to the ARLA, as consideration, we agreed to pay OSR additional license fees equal to up to €875,000 in total, which were paid on April 20, 2023 for €225,000, on December 31, 2023 for €150,000, and the remaining portion of €500,000 are to be paid upon our entering into a sublicense agreement with a third party sublicensee (pursuant to which we are entitled to receive an upfront payment in an amount exceeding a specified threshold from such sublicensee) during the period between September 30, 2022 and April 20, 2028 (with most of these additional license fees being triggered upon our entering into such a sublicense agreement). In addition, we have agreed to pay OSR royalties on a single digit percentage of the net sales of each licensed product. The royalty may be reduced upon the introduction of generic competition or patent stacking, but in no event would the royalty be less than half of what it would have otherwise been, but for the generic competition or patent stacking. We also agreed to pay OSR a royalty of our net sublicensing income for each licensed product and to pay OSR certain milestone payments upon the achievement of certain milestone events, such as the initiation of different phases of clinical trials of a licensed product, MAA approval by a major market country, MAA approval in the U.S., the first commercial sale of a licensed product in the U.S. and certain E.U. countries, and achievement of certain net sales levels.

As part of the ARLA, we have agreed to use reasonable efforts to involve OSR in Phase I clinical trials for licensed products in the field of use, subject to OSR maintaining any required quality standards and providing its services on customary and reasonable terms and consistent with then-applicable market standards. We are also obligated to carry out our development activities using qualified and experienced professionals and sufficient level of resources. In particular, consistent with the terms of the Original OSR License Agreement, the ARLA continues to require us to invest (a) at least €5,425,000 with respect to the development of the licensed products, and (b) at least €2,420,000 with respect to the manufacturing of such licensed products (subject to certain adjustments).

OSR maintains control of the preparation, prosecution and maintenance of the patents licensed. We are obligated to pay those costs unless additional licensees benefit from these rights, in which case the cost will be shared *pro rata*. OSR controls enforcement of the patents and know-how rights, at its own expense. In the event that OSR fails to file suit to enforce such rights after notice from us, we have the right to enforce the licensed technology within the field of use. Both we and OSR must consent to settlement of any such litigation, and all monies recovered will be shared, after reimbursement for costs, in relation to the damages suffered by each party, or failing a bona fide agreement between us and OSR, on a 50% - 50% basis.

The ARLA expires upon the expiry of the "Royalty Term" for all licensed products and all countries, unless terminated earlier. The Royalty Term begins on the first commercial sale of a licensed product in each country, on a country by country basis, and ends upon the later of the (a) expiration of the commercial exclusivity for such product in that country (wherein the commercial exclusivity refers to any remaining valid licensed patent claims covering such licensed product, any remaining regulatory exclusivity to market and sell such licensed product or any remaining regulatory data exclusivity for such licensed product), and (b) 10 years from the first commercial sale of such licensed product in such country.

The parties may terminate the agreement in the event the other party breaches its obligations therein, which termination shall become effective 60 business days following written notice thereof to the breaching party. The breaching party shall have the right to cure such breach or default during such 60 business days. OSR may terminate the agreement for failure to pay in the event that we fail to pay any of the upfront payment, additional license fees, sublicensing income or milestone payments within 30 days of due dates for each. In addition, OSR may terminate (with a 60-business-day prior written notice) our rights as to certain fields of use for our failure to achieve certain development milestones for specified licensed products within certain time periods, which may be subject to extension. In addition, OSR may terminate the agreement in the event that commercialization of a licensed product is not started within 24 months from the grant of both (i) the MAA approval and (ii) the pricing approval of such licensed product, provided that such termination will relate solely to such licensed product and to such country or region to which both such MAA approval and pricing approval were granted.

Amendment to Amended and Restated License Agreement with OSR

On September 28, 2023, we entered into an amendment to the ARLA, whereby we and OSR agreed that we had fulfilled the obligations as set forth in the ARLA specific to Candidate Products 1 pursuant to the CP1 SRA (as defined below). Furthermore, the amendment provides that we and OSR have no further obligations to negotiate and execute a sponsored research agreement for the performance of feasibility studies related to certain gene therapy products consisting of any lentiviral vectors regulated by miR126 and/or miR130 and/or other miRs with the same expression pattern as miR126 and miR130 in hematopoietic cells for the expression of cytokines and their variants (other than IFN or in addition to IFN) under the control of a Tie2 promoter, either alone or in combination with any immunotherapy ("Candidate Products 2"). Notwithstanding the removal of the obligation to enter into a sponsored research agreement with regards to Candidate Products 2, OSR granted us an exclusive option, to be exercised by sending written notice to OSR on or before September 30, 2025, to include certain intellectual property related to Candidate Products 2 and Candidate Products 2 as part of the licensed patents and licensed products under the ARLA. The option fee and our fee to extend the option period, if necessary, remain consistent with the prior fees to those costs reflected in the ARLA specific to Candidate Products 2. OSR will also have the right to prepare, file and prosecute patents and patent applications with respect to the results of Candidate Products 2. The amendment provides that the costs of the foregoing activities will be borne by us.

Sponsored Research Agreement

On August 1, 2023, we entered into a Sponsored Research Agreement ("CP1 SRA"), which was contemplated under the ARLA, pursuant to which we will fund feasibility studies for certain gene therapy products consisting of any lentiviral vectors regulated by miR126 and/or miR130 and/or other miRs with the same expression pattern as miR126 and miR130 in hematopoietic cells for the expression of IFN under the control of a Tie2 promoter, in combination with any immunotherapy ("Candidate Products 1"), along with three additional research projects, to be conducted at OSR. If OSR determines that additional funds are needed, OSR will inform us and provide an estimate for completing the research.

During the period from the date of execution from the CP1 SRA until six months from the last report delivered to us under the CP1 SRA (the "CP1 Option Period"), we have the exclusive option to include certain intellectual property related to Candidate Products 1 and Candidate Products 1 as part of the licensed patents and licensed products under the ARLA. To exercise this option, we must pay an option exercise fee. We also have the right to extend the CP1 Option Period twice for additional 24-month periods. The extension requires payment of an extension fee for each 24-month extension.

Know-How License Agreement with Fondazione Telethon

In February 2016, we entered into a Know-How License Agreement with Telethon (Telethon License Agreement). Telethon granted us a non-exclusive, perpetual, sublicensable (through multiple tiers), royalty-bearing, worldwide license to use its manufacturing know-how in the research and development, sale and export of any product, which is defined therein as any lentiviral vector regulated by miRNA 126 and/or miRNA 130 and/or other miRNAs with the same expression pattern as miRNA 126 and/or miRNA 130 in hematopoietic cells for the expression of any anticancer protein under the control of a Tie2 promoter or INF under the control of any promoter other than Tie2 for any cancer indication. As consideration for the license, we agreed to pay Telethon a royalty equal to a low single digit percentage of any actual payments (excluding taxes) to any CMO for the manufacturing of any product using the licensed know-how. The royalty payments must be made for eight (8) years from the effective date, or until February 2, 2024. At December 31, 2024, there were no royalties payments due. The parties may terminate the agreement in the event the other party breaches its obligations therein, which termination shall become effective sixty (60) business days following written notice thereof to the breaching party.

Legal Proceedings

From time to time, we may be involved in various claims and legal proceedings relating to claims arising out of our operations. We are not currently a party to any legal proceedings that, in the opinion of our management, are likely to have a material adverse effect on our business and have not been notified of any claims in respect thereof.

C. Organizational Structure

Genenta Science S.p.A. owns 100% of Genenta Science, Inc.

D. Plants, Property and Equipment

Our corporate headquarters is located in Milan, Via Olgettina 58 within OSR - San Raffaele Hospital, Italy, where we lease approximately 51 square meters of office space (three (3) offices). The lease commenced in January 2020 and has a six (6) year initial term. It will expire on December 1st, 2025, and may be renewed for an additional six (6) years. We also have an office in a co-working space located in Alexandria Center - LaunchLabs, 430 East 29th Street, New York, NY. We believe that our existing facilities are adequate for our near-term needs, and we believe that suitable additional or alternative office will be available as required in the future on commercially reasonable terms.

ITEM 4A. UNRESOLVED STAFF COMMENTS

None.

ITEM 5. OPERATING AND FINANCIAL REVIEW AND PROSPECTS

You should read the following discussion and analysis of our financial condition and results of operations in conjunction with our consolidated financial statements and related notes included in this Annual Report beginning on page F-1. The following discussion and analysis contain forward-looking statements that involve risks and uncertainties. Our actual results and the timing of selected events could differ materially from those anticipated in these forward-looking statements as a result of various factors, including those set forth under "Risk Factors" and elsewhere in this Annual Report.

A. Operating Results

Overview

We are a clinical-stage biotechnology company engaged in the development of hematopoietic stem cell gene therapies for the treatment of solid tumors. We have developed a novel biologic platform which involves the *ex-vivo* gene transfer of a therapeutic candidate into autologous hematopoietic stem/progenitor cells (HSPCs) to deliver immunomodulatory molecules directly to the tumor by infiltrating monocytes/macrophages (Tie2 Expressing Monocytes - TEMs). Our technology is designed to turn TEMs, which normally have an affinity for and travel to tumors, into a "Trojan Horse" to counteract cancer progression and prevent tumor relapse. Because our technology is not target dependent, we believe it can be used for treatment across a broad variety of cancers.

Since our inception in 2014, we have devoted substantially all our resources to organizing and staffing our company, business planning, raising capital, acquiring or discovering product candidates and securing related intellectual property rights, conducting discovery, research and development activities for our programs and planning for eventual commercialization. We do not have any products approved for sale and have not generated any revenue from product sales. To date, we have funded our operations with proceeds from the sales of equity securities and convertible debt securities, which through December 31, 2024, aggregated gross cash proceeds of approximately €68.5 million.

We do not have any products approved for sale, have not generated any revenue from commercial sales of our product candidates, and have incurred net losses each year since our inception. Our ability to generate product revenue sufficient to achieve profitability will depend heavily on the successful development and eventual commercialization of one or more of our current or future product candidates and programs. Our net losses for the years ended December 31, 2024, 2023 and 2022 were approximately €8.9 million, €11.6 million, and €8.5 million, respectively. At December 31, 2024, we had an accumulated deficit of approximately €56.0 million. Substantially all our operating losses resulted from costs incurred in connection with our research and development activities, including preclinical and clinical development of our gene therapy product candidates, namely our leading product candidate Temferon, and from general and administrative costs associated with our operations.

We expect to continue to incur significant expenses for at least the next several years as we advance our product candidates from discovery through preclinical development and clinical trials and seek regulatory approval of our product candidates. In addition, if we obtain marketing approval for any of our product candidates, we expect to incur significant commercialization expenses related to product manufacturing, marketing, sales, and distribution. We may also incur expenses in connection with the in-licensing or acquisition of additional product candidates. Furthermore, we expect to continue incurring additional costs associated with operating as a public company, including significant legal, accounting, investor relations, compliance, and other expenses.

As a result, for our long-term strategy, we will need substantial additional funding to support our continuing operations and pursue our growth strategy. Until such time as we can generate significant revenue from product sales, if ever, we expect to finance our operations with proceeds from outside sources, with most of such proceeds to be derived from sales of equity securities, including the net proceeds from our initial public offering ("IPO") in December 2021 and follow-on offerings, and proceeds from our mandatory convertible bond financing in March 2025. We also plan to pursue additional funding from outside sources, including but not limited to our entry into or expansion of new borrowing arrangements; research and development incentive payments, government grants, pharmaceutical companies, and other corporate sources; and our entry into potential future collaboration agreements with pharmaceutical companies or other third parties for one or more of our programs. We may be unable to raise additional funds or enter into such other agreements or arrangements when needed on favorable terms, or at all. If we fail to raise capital or enter into such agreements as, and when, needed, we may have to significantly delay, scale back or discontinue the development and eventual commercialization of one or more of our product candidates or delay our pursuit of potential in-licenses or acquisitions.

We are unable to predict the timing or amount of increased expenses or when or if we will be able to achieve or maintain profitability, mainly due to the numerous risks and uncertainties associated with product development and related regulatory filings, which we expect to make in multiple jurisdictions. When we are eventually able to generate product sales, those sales may not be sufficient to become profitable. If we fail to become profitable or are unable to sustain profitability on a continuing basis, we may be unable to continue our operations at planned levels and be forced to reduce or terminate our operations.

As of December 31, 2024, we had cash and cash equivalents of approximately €4.6 million and marketable securities of approximately €8.1 million. Our existing cash and cash equivalents as of December 31, 2024, plus €7.5 million in gross proceeds from our March 2025 mandatory convertible bond financing, will enable us to fund our operating expenses and capital expenditure requirements until approximately May 2026. We have based this estimate on assumptions that may prove to be wrong, and we could exhaust our available capital resources sooner than we expect. See "Liquidity and Capital Resources." To finance our continuing operations, we will need to raise additional capital, which cannot be assured.

Components of Operating Results

Revenue

We have not generated any revenue since inception and do not expect to generate any revenue from the sale of products in the near term until we obtain regulatory approval of, and commercialize, our product candidates.

Operating Expenses

Our current operating expenses consist of two components – research and development expenses, and general and administrative expenses.

Research and Development Expenses

We expense research and development costs as incurred. These expenses consist of costs incurred in connection with the development of our product candidates, including:

- license fees and milestone payments incurred in connection with our license agreements;
- expenses incurred under agreements with contract research organizations ("CROs"), contract manufacturing organizations ("CMOs"), as well as investigative sites and consultants that conduct or support our clinical trials, preclinical studies and other scientific development services;
- manufacturing scale-up expenses and the cost of acquiring and manufacturing preclinical and clinical trial materials and (in due course) commercial materials, including manufacturing validation batches;
- employee-related expenses, including salaries, social security charges, related benefits, severance indemnity in case of termination of employees' relationships, travel and share-based compensation expense for employees engaged in research and development functions and consulting fees;
- costs related to compliance with regulatory requirements; and
- facilities costs, depreciation, and other expenses, which include rent and utilities.

Our research and development expenses are tracked on a program-by-program basis for our product candidates and consist primarily of external costs, such as fees paid to outside consultants, CROs, CMOs, and central laboratories in connection with our preclinical development, process development, manufacturing, and clinical development activities. Our research and development expenses by program also include fees incurred under license agreements, as well as option agreements with respect to licensing rights. We do not allocate employee costs or facility expenses, including depreciation or other indirect costs, to specific programs because these costs are deployed across multiple programs and, as such, are not separately classified. We primarily use internal resources to oversee research and discovery activities as well as for managing our preclinical development, process development, manufacturing, and clinical development activities. These employees work across programs, and therefore, we do not track their costs by program. We elected to present the research and development expenditure net of research and development tax credit on the statements of operations and comprehensive loss. However, not all our research and development expenses are allocated by program:

	Year Ended December 31,		
	2024	2023	2022
		(in Euros)	
Direct research and development expenses by program:			
TEM-GBM Phase 1	€ 1,175,026	€ 1,331,166	984,458
TEM-GBM Phase 2	10,766	-	-
TEM-MM	-	-	1,331
TEM-LT	2,770	-	-
TEM-GU Phase 1	953,794	-	-
Unallocated costs:			
Personnel (including share-based compensation)	1,443,510	1,113,489	992,281
Consultants and other third parties	412,229	305,289	544634
Materials & supplies	783,880	3,639,920	2,790,982
Travel & entertainment	29,137	44,242	-
Other	1,742	40,335	25,276
Total research and development expenses	€ 4,812,854	€ 6,474,441	€ 5,338,962

Research and development activities are central to our business model. Product candidates in later stages of clinical development generally have higher development costs than those in earlier stages of clinical development, primarily due to the increased size and duration of later-stage clinical trials; however, manufacturing costs in earlier-stage clinical trials tend to be higher due to the high cost associated with scaling up the manufacturing process and the smaller number of patients over which to spread those costs.

Starting from 2023, we implemented a new management accounting system, enabling the division of expenses by project, allowing for a more precise allocation of direct costs, including manufacturing costs, to the respective projects. This process has consequently led to a reduction in the balance of manufacturing costs that are not specifically allocated to any project but are incurred for the general benefit of all ongoing research and development activities, as shown in the table above.

We had a decrease in research and development expenses in 2024, compared to 2023, that was due to several factors as explained in the section "—Results of Operations - *Comparison of Year Ended December 31, 2024 to Year Ended December 31, 2023*," but we expect that our research and development expenses, will increase substantially over the next several years, particularly as we increase the number of patients treated in our clinical trials, as well as due to increases in personnel costs, including share-based compensation, contractor costs and facilities costs, as we continue to advance the development of our product candidates. We also expect to incur additional expenses related to milestone and royalty payments payable to third parties with whom we have entered into license agreements to acquire the rights to our product candidates.

The successful development and commercialization of our product candidates is highly uncertain. At this time, we cannot reasonably estimate or know the nature, timing and costs of the efforts that will be necessary to complete the preclinical and clinical development of any of our product candidates or when, if ever, material net cash inflows may commence from any of our product candidates. This uncertainty is due to the numerous risks and uncertainties associated with product development and commercialization, including the uncertainty of:

- the scope, progress, outcome, and costs of our preclinical development activities, clinical trials and other research and development activities;
- establishing an appropriate safety profile with IND-enabling studies;
- successful patient enrollment in, and the design, initiation and completion of, clinical trials;
- the timing, receipt and terms of any marketing approvals from applicable regulatory authorities;
- establishing and maintaining clinical and commercial manufacturing capabilities or making arrangements with third party manufacturers;
- development and timely delivery of commercial-grade drug formulations that can be used in our clinical trials and for commercial launch;

- obtaining, maintaining, defending and enforcing patent claims and other intellectual property rights;
- significant and changing government regulations;
- qualifying for, and maintaining, adequate coverage and reimbursement by the government and other payors for any product candidate for which we obtain marketing approval;
- launching commercial sales of our product candidates, if and when approved, whether alone or in collaboration with others;
- addressing any competing technological and market developments; and
- maintaining a continued acceptable safety profile of the product candidates following approval.

We may never succeed in achieving regulatory approval for any of our product candidates. We may obtain unexpected results from our clinical trials. We may elect, or be forced by regulatory authorities, to discontinue, delay or modify clinical trials of some product candidates or focus on others. Any changes in the outcome of any of these variables with respect to the development of our product candidates in preclinical and clinical development could mean a significant change in the costs and timing associated with the development of these product candidates. For example, if AIFA, EMA, FDA, or another regulatory authority were to delay our planned start of clinical trials or require us to conduct clinical trials or other testing beyond those that we currently expect, or if we experience significant delays in enrollment in or treatment as part of any of our ongoing and planned clinical trials for any reason, we could be required to expend significant additional financial resources and time on the completion of clinical development of that product candidate. Identifying potential product candidates and conducting preclinical testing and clinical trials is a time-consuming, expensive, and uncertain process that takes years to complete, and we may never generate the necessary data or results required to obtain marketing approval and achieve product sales. In addition, our product candidates, if approved, may not achieve commercial success.

General and Administrative Expenses

General and administrative expenses consist primarily of salaries and consulting fees, related benefits, travel, and share-based compensation expense for personnel in executive, finance, and administrative functions. General and administrative expenses also include professional fees for legal, consulting, accounting, and audit services.

We anticipate that our general and administrative expenses will increase in the future as we increase our headcount to support our continued research activities and development of our product candidates. We also anticipate that we will continue to incur additional accounting, audit, legal, regulatory, compliance, director and officer insurance costs, as well as legal, investor and public relations expenses associated with being a public company. Additionally, if we believe a regulatory approval of a product candidate appears likely, we anticipate an increase in payroll and other expense in order to perpare for commercial operations, especially as it relates to the sales and marketing of our product candidate.

Other Income (Expense)

Other income (expense) consists primarily of interest income/(expense), foreign exchange income/(loss). For the year ended December 31, 2024, the net balance of other income/(expense) amounted to approximately €869,000 and mainly related to net financial interest income of approximately € 616,000, net unrealized foreign exchange gain of approximately € 260,000, and net realized foreign exchange loss of approximately €(7,000).

For the year ended December 31, 2023, the net balance of other income/(expense) amounted to approximately €87,000 and mainly related to net financial interest income of approximately € 304,000, net unrealized foreign exchange losses of approximately € (257,000), and net realized foreign exchange gain of approximately €40,000.

For the year ended December 31, 2022, other income (expense) consisted primarily of a tax benefit approved by the Italian Tax Agency of €180,000 related to the allowance for corporate equity (“ACE”), and financial fees reimbursement of approximately €28,000.

The differences between periods in the Other income (expense) category is due to the performance of our investment activities, which are influenced by the price trends of US Treasury Bills and Italian Government Bonds and interest rates, and to the macroeconomic situation that affects the purchasing power of currencies like US Dollar versus Euro.

Income taxes

We are subject to taxation in Italy and the U.S. Taxes are recorded on an accrual basis. These taxes therefore represent the allowances for taxes paid or to be paid for the year, calculated according to the current enacted rates and applicable laws. Due to the tax loss position reported, no income taxes were due for the years ended December 31, 2024, 2023, and 2022.

As of each reporting date, we consider existing evidence, both positive and negative, that could impact our view of the future realization of deferred tax assets. We believe that it is more likely than not that the benefit for deferred tax assets will not be realized. In recognition of this uncertainty, a full valuation allowance was applied to the deferred tax assets. Future realization depends on our future earnings, if any, the timing, and amount of which are uncertain as of December 31, 2024. In the future, should management conclude that it is more likely than not that the deferred tax assets are partially or fully realizable, the valuation allowance would be reduced to the extent of such expected realization and the amount would be recognized as a deferred income tax benefit in our Consolidated Statements of Operations and Comprehensive Loss.

There are open statutes of limitations for Italian tax authorities to audit our tax returns. There have been no material income tax-related interests or penalties assessed or recorded.

There is no liability related to uncertain tax positions reported in our consolidated financial statements.

In line with the legislation in force, as updated by the Italian Budget Law 2022, companies in Italy that invested in eligible research and development activities, regardless of the legal form and economic sector in which they operate, can benefit from a tax credit up to 10% of the increase of annual research and development expenses incurred, up to a maximum of €5.0 million, which can be used as compensation in order to reduce most taxes payable, including income tax or regional tax on productive activities, as well as of social security contributions.

The Italian Budget Law also established that the actual support of eligible expenses and its correspondence with the accounting documents must result from a specific certification issued by the person responsible for the legal audit and, in addition to the audit report, a technical report is also required. In addition, the tax credit due can only be used as compensation in three equal annual instalments. The measure is provided up to the tax period ending December 31, 2031; however, starting with the fiscal year 2023, and in respect subsequent fiscal periods, the tax credit rate was decreased from 20% to 10% of the eligible expenses, and the annual ceiling of the credit was increased from €4.0 million to €5.0 million.

For the years ended December 31, 2024, 2023 and 2022, we recorded research and development tax benefits of approximately €373,000, €428,000, and €890,000, respectively.

Results of Operations

Comparison of Year Ended December 31, 2024 to Year Ended December 31, 2023

The following table summarizes our results of operations for the years ended December 31, 2024, and 2023:

	Year Ended December 31,	
	2024	2023
	(in Euros)	
Operating expenses		
Research and development	€ 4,812,853	€ 6,474,441
General and administrative	4,951,456	5,258,501
Total operating expenses	9,764,31020	11,732,942
Loss from operations	(9,764,310)	(11,732,942)
Other income (expense)		
Others income (expense)	529,683	(4,875)
Finance income (expense)	81,140	309,253
Net exchange rate gain (loss)	240,992	(216,891)
Total other income (expense), net	851,815	87,487
Loss before income taxes	(8,912,495)	(11,645,455)
Income tax benefit (expense)	-	-
Net loss	€ (8,912,495)	€ (11,645,455)
Net loss per share - basic	€ (0.49)	€ (0.64)
Weighted average number of shares outstanding - basic and diluted	18,273,490	18,216,907
Other comprehensive income (loss)		
Total change of marketable debt securities	(118,750)	214,984
Change in foreign currency translation	(23,446)	(15,853)
Total other comprehensive income (loss)	(142,196)	199,131
Comprehensive loss	€ (9,054,691)	€ (11,446,324)

We have presented basic and diluted loss per share at December 31, 2024, which consists of our historical loss divided by the basic and diluted weighted average number of ordinary shares outstanding at December 31, 2024. There was no dilutive impact due to our net loss position.

Research and Development Expenses

Research and development expenses were approximately €4.8 million for the year ended December 31, 2024, as compared to approximately €6.5 million for the year ended December 31, 2023.

The decrease of €1.7 million was mainly due to:

(1) a decrease in manufacturing costs of approximately €0.4 million, as a net result of: i) a decrease in manufacturing activities and plasmid preparation of Lentiviral Vector ("LVV") of approximately €0.7 million; and ii) an increase in CRO fees due to the commencement in October 2024 of the TEM-GU clinical trial of approximately €0.3 million;
(2) a decrease in manufacturing costs of approximately €0.4 million related to the final phase of the scale-up manufacturing of LVV for gene therapy, mostly incurred in 2023;
(3) a decrease of approximately €0.3 million in the costs associated with the technology transfer from the AGC Biologics' Olgettina facility to its Bresso site for drug product manufacturing, mostly completed in 2023;
(4) a decrease in trial costs of approximately €0.1 million as a net result of: i) a decrease in trial costs related to the last cohort of our TEM-GBM Phase 1 dose-ranging study completed in May 2024, for approximately €0.2 million; and ii) an increase in trial costs related to TEM-GU clinical trial commenced in October 2024 of approximately €0.1 million; and
(5) a decrease in fees to OSR of approximately €0.5 million in line with the fee payment schedule provided by the ARLA and related Sponsored Research Agreement.

During the years ended December 31, 2024, and December 31, 2023, we utilized approximately €0.7 million per year of research and development tax credit to offset certain social contributions and taxes payable. The benefit recorded for the years ended December 31, 2024, and 2023, to offset research and development expenses was approximately €0.4 million per year.

General and Administrative Expenses

General and administrative expenses were approximately €5.0 million for the year ended December 31, 2024, as compared to approximately €5.3 million for the year ended December 31, 2023. The decrease of approximately €0.3 million was primarily due to a reduction in compensation expense, including stock option expenses of approximately €0.2 million as a result of two (2) employees who left the company in the second half of 2024, and a cumulative reduction of approximately €0.1 million in other general and administrative expenses mainly related to audit costs and insurance costs.

Other income (expense)

Other income (expense) was approximately €0.5 million at December 31, 2024, while other income (expense) was not material for the year ended December 31, 2023. The reason for this change was due to an increase in capital gain income from favorable performance of our financial investments.

Our net financial income was approximately €0.1 million for the year ended December 31, 2024, compared to a net financial income of approximately €0.3 million for the year ended December 31, 2023. The change was mainly related to financial interest income on financial investments made in 2024 and 2023 in U.S. Treasury bills and Italian government bonds.

Net exchange rate gain (loss)

The net exchange gain was approximately €0.3 million for the year ended December 31, 2024, compared to a net exchange loss of approximately €0.2 million for the year ended December 31, 2023. The change in respect of the preceding year was due to the fluctuation of the USD versus Euro exchange rate.

Net Loss

As a result of the foregoing, our net loss was approximately €8.9 million for the year ended December 31, 2024, as compared to approximately €11.6 million for the year ended December 31, 2023. The decrease in our net loss of approximately €2.7 million was primarily due to a decrease in research and development expenses of approximately €1.6 million, a decrease in general and administrative expenses of approximately €0.3 million, an increase in net financial income of approximately €0.3 million, and a positive exchange rate fluctuation effect of approximately €0.5 million compared to the previous year.

Comparison of Year Ended December 31, 2023 to Year Ended December 31, 2022

The following table summarizes our results of operations for the years ended December 31, 2023, and 2022:

	Year Ended December 31,	
	2023	2022
	(in Euros)	
Operating expenses		
Research and development	€ 6,474,441	€ 5,338,962
General and administrative	5,258,501	5,705,030
Total operating expenses	11,732,942	11,043,992
Loss from operations	(11,732,942)	(11,043,992)
Other income (expense)		
Others income (expense)	(4,875)	242,554
Finance income (expense)	309,253	36,985
Net exchange rate gain (loss)	(216,891)	2,286,690
Awards and subsidies	-	-
Total other income (expense), net	87,487	2,566,229
Loss before income taxes	(11,645,455)	(8,477,763)
Income tax benefit (expense)	-	-
Net loss	€ (11,645,455)	€ (8,477,763)
Net loss per share - basic and diluted	€ (0.64)	€ (0.47)
Weighted average number of shares outstanding - basic and diluted	18,216,907	18,216,858
Other comprehensive income/(loss)		
Change in fair value of marketable debt securities fair value measurement	214,984	-
Change in foreign currency translation	(15,853)	-
Total other comprehensive income	199,131	
Comprehensive loss	€ (11,446,324)	€ (8,477,763)

We have presented basic and diluted loss per share at December 31, 2023, which consists of our historical loss divided by the basic and diluted weighted average number of ordinary shares outstanding at December 31, 2023. There was no dilutive impact due to our net loss position.

Research and Development Expenses

Research and development expenses were approximately €6.5 million for the year ended December 31, 2023, as compared to approximately €5.3 million for the year ended December 31, 2022. The increase of approximately €1.2 million was mainly due to LVV (lentiviral vector for gene therapy) production activities. The increase in production activities related to the increase in the number of patients enrolled, the preparation of Phase II involving plasmid, cell banks production, and the cost of the manufacturing site transfer to a new location in Italy.

During the year ended December 31, 2023, we utilized approximately €0.7 million of research and development tax credit to offset certain social contributions and taxes payable, while we utilized approximately €0.6 million for such purpose during 2022. The benefit recorded for the years ended December 31, 2023 and 2022 to offset research and development expenses was approximately €0.4 million and €0.7 million, respectively. The decrease in the benefit recorded for the year ended December 31, 2023, compared to the year ended December 31, 2022, was primarily due to the R&D tax rate reduction from 20% to 10% of the eligible expenses, starting from January 2023, as provided by the 2022 Italian Budget Law.

General and Administrative Expenses

General and administrative expenses were approximately €5.3 million for the year ended December 31, 2023, as compared to approximately €5.7 million for the year ended December 31, 2022. The decrease was primarily due to a decrease in our insurance cost, as we were able to significantly reduce the cost of our directors and officers insurance without reducing coverage.

Other Income (Expense)

Other income (expense) was not material for the year ended December 31, 2023, as compared to approximately €243,000 for the year ended December 31, 2022, which was mainly due to a tax benefit to help our economic growth “ACE” (i.e., allowance for corporate equity) and a reimbursement for bank fees and commissions both accrued in 2022.

Our net financial income was approximately €309,000 for the year ended December 31, 2023, compared to a net financial loss of approximately €37,000 for the year ended December 31, 2022. The change was mainly related to financial interest income on financial investments made in 2023 in U.S. Treasury bills and Italian government bonds.

Net Exchange Rate Gain

The net exchange loss was approximately €(217,000) for the year ended December 31, 2023 compared to approximately €2.3 million for the year ended December 31, 2022. The change in respect of the preceding year was due to the fluctuation of the USD versus Euro exchange rate.

For the year ended December 31, 2023, the net exchange loss was due to a net unrealized foreign exchange loss of approximately €(257,000), and a net realized foreign exchange gain of approximately €40,000.

For the year ended December 31, 2022, the net exchange rate gain was mainly due to an approximately €1.6 million of net exchange rate gain realized on the conversion of $12.0 million of IPO proceeds collected in December 2021 to Euros, an approximately €0.4 million net exchange rate gain realized on USD trade payables and an approximately €0.3 million net exchange rate gain unrealized on USD bank deposits.

Net Loss

As a result of the foregoing, our net loss was approximately €11.6 million for the year ended December 31, 2023, as compared to approximately €8.5 million for the year ended December 31, 2022. The increase in our loss of approximately €3.2 million was primarily due to the net exchange rate loss compared to the net exchange rate gain in the prior year, the increase in our overall research and development spending, and the decrease in tax benefits recorded.

Critical Accounting Policies

Our consolidated financial statements are prepared in accordance with generally accepted accounting principles in the U.S. The preparation of our consolidated financial statements and related disclosures requires us to make estimates and judgments that affect the reported amounts of assets, liabilities, costs, and expenses, and the disclosure of contingent assets and liabilities in our consolidated financial statements. We base our estimates on historical experience, known trends, and events and various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. We evaluate our estimates and assumptions on an ongoing basis. Our actual results may differ from these estimates under different assumptions or conditions.

We believe that the accounting policies described below are critical to understand the judgements and estimates used in the consolidated financial statements and to fully understand and evaluate our financial condition and results of operations.

Accrued Research and Development Expenses

As part of the process of preparing our consolidated financial statements, we are required to estimate our accrued research and development expenses. This process involves reviewing open contracts and purchase orders, communicating with our personnel to identify services that have been performed on our behalf and estimating the level of service performed and the associated cost incurred for the service when we have not yet been invoiced or otherwise notified of actual costs. Many of our service providers invoice us in arrears for services performed, on a pre-determined schedule or when contractual milestones are met; however, some require advanced payments. We attempt to obtain estimates directly from vendors on work performed, if possible. If we are unable to obtain estimates from vendors, we estimate our accrued expenses as of each balance sheet date in the consolidated financial statements based on facts and circumstances known to us at that time. We periodically confirm the accuracy of these estimates with the service providers and make adjustments, if necessary. Examples of estimated accrued research and development expenses include fees paid to:

- vendors, including central laboratories, in connection with preclinical development activities, especially, OSR, a co-founding stockholder, significant related party vendor and a leading center for ex-vivo gene therapy for inherited diseases;
- CROs and investigative sites in connection with preclinical and clinical studies; and
- CMOs in connection with drug substance and drug product formulation of preclinical and clinical trial materials.

We base our expenses related to preclinical studies and clinical trials on our estimates of the services received and efforts expended pursuant to quotes and contracts with multiple research institutions and CROs that conduct and manage preclinical studies and clinical trials on our behalf. The financial terms of these agreements are subject to negotiation, vary from contract to contract and may result in uneven payment flows. There may be instances in which payments made to our vendors will exceed the level of services provided and result in a prepayment of the expense. Payments under some of these contracts depend on factors such as the successful enrollment of patients and the completion of clinical trial milestones. In accruing service fees, we estimate the time over which services will be performed and the level of effort to be expended in each period. If the actual timing of the performance of services or the level of effort varies from the estimate, we adjust the accrual or the amount of prepaid expenses accordingly. Although we do not expect our estimates to be materially different from amounts actually incurred, our understanding of the status and timing of services performed relative to the actual status and timing of services performed may vary and may result in reporting amounts that are too high or too low in any period. To date, there have not been any material adjustments to our prior estimates of accrued research and development expenses.

Share-based compensation

To reward the efforts of employees, officers, directors, and certain consultants, and to promote our growth and development, the Board may approve, upon occasion, various share-based awards. Our stock option plan (the "Equity Incentive Plan 2021–2025" or the "Plan"), pursuant to which stock options are granted, was originally approved on May 20, 2021.

In June 2023, our shareholders modified the 2021–2025 Equity Incentive Plan to extend the final deadline for the issuance of the ordinary shares until December 31, 2035, in order to allow that all stock options granted during the term of the Plan could provide for an exercise period of 10 years starting from the date of grant.

Currently, we have authorized options on 1,828,986 ordinary shares (i.e., 10% of the number of shares outstanding, which was 18,289,866 ordinary shares outstanding at December 31, 2024); however, as provided by the Plan, we may increase the authorized shares under the Plan up to a maximum of 2,700,000 ordinary shares without further shareholder approval. Therefore, as we raise additional capital, the Board has the authority to issue options on 1,828,986 to 2,700,000 ordinary shares, as the number of issued and outstanding ordinary shares grows, i.e., we do not have to obtain further authorization from shareholders to increase the number of ordinary shares available for equity grants until the outstanding ordinary shares exceed 27,000,000.

With the adoption of Accounting Standards Update ("ASU") No. 2018-07, Compensation—Stock Compensation (Topic 718): Improvements to Nonemployee Share-Based Payment Accounting on January 1, 2019, we measure our stock option awards granted to employees, officers, directors, and consultants based on their fair value on the date of the grant and recognize compensation expense for those awards over the requisite service period, which is normally the vesting period of the respective award. Forfeitures are accounted for as they occur. The measurement date for option awards is the date of the grant. We classify stock-based compensation expense in our Consolidated Statement of Operations and Comprehensive Loss in the same manner in which the award recipient's payroll costs are classified or in which the award recipient's service payments are classified.

We chose the Black-Scholes-Merton model because it is considered easier to apply and it is a defined equation and incorporates only one set of inputs. As a result, it is the model most commonly in use.

Research and Development Tax Credit Receivable

We account for our research and development tax credit receivable in accordance with IAS 20 *Accounting for Government Grants and Disclosure of Government Assistance*. The receivable is recognized when there is reasonable assurance that: (1) the recipient will comply with the relevant conditions and (2) the grant will be received. We elected to present the credit net of the related expenditure on the statements of operations and comprehensive loss. While these tax credits can be carried forward indefinitely, we recognized an amount which reflects management's best estimate of the amount that is reasonably assured to be realized or utilized in the foreseeable future based on historical benefits realized, adjusted for expected changes, as applicable.

Emerging Growth Company Status

We are an "emerging growth company." Under the Jumpstart Our Business Startups Act ("JOBS Act"), an emerging growth company can delay adopting new or revised accounting standards issued subsequent to the enactment of the JOBS Act until such time as those standards apply to private companies. We have irrevocably elected to avail ourselves of this exemption from new or revised accounting standards, and, therefore, will not be subject to the same new or revised accounting standards as public companies that are not emerging growth companies.

Off-Balance Sheet Arrangements

We have not engaged in any off-balance sheet arrangements, such as the use of unconsolidated subsidiaries, structured finance, special purpose entities, or variable interest entities.

We do not believe that any future off-balance sheet arrangements and commitments have or are reasonably likely to have a current or future effect on our financial condition, changes in financial condition, revenues or expenses, results of operations, liquidity, capital expenditures, or capital resources that is material to investors.

Quantitative and Qualitative Disclosure About Market Risk

We are exposed to market risks in the ordinary course of our business. Market risk represents the risk of loss that may impact our financial position due to adverse changes in financial market prices and rates. Our current investment policy is to invest available cash in bank deposits with banks that have a credit rating of at least A-. Accordingly, a substantial majority of our cash and cash equivalents, or marketable securities, is held in deposits that bear interest. Given the current rates of interest we receive, we will not be adversely affected if such rates are reduced. Our market risk exposure is primarily a result of foreign currency exchange rates, which is discussed in detail in the following paragraph.

Foreign Currency Exchange Risk

Our results of operations and cash flow are subject to significant fluctuations due to changes in foreign currency exchange rates. Our liquid assets and our expenses are denominated in EUR and USD.

As we continue to grow our business, our results of operations, and our cash flows might be subject to fluctuations due to changes in foreign currency exchange rates, which could adversely impact our results of operations.

A hypothetical movement of 10% in USD to the EUR exchange rate would have had an impact of approximately €0.5 million on our net result for the year ended December 31, 2024.

Currently, we do not hedge our foreign currency exchange risk. In the future, we may enter formal currency hedging transactions to decrease the risk of financial exposure from fluctuations in the exchange rates of our principal operating currencies. These measures, however, may not adequately protect us from the material adverse effects of such fluctuations.

B. Liquidity and Capital Resources

Overview

Since inception, we have not generated any revenue and have incurred significant operating losses and negative cash flows from our operations. We have funded our operations to date primarily with proceeds from the sales of quotas, in prior years as an S.r.l., and through our IPO of our shares as an S.p.A. We received gross cash proceeds of approximately €33.6 million from sales of quotas (pre-IPO), and approximately €32.7 million of gross proceeds from the IPO in December 2021. In addition, we received approximately €0.3 million of net proceeds from sales of our ADSs through our current and prior at-the-market ("ATM") offerings.

As of December 31, 2024, the Company had approximately €12.7 million in cash and cash equivalents and marketable securities.

The table below presents our cash flows for the years indicated:

	For the Year Ended December 31,		
	2024	**2023**	**2022**
		(in Euros)	
Net cash used in operating activities	€ (6,240,174)	€ (11,205,023)	€ (7,418,236)
Net cash (used in)/produced by investing activities	6,883,064	(14,892,666)	(27,070)
Net cash provided by financing activities	270,885	531	-
Effect of exchange rate changes	(23,446)	(6,278)	-
Net (decrease) increase in cash and cash equivalents	€ 890,329	€ (26,103,436)	€ (7,445,306)
Cash and cash equivalents at beginning of year	3,691,420	29,794,856	37,240,162
Cash and cash equivalents at end of year	€ 4,581,749	€ 3,691,420	€ 29,794,856

Operating Activities

During the year ended December 31, 2024, operating activities used approximately €6.2 million of cash and cash equivalents, resulting from our net loss of approximately €8.9 million, partially offset by non-cash charges of approximately €0.9 million and the cash generated by our operating assets and liabilities of approximately €1.9 million. The non-cash charges primarily included approximately €0.7 million of share-based compensation expense, approximately €0.1 million of unrealized gain on purchase of marketable securities, and other minor amounts of depreciation, retirement benefit obligation expense and cumulative translation adjustment. The net changes in our operating assets and liabilities were primarily due to: a decrease in other non-current assets due to a long-term VAT refund of approximately €0.4 million and the reduction of approximately €1.0 million from the research and development tax credit estimate; an increase in trade payables of approximately €0.2 million, primarily due to a lower premium for the D&O insurance policy, amounting to approximately €0.2 million; and an increase of approximately €0.2 million in accrued expenses -related parties, due to bonuses accrued at the end of 2023 that have not yet been paid.

During the year ended December 31, 2023, operating activities used approximately €11.0 million of cash and cash equivalents, resulting from our net loss of approximately €11.6 million, partially offset by non-cash charges of approximately €1.1 million and the cash generated by our operating assets and liabilities of approximately €0.4 million. The non-cash charges primarily included approximately €0.7 million of share-based compensation expense, approximately €0.2 million of unrealized gain on purchase of marketable securities, and other minor amounts of depreciation, retirement benefit obligation expense and cumulative translation adjustment. The net changes in our operating assets and liabilities were primarily due to a decrease in accounts payable. The decrease in accounts payable compared to the prior period, was mainly due to bills from certain suppliers, advisors, and legal consultants received in December 2022 that were paid in 2023.

During the year ended December 31, 2022, operating activities used approximately €7.4 million of cash and cash equivalents, resulting from our net loss of approximately €8.5 million, partially offset by non-cash charges of approximately €0.8 million and the cash generated by our operating assets and liabilities of approximately €0.2 million. The non-cash charges primarily included approximately €0.7 million of share-based compensation expense, and other minor amounts of depreciation, retirement benefit obligation expense and cumulative translation adjustment. The net changes in our operating assets and liabilities were primarily due to an increase in account payable and accrued expenses, as well as an increase in other current liabilities. The increase in account payable was mainly due to bills from certain suppliers, advisors, and legal consultants received in December 2022 that were paid in January 2023, as well as an increase in account payables to OSR, a related party. The increase in accrued expenses were mainly due to an increase in related parties-accrued expenses for invoices to be received from OSR and for senior management bonuses accrued at year end.

Investing Activities

During the year ended December 31, 2024, investing activities used approximately €16.4 million to purchase marketable securities (U.S. treasury bills and Italian government bonds), in order to deploy the liquidity available and not used in current operations more profitably, while respecting the principle of selecting low-risk profile assets. During the 2024, proceeds from the divestment of marketable securities amounted to approximately €23.2 million.

In addition, approximately €4,000 of our cash and cash equivalents were used to primarily purchase laptops and other work tools for new employees hired during the fiscal year ending on December 31, 2024.

During the year ended December 31, 2023, investing activities used approximately €14.9 million to purchase marketable securities (U.S. treasury bills and Italian government bonds), in order to deploy the liquidity available and not used in current operations more profitably, while respecting the principle of selecting low-risk profile assets. In addition, approximately €14,000 of our cash and cash equivalents were used to primarily purchase laptops and other work tools for new employees hired during the fiscal year ending on December 31, 2023.

During the year ended December 31, 2022, investing activities used €27,070 of our cash and cash equivalents to both improve our cyber security and support the implementation of our new ERP system.

Financing Activities

During the year ended December 31, 2024, the net cash provided by financing activities relates to the proceeds from our current and prior ATM offerings.

During the year ended December 31, 2023, there was no cash provided by financing activities.

During the year ended December 31, 2022, there was no cash provided by financing activities.

Current Outlook

To date, we have not generated revenue and do not expect to generate revenues from the sale of any product candidate in the near term.

As of December 31, 2024, our cash and cash equivalents, and marketable securities, were approximately €12.7 million. Our primary cash obligations relate to payments to AGC Biologic for manufacturing activities and to OSR pursuant to the ARLA and other providers of clinical trial related services and manufacturing activities.

Based on our existing cash and anticipated cash from short-term financing activities, we estimate that such funds will be sufficient to fund our operations and capital expenditure requirements into the second quarter of 2026. We have based this estimate on assumptions that may prove to be wrong, and we could use our available capital resources sooner than we currently expect.

In addition, our operating plans may change because of many factors that may currently be unknown to us, and we may need to seek additional funds sooner than planned. Our future capital requirements will depend on many factors, including:

- the progress and costs of our preclinical studies, clinical trials and other research and development activities;
- the scope, prioritization and number of our clinical trials and other research and development programs;

- any cost that we may incur under in- and out-licensing arrangements relating to our product candidate that we may enter into in the future;
- the costs and timing of obtaining regulatory approval for our product candidates;
- the costs of filing, prosecuting, enforcing, and defending patent claims and other intellectual property rights;
- the costs of, and timing for, amending current manufacturing agreements for production of sufficient clinical and (eventually) commercial quantities of our product candidates, or entering into new agreement with existing or new CMOs;
- the potential costs of contracting with third parties to provide marketing and distribution services for us or for building such capacities internally; and
- the costs of acquiring or undertaking the development and commercialization efforts for additional, future therapeutic applications of our product candidates and the magnitude of our general and administrative expenses.

Until we can generate significant revenues, if ever, we expect to satisfy our future cash needs through our existing cash, cash equivalents and short-term deposits as well as through additional financings, which we may seek through a combination of private and public equity offerings, debt financings and collaboration, in-licensing arrangements, joint ventures, strategic alliances or partnerships. For example, on May 12, 2023, we filed with the SEC a shelf registration statement, which was declared effective by the SEC on May 24, 2023 and permits us to sell from time to time additional ordinary shares, ordinary shares represented by ADSs or rights exercisable for ordinary shares or ADSs in one or more offerings in amounts, at prices and on the terms that we will determine at the time of offering for aggregate gross sales proceeds of up to $100.0 million. As of December 31, 2024, approximately $99.7 million of securities remained available under this registration statement. Further, we have entered into an ATM sales agreement, as amended (the "Sales Agreement"), with Virtu Americas LLC and Rodman & Renshaw LLC (the "Sales Agents") pursuant to which we may, but are not obligated to, offer and sell, from time to time, ADSs with an aggregate offering price up to $29,696,999 through the Sales Agents, subject to the terms and conditions described in the Sales Agreement and SEC rules and regulations (our "ATM offering"). As of December 31, 2024, approximately $29.7 million of capacity remained available under this ATM offering. In addition, in March 2025, we completed a mandatory convertible bond financing, pursuant to which we may receive up to €20 million in two tranches. Please see Note 1 – Nature of business and history – Shelf Registration Statement and Sales Agreement of our audited consolidated financial statements for further information.

We cannot be certain that additional funding will be available to us on acceptable terms, if at all. If funds are not available, we may be required to delay, reduce the scope of, or eliminate research or development plans for, or commercialization efforts with respect to, one or more applications of our product candidates.

This expected use of cash and cash equivalents represents our intentions based upon our current plans and business conditions, which could change in the future as our plans and business conditions evolve. We may also use a portion of the available cash and cash equivalents, and marketable securities, to in-license, acquire, or invest in additional businesses, technologies, products, or assets.

C. Research and Development

See "Item 4. Information on the Company—B. Business Overview—Intellectual Property Rights."

D. Trend Information

Other than as disclosed elsewhere in this Annual Report, we are not aware of any trends, uncertainties, demands, commitments or events for the fiscal year ended December 31, 2024 that are reasonably likely to have a material and adverse effect on our net revenues, income, profitability, liquidity or capital resources, or that would cause the disclosed financial information to be not necessarily indicative of future results of operations or financial conditions.

E. Critical Accounting Estimates

For our critical accounting estimates, see "Item 5. Operating and Financial Review and Prospects—A. Operating Results—Critical Accounting Policies."

ITEM 6. DIRECTORS, SENIOR MANAGEMENT AND EMPLOYEES

A. Directors and Senior Management

The members of the Board of Directors (the "Board") at December 31, 2024 were: John L. Cantello, Ph.D., Lauren H. Chung, Ph.D., Armon R. Sharei, Ph.D., Todd Wider, M.D., and Pierluigi Paracchi, who is the Chairman.

The term of office of the directors is one year, and the aggregate annual directors' compensation is €213,000.

The following table sets forth the name, age as of March 27, 2025, and position of the individuals who serve as our directors and executive officers. The following also includes certain information regarding the individual experience, qualifications, attributes and skills of our directors and executive officers as well as brief statements of those aspects of our directors' backgrounds that led us to conclude that they are qualified to serve as directors:

Name	Age	Position	Year elected or appointed
Pierluigi Paracchi	51	Chief Executive Officer, Chairman of the Board of Directors and General Manager	2014
Todd Michael Wider	60	Director (1) (2)	2024
John Louis Cantello	59	Director (1) (2)	2024
Lauren Haeyong Chung	52	Director (1) (2)	2024
Armon Reza Sharei	37	Director (1) (2)	2024
Richard B. Slansky	67	Chief Financial Officer	2021
Carlo Russo, M.D.	72	Chief Medical Officer, Head of Development	2021
Barbara Regonini	52	Finance Director	2021
Stefania Mazzoleni, Ph.D.	42	Scientific Project Manager and Communications Officer	2016

(1) Independent Director (as defined under Nasdaq Stock Market rules)

(2) Member of the Compensation, Nomination and Governance Committee

The Board consists of five (5) members and each of their terms will expire at the Company's general shareholders' meeting called to approve the financial statements for the year ending December 31, 2024 to be held in April 2025, or earlier upon resignation.

Pierluigi Paracchi, Chief Executive Officer, Chairman of the Board of Directors, and General Manager

Mr. Paracchi has over 15 years of combined experience as an investor and director of life science companies, including as Founder and CEO of Quantica SGR and in senior roles at Axòn Capital, Sofinnova Partners, and AurorA Science. He was also a board member and investor in Ethical Oncology Science, which was acquired in 2013 for a total deal of $470 million. Mr. Paracchi is a member of the Assobiotec Steering Committee, the Italian Association for the development of biotechnology. He also serves on the board of directors of the autoimmune disease and cancer company Altheia Science, as non-executive Chairman, at a medical device company, Lipogems International, and is a venture partner with AurorA Science, an independent biotech investment vehicle.

Richard B. Slansky, Chief Financial Officer

Mr. Slansky is a senior financial executive with more than 30 years of experience as Chief Financial Officer in various biopharmaceutical, diagnostic and life science companies, including Biological Dynamics, OncoSec Medical, GenMark Diagnostics, now part of Roche, and C-N Biosciences, now a part of Millipore Sigma, a division of Merck KGaA. His experience spans across public and private healthcare and technology companies at various stages of growth, pre-revenue to commercial. He has been responsible for strategic vision and oversight of financial and operational teams, organizational leadership, creating maximum stakeholder value, financial and governmental compliance, among other activities. He also serves on the board of directors of several private companies in the life science, aerospace and real estate market segments.

Carlo Russo, M.D., Chief Medical Officer & Head of Development

Dr. Russo has extensive experience as a biotech executive focused on medical affairs, research and development, and clinical studies. He has served as Head of Development of GSK's R&D Biopharm and Rare Disease Units and the Cardiovascular Metabolic Center. Previously, Dr. Russo served as an Executive VP and CMO of Adverum, CMO & Head of Research & Development of Annapurna, and President and CEO of VaxInnate Corporation, among other senior roles. Dr. Russo holds several senior positions at research institutions, including Cornell University Medical College, Columbia University, and Scripps Research Institute. He holds his MD and Board Certification in Hematology from the University of Genoa Medical School, and is the author of more than 70 scientific publications.

Barbara Regonini, Finance Director

Ms. Regonini is an experienced financial executive with skills in strategic finance, restructuring and reorganization processes, internal controls, and corporate governance systems implementation. Prior to joining Genenta, she was Head of Finance at OAM – Financial Supervisory Authority. She previously held CFO roles and was part of the Supervisory Body of a public company in the renewable energy field. Former senior manager at PriceWaterhouseCoopers, she has a significant finance background in the industrial and service field. She has a Master's degree at the University of Nicosia in Science of Digital Currency, a degree as Strategic CFO at Harvard Business School, a Master's degree in Business and Administration at the University of Parma, and she is a Chartered Public Accountant and Auditor.

Stefania Mazzoleni, Ph.D., Scientific Project Manager and Communications Officer

Dr. Mazzoleni manages and oversees the scientific development of parallel immuno-gene therapy studies in oncology indications and provides scientific support for investor interactions. Dr. Mazzoleni has more than 15 years' experience in life science research and development, oncology and project management, including over four years of drug development and cell and gene therapy experience acquired while working at various academic institutions (OSR - San Raffaele Hospital, National Institute of Molecular Genetics) and pharmaceutics (Nerviano Medical Sciences). Dr. Mazzoleni received a MSc in Medical Biotechnology in 2005, holds a PhD in Molecular and Cellular Biology from San Raffaele Vita-Salute University, has a second level vocational Master's degree in Pharmacy and Pharmaceutical Oncology and is a member of the European Academy of Tumor Immunology.

Board of Directors

Todd Michael Wider, M.D., Director

Todd Wider is a consultant to numerous entities in the biotechnology space, a co-founder and board member of Xanadu Bio and the prior Executive Chairman of Emendo Biotetherapeutics, a board member of Abeona Therapeutics, Arya Science Acquisition Corp. Todd is an active, honorary member of the medical staff of Mount Sinai Hospital in NYC. He received his AB, with high honors and Phi Beta Kappa, from Princeton University and his M.D. from Columbia University Vagelos College of Physicians and Surgeons.

Todd is also a principal in Wider Film Projects, a documentary film company focused on producing films with sociopolitical resonance that have won Academy, Emmy and Peabody Awards.

John Louis Cantello, Ph.D., Director

John is an independent advisor to the biopharma industry with over 20 years of experience. Former VP and Head of Business Development, Oncology Therapy Area at GlaxoSmithKline and VP and Head of Business Development, Respiratory & Immune Diseases at AstraZeneca. John has led teams accountable for assessing, valuing, and transacting M&A, pipeline & commercial asset deals covering oncology, respiratory, inflammation, metabolic and rare diseases. He has a track record of closing deals (transacting >$30B in deal value) representing primary care, specialty care and rare diseases.

Lauren Haeyong Chung, Ph.D., Director

Lauren is the CFO of Laxxon Medical, a pharma-technology company. Lauren has over 20 years of operating experience spearheading agile investment management strategies and tactical asset allocation in the healthcare industry. As the founder and CEO of Minleigh LLC, a healthcare focused strategic advisory firm, Lauren advised leadership, boards, and investment firms on global strategic plans, M&A, integration, and compliance. Previously, Lauren co-founded Tokum Capital Management, a global institutional healthcare fund, and successfully managed its merger with Perella Weinberg Partners. Lauren serves on public and private company boards. She has a Ph.D. in Biomedical Sciences from Columbia University Vagelos College of Physicians and Surgeons, an M.B.A. from Columbia Business School, and a B.A. in Biochemistry and Economics with Honors from Wellesley College.

Armon Reza Sharei, Ph.D., Director

Armon is Founder and CEO of Portal Bio and formerly the CEO and Founder of SQZ Biotechnologies (NYSE: SQZ), where he led the company from invention to post-IPO with over $300M in equity financing, a $1Bn collaboration with Roche, and three clinical trials. He graduated from Stanford University, obtained his Ph.D. at Massachusetts Institute of Technology and received his Post-Doctoral at Harvard Medical School.

Executive Scientific Board

Luigi Naldini, M.D., Ph.D., Chairman of the Executive Scientific Board

Prof. Naldini is a deeply experienced scientist and academic, considered by many to be the father of lentiviral gene therapy. Luigi Naldini is Professor of Cell and Tissue Biology and Cell and Gene Therapy at the Vita-Salute San Raffaele University School of Medicine in Milan, and Director of the San Raffaele-Telethon Institute for Gene Therapy and of the Division of Regenerative Medicine, Stem Cells & Gene Therapy at the San Raffaele Scientific Institute. He has previously served as President of the European Society of Gene and Cell Therapy and a member of the board of directors and Advisory Council of the American Society of Gene and Cell Therapy. Prof. Naldini is also a scientific advisor on EMEA and WHO committees for the evaluation of novel gene transfer medicines and has authored more than 250 scientific publications.

Bernhard Gentner, M.D., Member of the Executive Scientific Board

Dr. Gentner is a physician scientist, serving as Group Leader of the Translational Stem Cell and Leukemia Research Unit at the San Raffaele-Telethon Institute for Gene Therapy in Milan and Staff Hematologist in the Hematology and Bone Marrow Transplantation Unit of OSR - San Raffaele Hospital. Dr. Gentner completed his MD studies at the University of Heidelberg, Germany, the MD Anderson Cancer Center and Baylor College of Medicine, Houston, USA. He completed his internal medicine training at Erlangen University Hospital, Germany and his hematology training at San Raffaele Vita-Salute University and has authored more than 30 scientific publications.

Strategic Advisors

Advisors to the Company include:

Gaurav Shah: Gaurav Shah serves as CEO and President of Rocket Pharma (NASDAQ:RCKT), a publicly traded clinical-stage biotechnology company focused on developing first-in-class gene therapy options for rare, devastating diseases with a market cap ranging from $600 million to $1 billion in recent months. He is co-founder of Rocket Pharma and sits on the Board of Directors. Prior to this role Gaurav was a Global Program Head in the Cell & Gene Therapies Unit at Novartis, where he had strategic oversight of 12 functions and helped spearhead pivotal trials with CART-19 for patients with Leukemia and Lymphoma – later approved by the FDA as Kymriah. Earlier roles at Novartis included lead physician for Biosimilars and for Afinitor. Gaurav started his career in the pharmaceutical industry at ImClone/Eli Lilly as a Medical Director overseeing oncology trials focused on monoclonal antibodies. This work in industry has led to multiple drug approvals for children and adults with malignancies and other devastating disorders. Gaurav graduated from Harvard University (summa cum laude, Phi Beta Kappa) with a degree in Behavioral Neuroscience and currently serves as an interviewer for Admissions for Harvard College. He received his MD from Columbia (AOA), completed his internal medicine residency at Brigham and Women's Hospital/Harvard Medical School and hematology/oncology fellowship training at Memorial-Sloan Kettering. After receiving board certification in medical oncology, he served as an Adjunct Assistant Professor of Oncology at Columbia.

Family Relationships

There are no family relationships among our executive officers and directors.

Arrangements Concerning Election of Directors and Members of Management

There are no arrangements or understandings with major shareholders, customers, suppliers, or others pursuant to which any of our directors or members of senior management were selected as such.

B. Compensation

The following table presents in the aggregate all compensation we paid to all our directors and senior management as a group for the year ended December 31, 2024. The table does not include any amounts we paid to reimburse any of such persons for costs incurred in providing us with services during this period. We are not required to provide the compensation, on an individual basis, of our executive officers and directors under Italian law. As a matter of Italian law, the compensation of directors is established at the time of their appointment or by the shareholders' meeting. The compensation of the managing directors shall be established by the board of directors, with the opinion of the board of statutory auditors. Our bylaws provides that the shareholders' meeting may determine a total amount for the compensation of the directors, including managing directors.

The total amount paid to all directors and senior managers as a group was approximately €1.3 million for the year ended December 31, 2024.

	Salary, Bonuses and Related Benefits	Pension, Retirement and Other Similar Benefits	Share-Based Compensation
All directors and senior management as a group, consisting of 7 persons	€ 1,258,468	€ -	€ -

The total cost to the Company for the year ended December 31, 2024 related to all directors and senior managers as a group was approximately €2.2 million.

	Salary, Bonuses and Related Benefits	Pension, Retirement and Other Similar Benefits	Share-Based Compensation
All directors and senior management as a group, consisting of 7 persons	€ 1,859,094	€ 33,481	€ 293,845

The difference between the total amount paid by the Company and the total cost to the Company, stems from the fact that the Company's cost for each employee is higher than what is actually paid out during each fiscal year due to tax and contribution charges affecting labor costs. Additionally, according to the regulations applicable to Italian employees, severance pay is set aside annually and thus constitutes a cost for the Company, whereas it is disbursed and paid out only in the event of the employee's resignation or dismissal. Furthermore, provisions for unexercised stock options during the fiscal year are also included in the Company's cost.

C. Board Practices

Committees of the Board of Directors

We currently follow the historical Italian corporate governance system, with a board of directors (*consiglio di amministrazione*) and a separate board of statutory auditors (*collegio sindacale*) with supervisory functions. The two boards are separate, and no individual may be a member of both corporate bodies. Both the members of the board of directors and the members of the board of statutory auditors owe duties of loyalty and care to the Company. The board of statutory auditors acts as the Board's audit committee for purposes of SEC and Nasdaq compliance (see *Differences between Italian Laws and Nasdaq Requirements* below).

Board of Statutory Auditors

Our Board of Statutory Auditors for the three-year period of 2024-2026 consists of: Carlo Alberto Nicchio (Chairman), Jacopo Doveri, and Giuseppe Gentile, while Luca Domenico Maranzana and Adalberto Adriano Minazzi were appointed as alternates. The annual Board of Statutory Auditor compensation is €18,000 for the chairman and €12,000 for each active member while no compensation is provided for the alternates unless they replace an active member.

During 2024, our Board of Statutory Auditors received approximately €44,000 in compensation in the aggregate for their services to the Company.

Our Board of Statutory Auditors' term will therefore expire with our general shareholders' meeting called to approve the financial statements for the year ending December 31, 2026 to be held in 2027. The following table sets forth the name, age as of March 27, 2025, and position of the individuals who serve as our Board of Statutory Auditors, and their alternates.

Name	Age	Position	Year elected or re-appointed
Carlo-Alberto Nicchio	50	Chairman of the Board of Statutory Auditors	2024
Giuseppe Gentile	57	Statutory auditor	2024
Jacopo Doveri	52	Statutory auditor	2024
Luca Domenico Maranzana	57	Alternate auditor	2024
Adalberto Adriano Minazzi	75	Alternate auditor	2024

Each shareholder and shareholders belonging to the same group shall not submit, or contribute to submit, or to cast their vote for more than one slate, including through a nominee. Each candidate may only be listed on single slate or, otherwise, will be ineligible for election if named in multiple slates.

The Company relies on an exemption from the Rule 10A-3 requirements provided by Rule 10A-3(c)(3) of the Exchange Act for foreign private issuers with a board of statutory auditors established in accordance with local law or listing requirements and subject to independence requirements under local law or listing requirements.

Additional Board Committees

Although Italian law does not require that we adopt a Compensation, Nomination and Governance Committee, in connection with our Corporate Conversion from a limited liability company (società a responsabilità limitata, or "S.r.l.") to a joint stock company (società per azioni, or an "S.p.A."), we established a Compensation, Nomination and Governance Committee according to Nasdaq Listing Rule 5615(a)(3). The members of our Compensation, Nomination and Governance Committee include: Todd M. Wider, John L. Cantello, Lauren H. Chung, and Armon R. Sharei. They were nominated on May 2, 2024. The Compensation, Nomination and Governance Committee will assist our Board of Directors in overseeing our cash compensation and equity award recommendations for our executive officers along with the rationale for such recommendations, as well as summary information regarding the aggregate compensation provided to our executive officers.

Differences between Italian Laws and Nasdaq Requirements

The Sarbanes-Oxley Act, as well as related rules subsequently implemented by the SEC, requires foreign private issuers, such as us, to comply with various corporate governance practices. In addition, following the listing of the ADSs on Nasdaq, we are required to comply with the Nasdaq Stock Market Rules. Under those rules, we may elect to follow certain corporate governance practices permitted under Italian law in lieu of compliance with corresponding corporate governance requirements otherwise imposed by the Nasdaq Stock Market Rules for U.S. domestic registrants.

In accordance with Italian law and practice and subject to the exemption set forth in Rule 5615 of the Nasdaq Stock Market Rules, as a foreign private issuer, we have elected to rely on home country governance requirements and certain exemptions thereunder rather than the Nasdaq Stock Market Rules, with respect to the following requirements:

- *Composition of the board of directors*. Italian law does not require that the majority of our board of directors consist of independent directors. Our board of directors therefore may include fewer independent directors than would be required if we were subject to Nasdaq Listing Rule 5605(b) (1). In addition, we are not subject to Nasdaq Listing Rule 5605(b)(2), which requires that independent directors must regularly have scheduled meetings at which only independent directors are present.

- *Quorum*. In accordance with Italian law quorum requirements generally applicable to general meetings of shareholders are set forth in the Italian Civil Code therefore our bylaws may not provide a specific regulation of them. Our practice thus varies from the requirement of Nasdaq Listing Rule 5620(c), which requires an issuer to provide in its bylaws for a generally applicable quorum, and that such quorum may not be less than one-third of the outstanding voting stock.

  According to Italian law, the management report and the annual financial statements shall be communicated to Company's auditor and to the board of statutory auditors at least 30 days prior to the general meeting of shareholders convened for its approval. The board of statutory auditors must report to the shareholders' meeting on the results of the financial year and on the activities carried out in the performance of its duties and make observations and proposals regarding the financial statements and their approval. The financial statements, together with the reports of the directors, statutory auditors, and Company's auditors, must remain deposited at the Company's registered office for the 15 days preceding the shareholders' meeting called to approve them.

- *Proxy Solicitations*. Under Italian law shareholders may appoint attorneys-in-fact by delivering in writing appropriate power of attorney to represent them in an ordinary or extraordinary shareholders' meeting of the Company. Our directors, auditors, and employees may not be proxies. Italian law does not have a specific regulatory regime for the solicitation of proxies in private companies; thus, our practice varies from the requirement of Nasdaq Listing Rule 5620(b), which sets forth certain requirements regarding the solicitation of proxies.

- *Share Issuances*. Pursuant to Italian law, we have opted out of shareholder approval requirements by way of including authorized and conditional share capital for the issuance of securities in connection with certain events such as the acquisition of stock, assets or convertible notes, certain private placements and/or public offering. To this extent, our practice varies from the requirements of Nasdaq Listing Rule 5635, which generally requires an issuer to obtain shareholder approval for the issuance of securities in connection with such events.

- *Audit Committee*. U.S. companies listed on Nasdaq are required to have an audit committee that satisfies the requirements of Rule 10A-3 under the Exchange Act and certain additional requirements set by the Nasdaq. All members of this committee must be independent, and the committee must adopt a written charter. The committee's prescribed responsibilities include: (i) the appointment, compensation, retention and oversight of the external auditors; (ii) establishing procedures for handling "whistle blower" complaints regarding accounting, internal accounting controls, or auditing matters; (iii) engaging independent counsel and other advisers, as it determines necessary to carry out its duties; and (iv) determine appropriate funding for payments to the external auditor, advisors employed by the audit committee and other necessary administrative expenses of the audit committee. A company must also have an internal audit function, which may be outsourced, except to the independent auditor. We follow the "traditional" model of corporate governance for Italian companies and accordingly have established a board of statutory auditors established in accordance with Italian law which performs substantially the same functions and is accordingly exempt from the audit committee requirements established by Rule 10A-3 and Nasdaq rules. The Company's reliance on such exemption is based on the circumstance that the Company's board of statutory auditors meets the following requirements set forth in Exchange Act Rule 10A-3(c)(3):

  (i) the board of statutory auditors is established and selected pursuant to Italian law expressly permitting such a board;

  (ii) the board of statutory auditors is required under Italian law to be separate from the Company's board of directors;

  (iii) the board of statutory auditors is not elected by management of the Company and no executive officer of the Company is a member of the board of statutory auditors;

  (iv) Italian law provides for standards for the independence of the board of statutory auditors from the Company and its management; and

  (v) the board of statutory auditors, in accordance with applicable Italian law and the Company's governing documents, is responsible, to the extent permitted by Italian law, for the appointment, retention and oversight of the work (including, to the extent permitted by law, the resolution of disagreements between management and the auditor regarding financial reporting) of any registered public accounting firm engaged for the purpose of preparing or issuing an audit report or performing other audit, review or attest services for the Company.

  Our reliance on Rule 10A-3(c)(3) does not, in our opinion, materially adversely affect the ability of its board of statutory auditors to act independently and to satisfy the other requirements of Rule 10A-3.

- *Compensation Committee*. Italian law does not require the appointment of a compensation committee composed of independent directors as required by the Nasdaq Listing Rules. As a matter of Italian law applicable to Italian stock corporations whose shares are not listed on a regulated market in the E.U. and under our bylaws, the compensation of executive directors, including the CEO, is determined by the board of directors, after consultation with the board of statutory auditors, while the Company's shareholders, according to Italian law and our bylaws, may determine a total amount for the compensation of the directors, including managing directors. Compensation of the Company's executive officers is determined by Board of Directors or by the CEO, if duly empowered. Nevertheless, although not required under Italian law, the Company has established a Compensation, Nomination and Governance Committee.

- *Code of Conduct*. Pursuant to Italian law, we have adopted an "Organization and Operational Model" as required by Italian Legislative Decree of June 8, 2001, No. 231 (relating to administrative responsibility) that consists of: (i) a Code of Ethics; and (ii) operating procedures and reporting systems applicable to all of our directors, officers and employees, which may not comply with the requirements for a code of conduct meeting the criteria under Nasdaq Listing Rule 5610.

- *Loyalty Share Program*. As described in more detail in "Item 10. Additional Information. B. Memorandum and Articles of Association" we have established a loyalty share program. Under our loyalty share program, each ordinary share held in registered form entitles the shareholder to a double vote (i.e. two votes for each ordinary share) if the ordinary share has been held by the same shareholder for a continuous period of not less than twenty-four months from the date of its registration in the special list maintained by us, and an additional vote is also granted upon the expiration of each 12-month period, following the expiration of the period referred to above, in which such ordinary share has been held by the shareholder, up to a total maximum of ten votes per ordinary share. Pursuant to the home country exemption set forth under Nasdaq Stock Market Rule 5640, in establishing the loyalty share program, we elected to be exempt from the requirement under Nasdaq Stock Market Rule 5640, which provides that the voting rights of existing shareholders of publicly traded common stock registered under Section 12 of the Exchange Act cannot be disparately reduced or restricted through any corporate action or issuance.

D. Employees

As of March 26, 2025, we had 13 full-time employees, 11 located in Milan, Italy, and two (2) located in the U.S. We also rely on consultants, and several collaborators at SR-TIGET and OSR. Our full-time employees and consultants are engaged in clinical, research and development, product development, quality assurance, finance, accounting, and administrative activities. We consider our relationship with our employees to be good.

E. Share Ownership

See "Item 7.A. – Major Shareholders" below.

F. Disclosure of a Registrant's Action to Recover Erroneously Awarded Compensation

None.

ITEM 7. MAJOR SHAREHOLDERS AND RELATED PARTY TRANSACTIONS

A. Major Shareholders

The following table sets forth information regarding beneficial ownership of our ordinary shares as of March 26, 2025 by:

- each person, or group of affiliated persons, known to us to be the beneficial owner of more than 5% of our outstanding ordinary shares;
- each of our directors and executive officers; and
- all of our directors and executive officers as a group.

Percentage ownership is based on 18,289,866 ordinary shares (including ordinary shares represented by ADSs) outstanding on March 26, 2025. Beneficial ownership is determined in accordance with the rules of the SEC, which generally provide that a person has beneficial ownership of a security if he, she or it possesses sole or shared voting or investment power over that security or has the right to acquire a security, such as through the exercise of stock options, within 60 days. Shares subject to options that are currently exercisable or exercisable within 60 days of the date above are considered outstanding and beneficially owned by the person holding such options for the purpose of computing the percentage ownership of that person but are not treated as outstanding for the purpose of computing the percentage ownership of any other person.

Except as indicated in footnotes to this table, we believe that the shareholders named in this table have sole voting and investment power with respect to all shares shown to be beneficially owned by them, based on information provided to us by such shareholders. Our major shareholders do not have different voting rights than other holders of our ordinary shares. The information is not necessarily indicative of beneficial ownership for any other purpose. Unless otherwise noted below, each beneficial owner's address is: c/o Genenta Science S.p.A., Via Olgettina no. 58, 20132 Milan, Italy.

	No. of Shares Owned	No. of Shares Exercisable within 60 Days of March 28, 2025	No. of Shares Beneficially Owned	Percentage Owned		Percentage of Total Voting Power
Directors and executive officers						
Pierluigi Paracchi	2,296,129	36,603	2,332,732	12.75%	(1)	58.72%
John Cantello	-	20,163	20,163	*%	(2)	*%
Lauren Chung	-	20,163	20,163	*%	(3)	*%
Armon Sharei	-	20,163	20,163	*%	(4)	*%
Todd Wider	-	20,163	20,163	*%	(5)	*%
Richard B. Slansky	22,147	167,532	189,679	1.04%	(6)	*%
Carlo Russo	602,417	30,502	632,919	3.46%	(7)	1.54%
Luigi Naldini	1,386,145	-	1,386,145	7.58%		3.58%
Bernhard Gentner	692,871	-	692,871	3.79%		1.79%
Stefania Mazzoleni	30,321	53,726	84,047	*%	(8)	*%
Barbara Regonini	-	47,625	47,625	*%	(9)	*%
All directors and executive officers as a group (117 persons)	**5,030,030**	**416,638**	**5,446,668**	**29.78%**		**65.76%**
5% Shareholders						
OSR - San Raffaele Hospital	1,896,730		1,896,730	10.37%		4.89%

* Less than 1%.

(1) Consists of 2,296,129 shares (2,275,516 ordinary shares plus 20,613 ADSs) held by Mr. Paracchi and 36,603 shares underlying options to acquire ADSs of Genenta Science S.p.A. exercisable within 60 days of March 28, 2025. Mr. Paracchi is also enrolled in the Company's loyalty share program and based on his ten-year investment in the Company, has the right to vote 10 votes per share with respect to his ordinary shares. Currently, Mr. Paracchi is the only person enrolled in the Company's loyalty share program.
(2) Consists of 20,163 shares underlying options to acquire ADSs of Genenta Science S.p.A. exercisable within 60 days of March 28, 2025.
(3) Consists of 20,163 shares underlying options to acquire ADSs of Genenta Science S.p.A. exercisable within 60 days of March 28, 2025.
(4) Consists of 20,163 shares underlying options to acquire ADSs of Genenta Science S.p.A. exercisable within 60 days of March 28, 2025.
(5) Consists of 20,163 shares underlying options to acquire ADSs of Genenta Science S.p.A. exercisable within 60 days of March 28, 2025.
(6) Consists of 22,147 shares (19,947 ordinary shares plus 2,200 ADSs acquired through a 10b5-1 plan in July & August 2024) held directly by Mr. Slansky and 187,479 ordinary shares underlying options to acquire ordinary shares of Genenta Science S.p.A. exercisable within 60 days of March 28, 2025.
(7) Consists of 602,417 shares (598,417 ordinary shares plus 4,000 ADSs acquired through a 10b5-1 plan in September & October 2024) held by Dr. Russo and 30,502 shares underlying options to acquire ADSs of Genenta Science S.p.A. exercisable within 60 days of March 28, 2025.
(8) Consists of 30,321 ordinary shares held by Ms. Mazzoleni and 53,726 shares underlying options to acquire ADSs of Genenta Science S.p.A. exercisable within 60 days of March 28, 2025.
(9) Consists of 47,625 shares underlying options to acquire ADSs of Genenta Science S.p.A. exercisable within 60 days of March 28, 2025.

Significant Changes in Percentage Ownership

There are no significant changes in the percentage ownership held by our major shareholders since the IPO in December 2021.

Shareholders in the U.S.

To our knowledge, as of February 18, 2025, on the same basis of calculation as above, 45% of our total issued and outstanding ordinary shares were held by one record shareholder in the U.S., namely, The Bank of New York (formerly The Bank of New York Mellon), the depositary of our ADS program, which held 8,210,799 ordinary shares represented by 8,210,799 ADSs, or nine (9) brokers and institutional record holders. The actual number of holders is likely greater than these numbers of record holders and includes beneficial owners whose ordinary shares or ADSs are held in street name by brokers and other nominees. This number of holders of record also does not include holders whose shares may be held in trust by other entities.

Except for the above, we are not aware of any arrangement that may, at a subsequent date, result in a change of control of our company.

B. Related Party Transactions

We have not during the most recently completed financial year entered into transactions or loans with any (a) enterprises that are directly or indirectly controlled by or under common control with us; (b) our associates; (c) individuals directly or indirectly owning voting right which give them significant influence over us or close members of their respective families; (d) our directors, senior management or close members of their respective families; or (e) enterprises in which a substantial interest in the voting power is held or significantly influenced by any of the foregoing individuals (a "Related Party"), except as indicated below:

Agreements with OSR

We have a longstanding relationship with OSR. Beginning January 1, 2020, we entered into a six-year lease agreement for the use of office space in the OSR building. We paid OSR annual rent of approximately €15,000 in 2024 with a security deposit of €3,350.

In March 2023, we entered into an amended and restated license agreement (the "ARLA") with OSR. The ARLA replaced the Company's original license agreement originally entered into with OSR on December 15, 2014, as subsequently amended on March 16, 2017, February 1, 2019, December 23, 2020, September 28, 2021, January 22, 2022, September 29, 2022, and December 22, 2022 (the "Original OSR License Agreement").

The effectiveness of the ARLA was subject to Italy's Law Decree No. 21 of March 15, 2012 (i.e., the Italian Golden Power regulations), as subsequently amended and supplemented, and would not become effective until the applicable Italian governmental authority consented to the ARLA. On April 20, 2023, such consent was received and the ARLA became effective.

Pursuant to the terms of the ARLA, OSR has granted us an exclusive, royalty-bearing, non-transferrable (except with the prior written consent of OSR), sublicensable, worldwide license, subject to certain retained rights, to: (1) certain patents, patent applications and existing know-how for the use in the field(s) of Interferon ("IFN") gene therapy by lentiviral based-hematopoietic stem and progenitor cells ("HSPC") gene transfer with respect to: (a) any solid cancer indication (including glioblastoma and solid liver cancer) and/or (b) any lympho-hematopoietic indication for which we exercise an option (described below); and (2) certain gene therapy products (subject to certain specified exceptions related to replication competent viruses) developed during the license term for use in the aforementioned field(s) consisting of any lentivirals or other viral vectors regulated by miR126 and/or miR130 and/or other miRs with the same expression pattern as miR126 and miR130 in hematopoietic cells for the expression of IFN under the control of a Tie2 promoter. Lympho-hematopoietic indication means any indication related to lympho-hematopoietic malignancies and solid cancer indication means any solid cancer indication (e.g., without limitation, breast, pancreas, colon cancer), with each affected human organ counting as a specific solid cancer indication.

On August 1, 2023, we entered into a Sponsored Research Agreement ("CP1 SRA"), which was contemplated under the ARLA, pursuant to which we will fund feasibility studies for certain gene therapy products consisting of any lentiviral vectors regulated by miR126 and/or miR130 and/or other miRs with the same expression pattern as miR126 and miR130 in hematopoietic cells for the expression of IFN under the control of a Tie2 promoter, in combination with any immunotherapy ("Candidate Products 1"), along with three additional research projects, to be conducted at OSR. If OSR determines that additional funds are needed, OSR will inform us and provide an estimate for completing the research.

On September 28, 2023, we entered into an amendment to the ARLA, whereby we and OSR agreed that we had fulfilled the obligations as set forth in the ARLA specific to Candidate Products 1 pursuant to the CP1 SRA. Furthermore, the amendment provides that we and OSR have no further obligations to negotiate and execute a sponsored research agreement for the performance of feasibility studies related to certain gene therapy products consisting of any lentiviral vectors regulated by miR126 and/or miR130 and/or other miRs with the same expression pattern as miR126 and miR130 in hematopoietic cells for the expression of cytokines and their variants (other than IFN or in addition to IFN) under the control of a Tie2 promoter, either alone or in combination with any immunotherapy ("Candidate Products 2"). Notwithstanding the removal of the obligation to enter into a sponsored research agreement with regards to Candidate Products 2, OSR granted us an exclusive option, to be exercised by sending written notice to OSR on or before September 30, 2025, to include certain intellectual property related to Candidate Products 2 and Candidate Products 2 as part of the licensed patents and licensed products under the ARLA. The option fee and our fee to extend the option period, if necessary, remain consistent with the prior fees to those costs reflected in the ARLA specific to Candidate Products 2. OSR will also have the right to prepare, file and prosecute patents and patent applications with respect to the results of Candidate Products 2. The amendment provides that the costs of the foregoing activities will be borne by us.

For more information regarding the ALRA, CP1 SRA and the amendment to the ARLA, see "Item 4. Information on the Company—B. Business Overview—Collaboration / Licensing —Amended and Restated License Agreement with Ospedale San Raffaele" and "—Sponsored Research Agreement."

Employment Agreements with Senior Management

We entered into employment agreements with each of Mr. Paracchi, Dr. Russo, and Mr. Slansky effective upon the consummation of our IPO or, in the case of Mr. Slansky, November 1, 2021. Pursuant to such employment agreements, Mr. Paracchi, Dr. Russo and Mr. Slansky are entitled to gross annual base salaries of €420,000, $500,000 and $375,000, respectively. All these employment agreements are subject to annual review by and at the sole discretion of the Compensation, Nomination and Governance Committee of our board of directors. Mr. Paracchi is also eligible to receive an annual cash bonus of up to 40% of base salary, and Dr. Russo and Mr. Slansky are eligible to receive an annual cash bonus of up to 30% of base salary, provided that such individual achieves performance targets determined by the Compensation, Nomination and Governance Committee of the board of directors.

The employment agreements of Dr. Russo and Mr. Slansky, are governed by U.S. law and include the following terms and conditions, among others:

(a) each employment agreement has a term commencing on the date of consummation of our IPO or, in the case of Mr. Slansky, November 1, 2021, and continuing until terminated: (i) upon death of the employee; (ii) upon disability; (iii) for cause or good reason; (iv) without cause; or (v) voluntarily. The employment agreement also contains, among other things, the following material provisions: (i) reimbursement for all reasonable travel and other out-of-pocket expenses incurred in connection with such individual's employment; (ii) paid vacation leave; (iii) health benefits; and (iv) a severance payment equal to twelve (12) months of base salary and a prorated portion of the applicable cash bonus upon termination by such individual for just cause or by the Company without cause (each as defined in the relevant agreement), with restrictive covenants applicable for a corresponding period after termination.

(b) in the event such individual is terminated three months prior to, or one year after, a Change of Control (as defined in the agreement) by the Company for any reason other than cause, or by such individual for good reason, then the executive shall be entitled to receive a cash payment equal to a multiple of such individual's then-current annual base salary determined by the time elapsed since the commencement of the agreement (in the case of Dr. Russo) or two times such salary (in the case of Mr. Slansky). Such payment shall be in lieu of the severance payment described above.

The employment agreement of Mr. Paracchi is governed by Italian law and includes the following terms and conditions, among others:

(a) the duties of general manager (*direttore generale*) with direct report to the board of directors of the Company;

(b) reimbursement of reasonable expenses incurred in the performance of work duties, health benefits and, subject to the approval of the board of directors, a grant of an equity award under an equity incentive plan to be adopted after the offering;

(c) in case of Change of Control (as defined in the relevant agreement), in the event of termination not for "cause" by the Company or of resignation for "cause" by the executive (such terms as understood in accordance with Article 2119 of the Italian Civil Code), the executive shall be entitled to receive a cash payment equal to three times such individual's then-current annual base salary (such indemnity will replace any indemnity provided for by the applicable National Collective Labour Agreement in case of termination); and

(d) non-competition and non-solicitation obligations of the executive for a 12 month period after the termination of the employment in consideration for compensation equal to 12 months after termination at the executive's then-current monthly base salary for each obligation.

Such agreement has a term commencing on the date of consummation of our IPO and continuing until terminated, among other things: (a) upon death of the executive; (b) for just cause; (c) with objective or subjective reason; (d) by resignation of the executive; or (e) voluntarily by mutual agreement between the parties.

Consultancy Agreements

Prof. Naldini and Dr. Gentner have entered into consulting agreements in connection with their service on our Executive Scientific Board. The agreements provide for gross annual fees of €100,000 and €45,000, respectively. These agreements automatically renew each year.

Mr. Gaurav Shah has entered into consultancy agreements for the activity of support the development and the growth of the Company in the U.S. market. The agreement has been in effect on a calendar quarter-to-quarter basis until December 31, 2024. For the year ended December 31, 2024, the consultant invoiced the Company for a total $7,500.

Indemnification Agreements

We have entered into an indemnification agreement with our directors and executive officers which requires us to indemnify our directors and executive officers to the fullest extent permitted by law, save for a limited number of instances, including when: (i) officers and directors' acts or omissions constituted willful misconduct or gross negligence; (ii) officers and directors did not act in good faith, for a purpose which they reasonably believed to be in, or not opposed to, the best interests of the Company; and (iii) officers and directors are held liable towards the Company.

Insofar as indemnification of liabilities arising under the Securities Act may be permitted to executive officers and board members or persons controlling us pursuant to the foregoing provisions, we have been informed that, in the opinion of the SEC, such indemnification is against public policy as expressed in the Securities Act and is therefore unenforceable.

C. Interests of Experts and Counsel

Not Applicable.

ITEM 8. FINANCIAL INFORMATION

A. Consolidated Statements and Other Financial Information.

The Company's consolidated financial statements are stated in EUROs and are prepared in accordance with US GAAP.

Audited Financial Statements

Our consolidated financial statements for the 2024, 2023 and 2022 fiscal years as required under Item 17 are included immediately following the text of this Annual Report. The audit reports of the Company are included herein immediately preceding the consolidated financial statements.

Policy on Dividend Distributions

The Company has not paid any dividends on its outstanding ordinary shares since its incorporation and does not anticipate that it will do so in the foreseeable future. The payment of dividends in the future, if any, is within the discretion of the Board of Directors and will depend upon our earnings, our capital requirements and financial condition and other relevant factors. We do not anticipate declaring or paying any dividends in the foreseeable future.

Legal Proceedings

See "Item 4. Information on the Company—B. Business Overview—Legal Proceedings."

B. Significant Changes

Except as disclosed elsewhere in this Annual Report, we have not experienced any significant changes since the date of our audited consolidated financial statements included in this Annual Report.

ITEM 9. THE OFFER AND LISTING

A. Offer and Listing Details

Our ordinary shares are listed on The Nasdaq Capital Market in the form of ADSs under the symbol "GNTA." Neither the Company's ordinary shares nor its ADSs are listed on a securities exchange outside the U.S. Bank of New York Mellon is the Company's depositary for purposes of issuing ADSs. Trading in the ADSs on The Nasdaq Capital Market commenced on December 15, 2021.

B. Plan of Distribution

Not applicable.

C. Markets

See "Item 9. The Offer and Listing—A. Offer and Listing Details.

D. Selling Shareholders

Not applicable.

E. Dilution

Not applicable.

F. Expenses of the Issue

Not applicable.

ITEM 10. ADDITIONAL INFORMATION

A. Share Capital

Not applicable.

B. Memorandum and Articles of Association

The description of certain terms and provisions of our bylaws (our "Bylaws") is incorporated by reference to our Registration Statement on Form F-1 (File No. 333-260923) filed with the SEC and as declared effective on December 14, 2021, and to our Form 6-K filed with the SEC on May 3, 2024.

At our 2024 Ordinary and Extraordinary Shareholders' Meeting, our shareholders approved an amendment to our Bylaws that established a loyalty share program. Under the loyalty share program, each ordinary share held in registered form entitles the shareholder to a double vote (i.e. two votes for each ordinary share) if the ordinary share has been held by the same shareholder for a continuous period of not less than twenty-four months from the date of its registration in the special list maintained by us, and an additional vote is also granted upon the expiration of each 12-month period, following the expiration of the period referred to above, in which such ordinary share has been held by the shareholder, up to a total maximum of ten votes per ordinary share.

To effect the loyalty share program, a special list (the "Special List") is maintained by us. To be added to the Special List, the registered shareholder would need to submit a specific application, enclosing a communication certifying the ordinary share ownership – which may also concern only part of the ordinary shares held by the registered shareholder – issued by the intermediary with whom the ordinary shares are deposited pursuant to the laws in force. In the case of entities other than individuals, the application would need to specify whether the entity is subject to direct or indirect control by third parties and the identification data of the controlling entity, if any. The Special List is updated by us. Cancellation from the Special List results from the following cases: renunciation of the interested party; communication of the interested party or of the intermediary proving the loss of the prerequisites for the increase of the voting right or the loss of the ownership of the right; ex officio, when we are informed of the occurrence of facts that entail the loss of the prerequisites for the increase of the voting right or the loss of the ownership of the right.

C. Material Contracts

We have not entered into any material contracts other than in the ordinary course of business and other than those described in "Item 4. Information on the Company" or elsewhere in this Annual Report.

D. Exchange Controls

Under Italian law, there are no exchange control restrictions on investments in, or payments on, the Genenta ordinary shares. There are no special restrictions in the Genenta Articles of Association or Italian law that limit the right of shareholders who are not citizens or residents of Italy to hold or vote the Genenta ordinary shares.

E. Taxation

Italian Tax Consequences

General. Under Italian law, financial instruments issued by an Italian company are subject to the same tax regime as are shares, provided that their remuneration is entirely represented by participation in the economic results of the issuer. Pursuant to Article 10(3) of the Income Tax Convention, the tax regime of dividends applies to income from corporate rights of an Italian company, which is subject to the same taxation treatment as income from shares under the laws of Italy.

Income Tax Withholding on Dividends. We do not anticipate making any distributions on our ordinary shares in the foreseeable future. However, if we were to make distributions on our ordinary shares, we would generally be required under Italian law, except as otherwise discussed below, to apply a definitive withholding tax on payments made to holders of our ordinary shares who are not residents of Italy for tax purposes.

Notably, dividends paid to beneficial owners who are not Italian residents and do not have a permanent establishment in Italy are generally subject to a 26 percent substitute tax rate. Therefore, the amount of the dividends that the holders of American Depository Receipts ("ADRs")or holders of equity shares not residing in Italy will initially receive will be net of such Italian substitute tax.

All non-Italian resident owners of equity shares or ADRs may benefit from reduced withholding tax settled in the relevant anti-double tax treaty undersigned between Italy and the country of residence for tax purposes of the owners of equity shares or ADRs. The reduced withholding tax rate under the relevant anti-double tax treaty will be applicable provided that the non-resident owners of the equity shares or ADRs are able to produce the documentation attesting the requirements to be eligible for the application of the relevant anti-double tax treaty.

Under Italian law, U.S. owners can claim, in accordance with Presidential Decree No. 600 of October 16, 1973, Article 27(3), a refund of up to eleven-twenty-sixths (*i.e.,* 11/26) of the Italian withholding tax withheld on dividends upon presenting evidence to the Italian tax authorities that income taxes have been fully paid on the dividends in the country of residence of the U.S. owners in an amount at least equal to the total refund claimed. U.S. holders should consult an independent tax advisor concerning the availability of this refund, which has traditionally become payable only after extensive delays.

Under the double tax treaty in force between Italy and the U.S. ("U.S./Italy Income Tax Treaty"), if the payee is the beneficial owner of the payment, dividends paid to U.S. owners will be subject to Italian withholding tax at a reduced rate of: 1) 5%, if the beneficiary is a company owning at least 25% of the payer's voting shares (for at least 12 months preceding the dividend distribution); or 2) 15% in any other case. The aforementioned regime (both 1 and 2) is applicable only if the payee does not carry out an entrepreneurial activity in Italy through a permanent establishment or performs independent personal services through a fixed place situated therein.

Companies or entities subject to corporation tax and resident in States that are E.U. Member States or participants in the EEA (included in the list provided for by Italian Ministerial Decree, September 4, 1996, amended and supplemented by Ministerial Decree March 23, 2017) may be entitled to a reduced tax rate of 1.2% on dividends distributed. The pensions funds established in an E.U. Member State or EEA country may be entitled to a reduced tax rate of 11% or, under certain conditions, to exemption from Italian taxation on dividends.

Income Tax on Capital Gains

Generally, gains from shares in Italian companies, under custody in Italy, could give rise to a taxable income for the non-resident transferor.

Capital gains exempt from taxation in Italy - "Non-qualified shareholdings" are those which are below 2% of the voting rights and 5% of the capital of an exchange-listed company. Gains from the disposal of non-qualified share investments in Italian listed companies by non-Italian residents are not subject to Italian income tax under domestic rule.

Capital gains subject to tax in Italy - "Qualified shareholdings" in a listed company are those representing more than the 2% of the voting rights or more than the 5% of the capital of an exchange-listed company. Capital gains from the disposal of a qualified shareholding in a listed company are subject to a withholding tax of 26% under the domestic rule.

The "qualified shareholding" thresholds must be verified over a 12-month monitoring period, starting from the day on which the investor has held at least a qualifying stake, either actual or potential (this rule aimed at preventing that a buy/sale kind of trading resulting in an overall disposition of over 2% in 12 months may result in a qualifying gain having to be declared even when the investor has never owned an actual or potential qualifying stake). Consequently, all trades cumulatively carried out in a 12-month period should be considered. More in details: (i) until the investor holds a qualifying shareholding at any point in time, trades are not relevant for capital gain purposes, even if the overall amount disposed in a 12-month period exceeds the relevant thresholds; and (ii) starting from the day when the taxpayer holds a qualifying shareholding, all the trades carried out in any consecutive 12 months give rise to qualified capital gains if the overall amount disposed of exceeds one of the relevant thresholds.

However, please be informed that in accordance with rules stated in the anti-double tax treaty, in force between Italy and the country of residence for tax purposes of the transferor, is possible to claim the benefit of exemption of the 26% taxation on capital gains. In principle, and more in details, the art. 13 of the OECD model convention basically states that the capital gain is only taxed in the transferor's country of tax residence. The Italy – U.S. anti-double treaty tax convention states a taxation criterion in line with the above. In the light of the above and upon conditions that all the requirements relevant for the application of the Italy – U.S. anti-double treaty tax convention are met, an U.S. investor may benefit from the fully exemption of taxation in Italy.

Furthermore, save for any applicable anti-avoidance provision, pursuant to the Income Tax Convention, a U.S. owner will not be subject to Italian capital gain tax or to Italian individual or corporate income tax unless such U.S. owner has a permanent establishment or fixed base in Italy to which the owner's ordinary shares is effectively connected. To this end, U.S. owners selling ordinary shares and claiming benefits under the Income Tax Convention may be required to produce appropriate documentation establishing that the above-mentioned conditions have been met.

Estate and Gift Tax. Inheritance and gift taxes, which were abolished in 2001, have been re-introduced in the Italian system by Law Decree No. 262 of October 3, 2006 (converted into law, with amendments, by Law Decree No. 286 of November 24, 2006), as amended. Such taxes will apply to the overall net value of the relevant assets, at the following rates, depending on the relationship between the testate (or donor) and the beneficiary (or donee): (a) 4%, if the beneficiary (or donee) is the spouse or a direct ascendant or descendant (such rate only applying on the net asset value exceeding, for each person, €1.0 million); (b) 6%, if the beneficiary (or donee) is a brother or sister (such rate only applying on the net asset value exceeding, for each person, €0.1 million); (c) 6% if the beneficiary (or donee) is another relative within the fourth degree or a direct relative-in-law as well as an indirect relative-in-law within the third degree; and (d) 8% if the beneficiary is a person other than those mentioned under (a), (b) and (c), above. If the beneficiary has a serious disability recognized under applicable law, inheritance and gift taxes will apply to its portion of the net asset value exceeding €1.5 million.

Transfer tax. In connection with the Italian stamp duty tax on the transfer of shares, according to article 37 of Law No. 248 of December 31, 2007, converted with amendments into Law No. 31 of February 28, 2008, the stamp duty has been abolished regarding contracts having as their object the transfer of shares. In certain cases, the relevant transfer acts would be subject to the registration tax at a flat amount equal to €200.

Communications Stamp Duty. A stamp duty has been introduced under article 19 of Law Decree No. 201 of December 6, 2011, converted into Law No. 214 of December 22, 2011, to be imposed on communications (issued by banks and financial intermediaries) to clients relating to securities, even where the deposit of such securities is not mandatory (although certain entities are excluded). The amount of the stamp duty is based on the market value of the securities or, in the absence of a market value, on the nominal amount or the amount payable on redemption. As a general comment, the stamp duty rate is 0.2% on a yearly *pro-rata temporis* basis (from January 1 up to December 31). The minimum amount is fixed of €34.20 up to a maximum amount of €14,000 for persons other than individuals. The communication is deemed to be sent to clients at least once a year, even where there is no obligation to issue any such communication.

Financial Transaction Tax. Law 228 of December 24, 2012, Article 1(491 – 500) introduced the Italian Financial Transaction Tax applicable: (i) to the transfer of shares and other participative financial instruments issued by companies resident in Italy ("Italian Equity") and securities representing Italian Equity, regardless of the country where the issuer has its residence (together with Italian Equity are referred to as "Qualifying Equity"); (ii) on the basis of the "value of the transaction"; (iii) regardless of the place where the transaction is concluded and of the State where the parties have their residence; (iv) to transactions on "regulated markets and on multilateral trading facilities" with a reduced rate; and (v) to over-the-counter transactions with a full rate.

The taxable event, triggering Italian Financial Transaction Tax, is the transfer of ownership of Qualifying Equity. Securities representing Italian Equity are in scope of the Italian Financial Transaction Tax, regardless of the State where the issuer has its residence. This provision is aimed at including in the scope of the Italian Financial Transaction Tax, ADRs, Global Depository Receipts and any other certificate of deposit, where the underlying securities are Italian Equity.

The value of the transaction is determined based on the net balance of the transactions settled daily, calculated for each taxpayer with reference to the number of securities traded under the transactions settled in the same day and relating to the same financial instrument.

The calculation is made by the financial intermediary responsible for the payment of the tax, i.e., the one receiving the order to execute the transaction directly from the purchaser or final counterparty.

The Italian Financial Transaction Tax is due by the person in whose favor the transfer of ownership of the Qualifying Equities occurs.

The tax rate applicable is 0.20% while the reduced rate for transactions on "regulated markets and on multilateral trading facilities" is 0.10%.

The tax shall be paid by the 16th day of the month following the one in which the relevant triggering event occurs.

The Italian Financial Transaction Tax does not apply to the transfer of ownership of Italian Equity where the issuing companies are listed in regulated markets and have a market capitalization below 500 million Euros. Such exclusion also applies to the transfer of ownership of securities representing Italian Equity.

U.S. Federal Income Taxation

THE FOLLOWING SUMMARY IS INCLUDED HEREIN FOR GENERAL INFORMATION AND IS NOT INTENDED TO BE, AND SHOULD NOT BE CONSIDERED TO BE LEGAL OR TAX ADVICE. EACH U.S. HOLDER SHOULD CONSULT WITH HIS OR HER OWN TAX ADVISOR AS TO THE PARTICULAR U.S. FEDERAL INCOME TAX CONSEQUENCES OF THE PURCHASE, OWNERSHIP AND SALE OF ADS'S, INCLUDING THE EFFECTS OF APPLICABLE STATE, LOCAL, FOREIGN OR OTHER TAX LAWS AND POSSIBLE CHANGES IN THE TAX LAWS.

Subject to the limitations described in the next paragraph, the following discussion summarizes the material U.S. federal income tax consequences to a "U.S. Holder" arising from the purchase, ownership, and sale of the ADSs. For this purpose, a "U.S. Holder" is a holder of ADSs that is: (1) an individual citizen or resident of the U.S., including an alien individual who is a lawful permanent resident of the U.S. or meets the substantial presence residency test under U.S. federal income tax laws; (2) a corporation (or entity treated as a corporation for U.S. federal income tax purposes) or a partnership (other than a partnership that is not treated as a U.S. person under any applicable U.S. Treasury regulations) created or organized under the laws of the U.S. or the District of Columbia or any political subdivision thereof; (3) an estate, the income of which is includable in gross income for U.S. federal income tax purposes regardless of source; (4) a trust if a court within the U.S. is able to exercise primary supervision over the administration of the trust and one or more U.S. persons have authority to control all substantial decisions of the trust; or (5) a trust that has a valid election in effect to be treated as a U.S. person to the extent provided in U.S. Treasury regulations.

This summary is for general information purposes only and does not purport to be a comprehensive description of all the U.S. federal income tax considerations that may be relevant to a decision to invest in or dispose of the ADSs. This summary generally considers only U.S. Holders that will own the ADSs as capital assets and who will not hold the ADSs as part of a permanent establishment in Italy. This summary does not consider the U.S. federal tax consequences to a person that is not a U.S. Holder, nor does it describe the rules applicable to determine a taxpayer's status as a U.S. Holder. This summary is based on the provisions of the Internal Revenue Code of 1986, as amended, or the Code, final, temporary and proposed U.S. Treasury regulations promulgated thereunder, administrative and judicial interpretations thereof, and the U.S./Italy Income Tax Treaty, all as in effect as of the date hereof and all of which are subject to change, possibly on a retroactive basis, and all of which are open to differing interpretations. We will not seek a ruling from the IRS regarding the U.S. federal income tax treatment of an investment in the ADSs by U.S. Holders and, therefore, can provide no assurances that the IRS will agree with the conclusions set forth below.

This discussion does not address all the aspects of U.S. federal income taxation that may be relevant to a particular U.S. holder based on such holder's particular circumstances and does not discuss any estate, gift, generation-skipping, transfer, state, local, excise or foreign tax considerations. In addition, this discussion does not address the U.S. federal income tax treatment of a U.S. Holder who is: (1) a bank, life insurance company, regulated investment company, or other financial institution or "financial services entity;" (2) a broker or dealer in securities or foreign currency; (3) a person who acquired our securities in connection with employment or other performance of services; (4) a U.S. Holder that is subject to the U.S. alternative minimum tax; (5) a U.S. Holder that holds our securities as a hedge or as part of a hedging, straddle, conversion or constructive sale transaction or other risk-reduction transaction for U.S. federal income tax purposes; (6) a tax-exempt entity; (7) real estate investment trusts or grantor trusts; (8) an expatriate or a former long-term resident of the U.S.; or, (9) a U.S. Holder having a functional currency other than the U.S. dollar. This discussion does not address the U.S. federal income tax treatment of a U.S. Holder that owns, directly or constructively, at any time, securities representing 10% or more of the voting power or value of our shares.

Additionally, the U.S. federal income tax treatment of partnerships (or other pass-through entities) or persons who hold securities through a partnership or other pass-through entity are not addressed. If a partnership (including any entity treated as a partnership for U.S. federal income tax purposes) holds ADSs, the U.S. federal income tax consequences to the partners of such partnership will depend on the activities of the partnership and the status of the partners.

Each investor is advised to consult his or her own tax adviser for the specific tax consequences to that investor of purchasing, holding, or disposing of our securities, including the effects of applicable state, local, foreign or other tax laws and possible changes in the tax laws.

Taxation of Dividends Paid on Ordinary Shares

We do not intend to pay dividends in the foreseeable future. In the event that we do pay dividends, and subject to the discussion under the heading "Passive Foreign Investment Companies" below and the discussion of "qualified dividend income" below, a U.S. Holder, other than certain U.S. Holders that are U.S. corporations, will be required to include in gross income as ordinary income the U.S. dollar amount of any distribution paid on ordinary shares (including the amount of any Italy tax withheld on the date of the distribution), to the extent that such distribution does not exceed our current and accumulated earnings and profits, as determined for U.S. federal income tax purposes. The amount of a distribution which exceeds our earnings and profits will be treated first as a non-taxable return of capital, reducing the U.S. Holder's tax basis for the ordinary shares to the extent thereof, and then as capital gain. We do not expect to maintain calculations of our earnings and profits under U.S. federal income tax principles and, therefore, U.S. Holders should expect that the entire amount of any distribution generally will be reported as dividend income. Any dividends we pay with respect to the ADSs, or ordinary shares are expected to constitute foreign source income for foreign tax credit purposes.

In general, preferential tax rates for "qualified dividend income" and long-term capital gains are applicable for U.S. Holders that are individuals, estates, or trusts. For this purpose, "qualified dividend income" means, inter alia, dividends received from a "qualified foreign corporation." A "qualified foreign corporation" is a corporation that is entitled to the benefits of a comprehensive tax treaty with the U.S. which includes an exchange of information program. The IRS has stated that the Italy/U.S. Tax Treaty satisfies this requirement and we believe we are eligible for the benefits of that treaty.

In addition, our dividends will be qualified dividend income if our ordinary shares are readily tradable on Nasdaq or another established securities market in the U.S. Dividends will not qualify for the preferential rates if we are treated, in the year the dividend is paid or in the prior year, as a PFIC, as described below under "Passive Foreign Investment Companies." A U.S. Holder will not be entitled to the preferential rate: (1) if the U.S. Holder has not held our ordinary shares for at least 61 days of the 121 day period beginning on the date which is 60 days before the ex-dividend date; or (2) to the extent the U.S. Holder is under an obligation to make related payments on substantially similar property. Any days during which the U.S. Holder has diminished its risk of loss on our ordinary shares are not counted towards meeting the 61-day holding period. Finally, U.S. Holders who elect to treat the dividend income as "investment income" pursuant to Code section 163(d)(4) will not be eligible for the preferential rate of taxation.

The amount of a distribution with respect to our ordinary shares will be measured by the amount of the fair market value of any property distributed, and for U.S. federal income tax purposes, the amount of any Italian taxes withheld therefrom. Cash distributions paid by us in Euros will be included in the income of U.S. Holders at a U.S. dollar amount based upon the spot rate of exchange in effect on the date the dividend is includible in the income of the U.S. Holder, and U.S. Holders will have a tax basis in such Euros for U.S. federal income tax purposes equal to such U.S. dollar value. If the U.S. Holder subsequently converts the Euros into U.S. dollars or otherwise disposes of it, any subsequent gain or loss in respect of such Euros arising from exchange rate fluctuations will be U.S. source ordinary exchange gain or loss.

Subject to certain limitations, Italian withholding tax, if any, paid in connection with any distribution with respect to ADSs may be claimed as a credit against a U.S. Holder's U.S. federal income tax liability if the U.S. Holder elects not to take a deduction for any non-U.S. income taxes for that taxable year; otherwise, such Italian withholding tax may be taken as a deduction. If a U.S. Holder is eligible for benefits under the Treaty or is otherwise entitled to a refund for the taxes withheld, the U.S. Holder will not be entitled to a foreign tax credit or deduction for the amount of any Italian taxes withheld in excess of the maximum rate under the Treaty or for the taxes with respect to which the U.S. Holder can obtain a refund from the Italian taxing authorities. As the relevant rules are very complex, U.S. Holders should consult their own tax advisors concerning the availability and utilization of the foreign tax credit or deductions for non-U.S. taxes in their circumstances.

Taxation of the Disposition of Ordinary Shares

Except as provided under the PFIC rules described below under "Passive Foreign Investment Companies," upon the sale, exchange or other disposition of our ordinary shares, a U.S. Holder will recognize capital gain or loss in an amount equal to the difference between such U.S. Holder's tax basis for the ordinary shares in U.S. dollars and the amount realized on the disposition in U.S. dollar (or its U.S. dollar equivalent determined by reference to the spot rate of exchange on the date of disposition, if the amount realized is denominated in a foreign currency). The gain or loss realized on the sale, exchange or other disposition of ordinary shares will be long-term capital gain or loss if the U.S. Holder has a holding period of more than one year at the time of the disposition. Individuals who recognize long-term capital gains may be taxed on such gains at reduced rates of tax. The deduction of capital losses is subject to various limitations.

Passive Foreign Investment Companies

Special U.S. federal income tax laws apply to U.S. taxpayers who own shares of a corporation that is a PFIC. We will be treated as a PFIC for U.S. federal income tax purposes for any taxable year that either:

- 75% or more of our gross income (including our pro rata share of gross income for any company, in which we are considered to own 25% or more of the shares by value), in a taxable year is passive; or

- At least 50% of our assets, averaged over the year and generally determined based upon fair market value (including our pro rata share of the assets of any company in which we are considered to own 25% or more of the shares by value) are held for the production of, or produce, passive income.

For this purpose, passive income generally consists of dividends, interest, rents, royalties, annuities, and income from certain commodities transactions and from notional principal contracts. Cash is treated as generating passive income.

Our status as a PFIC will depend on the nature and composition of our income and the nature, composition and value of our assets. Our status may also depend, in part, on how quickly we utilize cash proceeds received from previous offerings of our ADSs or ordinary shares in our business. Based on preliminary analysis, we believe that we were likely classified as a PFIC in 2024, and we may be classified as a PFIC for 2025 and future years. In particular, so long as we do not generate revenue from operations for any taxable year and do not receive any research and development grants, or even if we receive a research and development grant, if such grant does not constitute gross income for United States federal income tax purposes, we likely will be classified as a PFIC in any taxable year due to the gross income from investment of cash reserves and other passive sources that we derive.

If we currently are or become a PFIC during the holding period of a U.S. Holder, the U.S. Holder would be subject to potentially materially greater amounts of tax and subject to additional U.S. tax form filing requirements. In addition, a non-corporate U.S. Holder will not be eligible for qualified dividend income treatment on dividends received from us if we are treated as a PFIC for the taxable year in which the dividends are received or for the preceding taxable year. Specifically, each U.S. Holder who has not elected to mark the shares to market (as discussed below), would, upon receipt of certain distributions by us and upon disposition of our ordinary shares at a gain: (1) have such distribution or gain allocated ratably over the U.S. Holder's holding period for the ordinary shares, as the case may be; (2) the amount allocated to the current taxable year and any period prior to the first day of the first taxable year in which we were a PFIC would be taxed as ordinary income; and (3) the amount allocated to each of the other taxable years would be subject to tax at the highest rate of tax in effect for the applicable class of taxpayer for that year, and an interest charge for the deemed deferral benefit would be imposed with respect to the resulting tax attributable to each such other taxable year. In addition, when shares of a PFIC are acquired by reason of death from a decedent that was a U.S. Holder, the tax basis of such shares would not receive a step-up to fair market value as of the date of the decedent's death, but instead would be equal to the decedent's basis if lower, unless all gain were recognized by the decedent. Indirect investments in a PFIC may also be subject to these special U.S. federal income tax rules.

The PFIC rules described above would not apply to a U.S. Holder who makes a QEF election for all taxable years that such U.S. Holder has held the ordinary shares while we are a PFIC, provided that we comply with specified reporting requirements. Instead, each U.S. Holder who has made such a QEF election is required for each taxable year that we are a PFIC to include in income such U.S. Holder's pro rata share of our ordinary earnings as ordinary income and such U.S. Holder's pro rata share of our net capital gains as long-term capital gain, regardless of whether we make any distributions of such earnings or gain. In general, a QEF election is effective only if we make available certain required information. However, we provide no assurance as to whether we will calculate our "ordinary earnings" or "net capital gain" under U.S. tax principles or supply U.S. Holders with the required "PFIC Annual Information Statement." If we do not provide this information for any reason, it generally will not be possible for a U.S. Holder to make a QEF election if we are, or if we become, a PFIC.

In addition, the PFIC rules described above would not apply if we were a PFIC and a U.S. Holder made a mark-to-market election. A U.S. Holder of our ordinary shares which are regularly traded on a qualifying exchange, including the Nasdaq Capital Market, can elect to mark the ordinary shares to market annually, recognizing as ordinary income or loss each year an amount equal to the difference as of the close of the taxable year between the fair market value of the ordinary shares and the U.S. Holder's adjusted tax basis in the ordinary shares. Losses are allowed only to the extent of net mark-to-market gain previously included income by the U.S. Holder under the election for prior taxable years.

U.S. Holders who hold our ordinary shares during a period when we are a PFIC will be subject to the foregoing rules, even if we cease to be a PFIC. U.S. Holders are strongly urged to consult their tax advisors about the PFIC rules.

Tax on Net Investment Income

U.S. Holders who are individuals, estates, or trusts will generally be required to pay a 3.8% Medicare tax on their net investment income (including dividends on and gains from the sale or other disposition of our ordinary shares), or in the case of estates and trusts on their net investment income that is not distributed. In each case, the 3.8% Medicare tax applies only to the extent the U.S. Holder's total adjusted income exceeds applicable thresholds.

Information Reporting and Withholding

A U.S. Holder may be subject to backup withholding at a rate of 24% with respect to cash dividends and proceeds from a disposition of ordinary shares. In general, backup withholding will apply only if a U.S. Holder fails to comply with specified identification procedures. Backup withholding will not apply with respect to payments made to designated exempt recipients, such as corporations and tax-exempt organizations. Backup withholding is not an additional tax and may be claimed as a credit against the U.S. federal income tax liability of a U.S. Holder, provided that the required information is timely furnished to the IRS.

U.S. federal income tax law requires certain U.S. investors to disclose information relating to investments in securities of a non-U.S. issuer. Failure to comply with applicable disclosure requirements could result in the imposition of substantial penalties. U.S. Holders should consult their own tax advisors regarding any disclosure obligations.

F. Dividends and Paying Agents

Not applicable.

G. Statement by Experts

Not applicable.

H. Documents on Display

Documents concerning us that are referred to in this document may be inspected at our office at Via Olgettina No. 58, 20132 Milan, Italy.

In addition, we file annual reports and other information with the Securities and Exchange Commission. We file annual reports on Form 20-F and submit other information under cover of Form 6-K. As a foreign private issuer, we are exempt from the proxy requirements of Section 14 of the Exchange Act and our officers, directors, and principal shareholders are exempt from the insider short-swing disclosure and profit recovery rules of Section 16 of the Exchange Act. The Commission maintains a web site that contains reports and other information regarding registrants (including us) that file electronically with the Commission which can be assessed at http://www.sec.gov.

I. Subsidiary Information

Not required.

J. Annual Report to Security Holders

Not applicable.

ITEM 11. QUANTITATIVE AND QUALITATIVE DISCLOSURE ABOUT MARKET RISK

Genenta's activities expose it to a variety of financial risks: market risk (including foreign currency risk and interest rate risk), credit risk, and liquidity risk. The overall risk management strategy focuses on the unpredictability of the finance markets and seeks to minimize the potential adverse effects on the financial performance. Genenta uses different methods to measure different types of risk to which it is exposed. These methods include sensitivity analysis in the case of interest rate, foreign exchange, and other price risks, aging analysis for credit risk and beta analysis in respect of investment portfolios to determine market risk. Risk management is carried out under the direction of the Board. Please see Note 1 – Nature of business and history - to our audited consolidated financial statements for further information with respect to certain of these risks.

ITEM 12. DESCRIPTION OF SECURITIES OTHER THAN EQUITY SECURITIES

A. Debt Securities

Not applicable.

B. Warrants and Rights

Not applicable.

C. Other Securities

Not applicable.

D. American Depositary Shares

The Bank of New York Mellon, as depositary, collects its fees for delivery and surrender of ADSs directly from investors depositing shares or surrendering ADSs for the purpose of withdrawal or from intermediaries acting for them. The depositary collects fees for making distributions to investors by deducting those fees from the amounts distributed or by selling a portion of distributable property to pay the fees. The depositary may collect its annual fee for depositary services by deduction from cash distributions or by directly billing investors or by charging the book-entry system accounts of participants acting for them. The depositary may collect any of its fees by deduction from any cash distribution payable (or by selling a portion of securities or other property distributable) to ADS holders that are obligated to pay those fees. The depositary may generally refuse to provide fee-attracting services until its fees for those services are paid.

Persons depositing or withdrawing shares or ADS holders must pay:	***For:***
$5.00 (or less) per 100 ADSs (or portion of 100 ADSs).	Issuance of ADSs, including issuances resulting from a distribution of shares or rights or other property. Cancellation of ADSs for the purpose of withdrawal, including if the deposit agreement terminates.
$.05 (or less) per ADS. A fee equivalent to the fee that would be payable if securities distributed to you had been shares and the shares had been deposited for issuance of ADSs.	Any cash distribution to ADS holders distribution of securities distributed to holders of deposited securities (including rights) that are distributed by the depositary to ADS holders depositary services.
$.05 (or less) per ADS per calendar year. Registration or transfer fees. Expenses of the depositary.	Transfer and registration of shares on our share register to or from the name of the depositary or its agent when you deposit or withdraw shares. Cable (including SWIFT) and facsimile transmissions (when expressly provided in the deposit agreement) Converting foreign currency to U.S. dollars, as necessary.
Taxes and other governmental charges the depositary or the custodian has to pay on any ADSs or shares underlying ADSs, such as stock transfer taxes, stamp duty or withholding taxes. Any charges incurred by the depositary or its agents for servicing the deposited securities.	As necessary.

From time to time, the depositary may make payments to us to reimburse us for costs and expenses generally arising out of establishment and maintenance of the ADS program, waive fees and expenses for services provided to us by the depositary or share revenue from the fees collected from ADS holders. In performing its duties under the deposit agreement, the depositary may use brokers, dealers, foreign currency dealers or other service providers that are owned by or affiliated with the depositary and that may earn or share fees, spreads, or commissions.

The depositary may convert currency itself or through any of its affiliates, or the custodian or we may convert currency and pay U.S. dollars to the depositary. Where the depositary converts currency itself or through any of its affiliates, the depositary acts as principal for its own account and not as agent, advisor, broker, or fiduciary on behalf of any other person and earns revenue, including, without limitation, transaction spreads, that it will retain for its own account. The revenue is based on, among other things, the difference between the exchange rate assigned to the currency conversion made under the deposit agreement and the rate that the depositary or its affiliate receives when buying or selling foreign currency for its own account. The depositary makes no representation that the exchange rate used or obtained by it or its affiliate in any currency conversion under the deposit agreement will be the most favorable rate that could be obtained at the time or that the method by which that rate will be determined will be the most favorable to ADS holders, subject to the depositary's obligation to act without negligence or bad faith. The methodology used to determine exchange rates used in currency conversions made by the depositary is available upon request. Where the custodian converts currency, the custodian has no obligation to obtain the most favorable rate that could be obtained at the time or to ensure that the method by which that rate will be determined will be the most favorable to ADS holders, and the depositary makes no representation that the rate is the most favorable rate and will not be liable for any direct or indirect losses associated with the rate. In certain instances, the depositary may receive dividends or other distributions from the us in U.S. dollars that represent the proceeds of a conversion of foreign currency or translation from foreign currency at a rate that was obtained or determined by us and, in such cases, the depositary will not engage in, or be responsible for, any foreign currency transactions and neither it nor we make any representation that the rate obtained or determined by us is the most favorable rate and neither it nor we will be liable for any direct or indirect losses associated with the rate.

PART II

ITEM 13. DEFAULTS, DIVIDEND ARREARAGES AND DELINQUENCIES

Not applicable.

ITEM 14. MATERIAL MODIFICATIONS TO THE RIGHTS OF SECURITY HOLDERS AND USE OF PROCEEDS Material Modifications to the Rights of Security Holders

See "Item 10. Additional Information" for a description of the rights of securities holders, which remain unchanged.

ITEM 15. CONTROLS AND PROCEDURES

Disclosure Controls and Procedures

Disclosure controls and procedures are designed to ensure that information required to be disclosed by us in reports filed or submitted under the Securities Exchange Act of 1934, as amended (the "Exchange Act"), is recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms. Disclosure controls include, without limitation, controls and procedures designed to ensure that information required to be disclosed under the Exchange Act is accumulated and communicated to management, including principal executive and financial officers, as appropriate, to allow timely decisions regarding required disclosure. There are inherent limitations to the effectiveness of any system of disclosure controls and procedures, including the possibility of human error and the circumvention or overriding of the controls and procedures. Accordingly, even effective disclosure controls and procedures can only provide reasonable assurance of achieving their control objectives.

Our management carried out an evaluation, under the supervision of our chief executive officer and chief financial officer, of the effectiveness of our disclosure controls and procedures as such term is defined under Rule 13a-15(e) promulgated under the Exchange Act as of December 31, 2022. Based on that evaluation, our management, including our chief executive officer and chief financial officer, has concluded that the Company's disclosure controls and procedures were effective as of December 31, 2024.

Management's Annual Report on Internal Control over Financial Reporting

The Company's internal control over financial reporting is a process designed under the supervision of the chief executive officer and chief financial officer to provide reasonable assurance as to the reliability of the Company's financial reporting and the preparation of its consolidated financial statements for external purposes in accordance with generally accepted accounting principles. Our management is responsible for establishing and maintaining adequate internal control over financial reporting, as such term is defined in Rule 13a-15(f) under the Securities Exchange Act of 1934, as amended.

Internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of consolidated financial statements in accordance with U.S. GAAP and includes those policies and procedures that (1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of a company's assets; (2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of consolidated financial statements in accordance with generally accepted accounting principles, and that a company's receipts and expenditures are being made only in accordance with authorizations of a company's management and directors; and (3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of a company's assets that could have a material effect on the consolidated financial statements.

Because of its inherent limitations, a system of internal control over financial reporting can provide only reasonable assurance with respect to consolidated financial statements preparation and presentation and may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

Management evaluated the effectiveness of our internal control over financial reporting as of December 31, 2024 and concluded our internal control over financial reporting was effective as of December 31, 2024. In making this evaluation, management used the framework established in Internal Control — Integrated Framework (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission ("COSO"). The COSO framework summarizes each of the components of a company's internal control system, including the control environment, risk assessment, control activities, information and communication, and monitoring activities.

Remediation of Previously Disclosed Material Weaknesses

As previously disclosed in Item 15 "Controls and Procedures" of our prior Annual Reports on Form 20-F, management previously identified and disclosed material weaknesses in internal control over financial reporting, including but not limited to our lack of adequate staff to: (i) process financial information in a timely manner; (ii) analyze and account for complex, non-routine transactions - including those subject to the Company's critical accounting policies; and (iii) maintain adequate segregation of duties; and the lack of documentation related to the Company's internal control over financial reporting including its policy over related party relationships and transactions. During the quarter ended December 31, 2023, we remediated our previously reported material weaknesses related to these matters.

In particular, our management, with oversight from our board of statutory auditors, executed a remediation plan, in order to fully remediate the historical causes of the material weaknesses. As of December 31, 2024, the Company had taken the following steps to address the internal control deficiencies that contributed to the material weaknesses in prior periods, including, but not limited to, the following:

- new hires of additional finance and accounting personnel with high professional skills, prior experience working for finance departments, and technical accounting experience, supplemented by third-party resources, maintain the overall control over the relevant operating activities, having in place incremental and compensating controls;

● implementation of a new accounting and reporting system - cloud-based ERP system - with controlled access, approval workflow and segregation of duties to avoid to rely on third party service provider for the accounting and financial reporting closing process;

● improvement of the documentation and formally assessed our accounting and financial reporting policies and procedures; and

● increase in the use of third-party consultants in assessing significant accounting transactions and other technical accounting and financial reporting issues, preparing accounting memoranda addressing these issues and maintaining these memoranda in our corporate records.

Attestation Report of Independent Registered Public Accounting Firm

Not required.

Changes in Internal Controls over Financial Reporting

Except as described above under "—Management's Annual Report on Internal Control over Financial Reporting—Remediation of Previously Disclosed Material Weaknesses," there were no changes in our internal control over financial reporting (as defined in Rule 13a-15(f) of the Exchange Act, as amended) that occurred during the year ended December 31, 2024 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

ITEM 16. [RESERVED]

ITEM 16A. AUDIT COMMITTEE FINANCIAL EXPERT.

Our Board of Directors has determined that, because of the existence and nature of its board of statutory auditors, it qualifies for an exemption provided by Rule 10A-3(c)(3) of the Exchange Act from many of the Rule 10A-3 audit committee requirements. The board of statutory auditors has determined that each of its members is an "audit committee financial expert" as defined in Item 16A of Form 20-F. For the names of the members of the board of statutory auditors, see "Item 6. Directors, Senior Management and Employees—Statutory Auditors".

Each of the audit committee financial experts is independent under the Nasdaq Independence Standards that would apply to audit committee members in the absence of our reliance on the exemption in Rule 10A-3(c)(3).

ITEM 16B. CODE OF ETHICS.

The Company has adopted a Code of Conduct that applies to its Chief Executive Officer and all of its directors, officers and employees, or persons performing similar functions. A copy of our Code of Conduct is available at its website. Any future changes to the Code of Conduct will be posted on the Company's website or filed as an exhibit to a report filed with the SEC within five business days of the change being effective.

ITEM 16C. PRINCIPAL ACCOUNTANT FEES AND SERVICES.

The following table represents aggregate fees billed to the Company for fiscal years ended December 31, 2024 and 2023 by Dannible & McKee, LLP ("Dannible & McKee" or "DM"), the Company's principal accounting firm, and Mayer, Hoffman McCann P.C. ("MHM"), the Company's former principal accounting firm.

Accountant Fees and Services (in Euros)	**2024**	**2023**
Audit Fees	€ 282,006	€ 433,884
	€ 282,006	€ 433,884

For the fiscal year ended December 31, 2024, Dannible & McKee billed €270,006.

For the fiscal year ended December 31, 2023, Dannible & McKee billed €312,629, MHM billed €121,255.

Audit Fees

The audit fees for the years ended December 31, 2024 and 2023 respectively, were paid for professional services rendered for the audits of our consolidated financial statements, half year reviews, consents, and assistance with review of documents filed with the SEC.

Tax Fees

Not applicable.

Other Fees

Not applicable.

Pre-Approval Policies and Procedures

Prior to engaging , Dannible & McKee to perform audit services, our Board obtains an estimate for the service to be performed. All of the services described above were approved by the members of the board of statutory auditors in accordance with its procedures.

ITEM 16D. EXEMPTIONS FROM THE LISTING STANDARDS FOR AUDIT COMMITTEES.

Genenta is relying on the exemption from listing standards for audit committees provided by Exchange Act Rule 10A-3(c)(3). The basis for this reliance is that Genenta's board of statutory auditors meets the following requirements set forth in Exchange Act Rule 10A-3(c)(3):

- the board of statutory auditors is established and selected pursuant to Italian law expressly permitting such a board;
- the board of statutory auditors is required under Italian law to be separate from Genenta's board of directors;
- the board of statutory auditors is not elected by management of Genenta and no executive officer of Genenta is a member of the board of statutory auditors;
- Italian law provides for standards for the independence of the board of statutory auditors from Genenta and its management;
- the board of statutory auditors, in accordance with applicable Italian law and Genenta's governing documents, is responsible, to the extent permitted by Italian law, for the appointment, retention and oversight of the work (including, to the extent permitted by law, the resolution of disagreements between management and the auditor regarding financial reporting) of any registered public accounting firm engaged for the purpose of preparing or issuing an audit report or performing other audit, review or attest services for Genenta, and
- to the extent permitted by Italian law, the audit committee requirements of paragraphs (b)(3), (b)(4) and (b)(5) of Rule 10A-3 apply to the board of statutory auditors.

The Company's reliance on Rule 10A-3(c)(3) does not, in its opinion, materially adversely affect the ability of its board of statutory auditors to act independently and to satisfy the other requirements of Rule 10A-3.

ITEM 16E. PURCHASES OF EQUITY SECURITIES BY THE ISSUER AND AFFILIATED PURCHASERS.

Not applicable.

ITEM 16F. CHANGE IN REGISTRANT'S CERTIFYING ACCOUNTANT.

Not applicable.

ITEM 16G. CORPORATE GOVERNANCE.

See "Item 6. Directors, Senior Management and Employees – C. Board Practices – Differences between Italian Laws and Nasdaq Requirements."

ITEM 16H. MINE SAFETY DISCLOSURE.

Not applicable.

ITEM 16I. DISCLOSURE REGARDING FOREIGN JURISDICTIONS THAT PREVENT INSPECTIONS.

Not applicable.

ITEM 16J. INSIDER TRADING POLICIES

We have adopted an insider trading policy and related procedures that govern the purchase, sale, and other disposition of our securities by directors, officers, and employees, as well as consultants and contractors who have access to material nonpublic information. We believe our insider trading policy and procedures are reasonably designed to promote compliance with insider trading laws, rules and regulations, and applicable Nasdaq listing standards. Our insider trading policy and procedures prohibit our directors, officers and employees, and consultants and contractors who have access to material nonpublic information, from trading in our securities while in possession of material, non-public information, among other things.

The foregoing description of our insider trading policy and procedures does not purport to be complete and is qualified in its entirety by the terms and conditions of our insider trading policy, a copy of which is attached hereto as Exhibit 11.1 and is incorporated herein by reference.

ITEM 16K. CYBERSECURITY.

We recognize the critical importance of maintaining the trust and confidence of our patients, business partners, employees and other stakeholders. As a result, cybersecurity risk management is an integral part of our overall risk management and compliance program and our current cybersecurity risk management processes are modeled after industry best practices, such as the National Institute of Standards and Technology Cybersecurity Framework, for handling cybersecurity threats and incidents, including threats and incidents associated with the use of applications developed by third-party service providers, and facilitate coordination across different departments of our Company.

Our board of directors has overall oversight responsibility for our cybersecurity risk management; however, it delegates cybersecurity risk management oversight to our management and board of statutory auditors. Our management and board of statutory auditors is responsible for ensuring that we have processes in place designed to identify and evaluate cybersecurity risks to which we are exposed and implement processes and programs to manage cybersecurity risks and mitigate cybersecurity incidents.

These processes include steps for assessing the severity of a cybersecurity threat, identifying the source of a cybersecurity threat, including whether the cybersecurity threat is associated with a third-party service provider, implementing cybersecurity countermeasures and mitigation strategies, and informing management and our board of directors of material cybersecurity threats and incidents. Our information technology consultant is responsible for assessing our cybersecurity risk management program, and we currently do not engage other third parties for such assessment.

Our cybersecurity program is under the direction of our Chief Financial Officer and Finance Director, who receive reports from our information technology consultant and monitors the prevention, detection, mitigation, and remediation of cybersecurity incidents. Our Chief Financial Officer and Finance Director together have over 50 years of information technology experience in various roles of increasing importance. Their experience includes overseeing and supervising information technology risk management processes. Among their other duties as Chief Financial Officer and Finance Director, respectively, they manage our cybersecurity consultant, who is a certified and experienced information security professional, and he has been instrumental in the implementation and monitoring of our various cybersecurity systems and tools.

Management is responsible for identifying, considering, and assessing material cybersecurity risks on an ongoing basis, establishing processes to ensure that such potential cybersecurity risk exposures are monitored, putting in place appropriate mitigation measures and maintaining cybersecurity programs, including:

- implementing a comprehensive, cross-functional approach to identifying, preventing and mitigating cybersecurity threats and incidents, while also implementing controls and procedures that provide for the prompt escalation of certain cybersecurity incidents so that decisions regarding the public disclosure and reporting of such incidents can be made by management in a timely manner;

- deploying technical safeguards that are designed to protect our information systems from cybersecurity threats, including firewalls, intrusion prevention and detection systems, anti-malware functionality and access controls, which are evaluated and improved through vulnerability assessments and cybersecurity threat intelligence;

- establishing and maintaining comprehensive incident response and recovery plans that fully address our response to a cybersecurity incident, and such plans are tested and evaluated on a regular basis; and

- providing regular, mandatory training for personnel regarding cybersecurity threats as a means to equip our personnel with effective tools to address cybersecurity threats, and to communicate our evolving information security policies, standards, processes and practices

Management, including our Chief Financial Officer and Finance Director, regularly update our board of statutory auditors on our cybersecurity processes, material cybersecurity risks and mitigation strategies. Our board of statutory auditors reports all material cybersecurity risks to our board of directors.

During the year ended December 31, 2024, we augmented our cybersecurity program to be a more comprehensive cybersecurity risk management program. Our roadmap for the future is centered on improving cybersecurity risk awareness for our employees and collaborators to strengthen our defenses, enhance our threat detection capabilities, and ensure the confidentiality, integrity, and availability of our critical systems and data.

Although we are subject to ongoing and evolving cybersecurity threats, we are not aware of any material risks from cybersecurity threats in 2024 that have materially affected or are reasonably likely to materially affect us, including our business strategy, results of operations or financial condition. For more information on our cybersecurity risks, see "Risk Factors — Our internal information technology systems, or those of our third party vendors, collaborators, or other contractors or consultants, may fail or suffer cyber security breaches or other unauthorized or improper access, which could result in a significant disruption of our product development programs, give rise to significant liability, subject us to costly and protracted litigation, cause significant reputational harm, and impact our ability to operate our business effectively."

PART III

ITEM 17. CONSOLIDATED FINANCIAL STATEMENTS

Our audited Consolidated Financial Statements are included as the "F" pages attached to this report.

All consolidated financial statements in this Annual Report, unless otherwise stated, are presented in accordance with US GAAP.

ITEM 18. CONSOLIDATED FINANCIAL STATEMENTS

The Company has elected to provide consolidated financial statements pursuant to ITEM 17.

ITEM 19. EXHIBITS

Exhibit No.	Description
2.4	Description of Securities
3.1*	Deed of Incorporation of Genenta Science S.p.A.
3.2****	Amended and Restated Bylaws of Genenta Science S.p.A.
3.3*****	Amendment to the Amended and Restated Bylaws of Genenta Science S.p.A.
4.1*	Deposit Agreement dated December 17, 2021 between the Company and The Bank of New York Mellon, as depositary.
4.2*	Form of American Depositary Receipt (included in exhibit 4.1)
4.3**	Underwriter Warrants dated December 17, 2021
8.1	List of subsidiaries of the registrant
10.1****,†	Amended and Restated License Agreement between Genenta Science S.p.A. and Ospedale San Raffaele S.r.l. ("OSR") dated March 23, 2023 (the "ARLA")
10.2###,†	Amendment to ARLA dated September 28, 2023
10.3###,†	Sponsored Research Agreement with OSR dated August 1, 2023
10.4*,†	Sponsored Research Agreement with OSR dated February 12, 2021
10.5*	Know-How License Agreement with Fondazione Telethon dated February 2, 2016
10.6*,†	Master Service Agreement dated March 6, 2019, between Molecular Medicine S.p.A. and Genenta Science S.p.A.
10.7*	2021-2025 Genenta Science Employee Share Option Plan with Chairman Sub-Plan
10.8*	Employment Agreement of Pierluigi Paracchi
10.9*	Employment Agreement of Carlo Russo
10.11*	Employment Agreement of Richard B. Slansky
10.12##,†	Development and Manufacturing Services Agreement dated January 20, 2023 between AGC Biologics S.p.A. and Genenta Science S.p.A.
10.13####	Amendment to the AGC Master Service Agreement dated September 19, 2024.
10.14####	Agreement for the Conduct of Clinical Trials on Medicinal Products with OSR dated October 14, 2024.
10.15#####	ATM Sales Agreement, dated April 26, 2024, among the Company and the Sales Agents
10.16######	Amendment No. 1 to ATM Sales Agreement, dated December 20, 2024, among the Company and the Sales Agents
10.17#######†	Second Amendment to Development and Master Services Agreement, by and between the Company and AGC Biologics S.p.A., effective as of December 24, 2024.
10.18########	Subscription Agreement
10.19########	Mandatory Convertible Bond Regulation
11.1**	Code of Business Conduct and Ethics of the Registrant
11.2	Insider Trading Policy
12.1	Certification of the Chief Executive Officer (Principal Executive Officer) pursuant to Rule 13a-14(a) of the Securities Exchange Act, as amended
12.2	Certification of the Chief Financial Officer (Principal Financial Officer) pursuant to Rule 13a-14(a) of the Securities Exchange Act, as amended
13.1	Certification of the Chief Executive Officer and Chief Financial Officer pursuant to 18 U.S.C. 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002
23.1	Consent of Dannible & McKee, LLP
97.1**	Compensation Recovery Policy of Registrant
101.INS	Inline XBRL Instance Document
101.SCH	Inline XBRL Taxonomy Extension Schema Document
101.CAL	Inline XBRL Taxonomy Extension Calculation Linkbase Document
101.DEF	Inline XBRL Taxonomy Extension Definition Linkbase Document
101.LAB	Inline XBRL Taxonomy Extension Label Linkbase Document
101.PRE	Inline XBRL Taxonomy Extension Presentation Linkbase Document
104	Cover Page Interactive Data File (formatted as Inline XBRL and contained in Exhibit 101).

* Incorporated by reference to the registration statement on Form F-1 of the Registrant (File No. 333-260923).

** Incorporated by reference to the Annual Report on Form 20-F of the Registrant filed on March 29, 2024.

*** Incorporated by reference to the Form 6-K of the Registrant filed on October 3, 2022.

**** Incorporated by reference to the Annual Report on Form 20-F of the Registrant filed on April 21, 2023.

***** Incorporated by reference to the Form 6-K of the Registrant filed on May 3, 2024.

Incorporated by reference to the Form 6-K of the Registrant filed on December 22, 2022.

Incorporated by reference to the Form 6-K of the Registrant filed on February 1, 2023.

Incorporated by reference to the Form 6-K of the Registrant filed on October 20, 2023.

Incorporated by reference to the Form 6-K of the Registrant filed on October 29, 2024.

Incorporated by reference to the Form 6-K of the Registrant filed on April 26, 2024.

####### Incorporated by reference to the Form 6-K of the Registrant filed on December 20, 2024.

######## Incorporated by reference to the Form 6-K of the Registrant filed on December 30, 2024.

######### Incorporated by reference to the Form 6-K of the Registrant filed on March 19, 2025.

† Portions of these exhibits (indicated with markouts) have been redacted in accordance with Item 601(b)(10)(iv).

SIGNATURES

The Registrant hereby certifies that it meets all of the requirements for filing on Form 20-F and that it has duly caused and authorized the undersigned to sign this annual report on its behalf.

GENENTA SCIENCE S.P.A.

By:	***/s/ Pierluigi Paracchi***	**By:**	***/s/ Richard B. Slansky***
Name:	**Pierluigi Paracchi**	**Name:**	**Richard B. Slansky**
Title:	**Chief Executive Officer (Principal Executive Officer)**	**Title:**	**Chief Financial Officer (Principal Financial and Accounting Officer)**
Date:	**March 28, 2025**	**Date:**	**March 28, 2025**

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

Report of Independent Registered Public Accounting Firm

To the Board of Directors and Shareholders of Genenta Science S.p.A.:

Opinion on the Consolidated Financial Statements

We have audited the accompanying consolidated Balance Sheets of Genenta Science S.p.A. ("the Company") as of December 31, 2024, 2023, and 2022 and the related consolidated statements of operations and comprehensive loss, changes in shareholders' equity, and cash flows for each of the years in the three-year period ended December 31, 2024, and the related notes to the consolidated financial statements (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2024, 2023 and 2022 and the results of its operations and its cash flows for each of the years in the three-year period ended December 31, 2024, in conformity with accounting principles generally accepted in the United States of America.

Basis for Opinion

These consolidated financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these consolidated financial statements based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) ("PCAOB") and are required to be independent with respect to the Company in accordance with the U.S. Federal Securities Laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audits to obtain reasonable assurance about whether the consolidated financial statements are free of material misstatement, whether due to error or fraud. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. As part of our audits, we are required to obtain an understanding of internal control over financial reporting but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion.

Our audits included performing procedures to assess the risks of material misstatement of the consolidated financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the consolidated financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the consolidated financial statements. We believe that our audits provide a reasonable basis for our opinion.

We have served as the Company's auditor since 2021.

/s/ Dannible & McKee, LLP

Syracuse, New York
March 28, 2025

Genenta Science S.p.A.
Consolidated Statements of Operations and Comprehensive Loss

	Year Ended December 31,		
	2024	**2023**	**2022**
		(in Euros)	
Operating expenses			
Research and development	€ 4,812,854	€ 6,474,441	€ 5,338,962
General and administrative	4,951,456	5,258,501	5,705,030
Total operating expenses	9,764,310	11,732,942	11,043,992
Loss from operations	(9,764,310)	(11,732,942)	(11,043,992)
Other income (expense)			
Others income (expense)	529,683	(4,875)	242,554
Finance income	81,140	309,253	36,985
Net exchange rate gain (loss)	240,992	(216,891)	2,286,690
Total other income (expense), net	851,815	87,487	2,566,229
Loss before income taxes	(8,912,495)	(11,645,455)	(8,477,763)
Income tax benefit (expense)	-	-	
Net loss	€ (8,912,495)	€ (11,645,455)	€ (8,477,763)
Net loss per share - basic	€ (0.49)	€ (0.64)	€ (0.47)
Weighted average number of shares outstanding - basic and diluted	18,273,490	18,216,907	18,216,858
Other comprehensive income (loss)			
Total change of marketable debt securities	(118,750)	214,984	-
Change in foreign currency translation	(23,446)	(15,853)	-
Total other comprehensive income (loss)	(142,196)	199,131	-
Comprehensive loss	€ (9,054,691)	€ (11,446,324)	€ (8,477,763)

The accompanying notes are an integral part of these consolidated financial statements.

Genenta Science S.p.A.
Consolidated Balance Sheets

	At December 31, 2024	At December 31, 2023	At December 31, 2022
	(in Euros)		
Assets			
Current assets			
Cash and cash equivalents	€ 4,581,749	€ 3,691,420	€ 29,794,856
Marketable Securities	8,078,002	15,084,284	-
Prepaid expenses and other current assets	1,813,226	2,480,554	1,926,512
Total current assets	14,472,977	21,256,258	31,721,368
Non-current assets			
Fixed assets, net	€ 42,922	€ 82,977	€ 111,639
Other non-current assets	304,744	1,004,560	1,601,503
Other non-current assets - related party	3,350	3,350	3,350
Total non-current assets	351,016	1,090,887	1,716,492
Total assets	€ 14,823,993	€ 22,347,145	€ 33,437,860
Liabilities and shareholders' equity			
Current liabilities			
Accounts payable	€ 317,830	€ 294,975	€ 1,042,054
Accounts payable - related party	180,116	170,888	151,988
Accrued expenses	232,307	153,136	202,389
Accrued expenses - related party	1,031,345	861,578	489,207
Other current liabilities	337,764	255,062	297,875
Total current liabilities	2,099,362	1,735,639	2,183,513
Non-current liabilities			
Other non current liabilities	1,158	14,594	27,218
Retirement benefit obligation	227,767	164,655	88,963
Total long-term liabilities	228,925	179,249	116,181
Commitments and contingencies	-	-	-
Shareholders' equity			
Ordinary shares, no par value, 59,700,000 shares authorized and 18,289,866 and 18,216,958 shares issued and outstanding respectively	68,462,280	67,344,140	66,603,725
Accumulated deficit	(56,055,520)	(47,143,025)	(35,465,559)
Accumulated other comprehensive income	88,946	231,142	-
Total shareholders' equity	12,495,706	20,432,257	31,138,166
Total liabilities and shareholders' equity	€ 14,823,993	€ 22,347,145	€ 33,437,860

The accompanying notes are an integral part of these consolidated financial statements.

Genenta Science S.p.A.
Consolidated Statement of Changes in Shareholders' Equity

	Common shares outstanding	Common stock, no par value	Accumulated deficit	Accumulated other comprehensive income	Total
Balance at December 31, 2021	18,216,858	€ 65,880,990	€ (27,019,807)	€ -	€ 38,861,183
Share-based compensation	-	722,735	-	-	722,735
Cumulative Translation Adjustment	-	-	32,011	-	32,011
Net loss	-	-	(8,477,763)	-	(8,477,763)
Balance at December 31, 2022	18,216,858	€ 66,603,725	€ (35,465,559)	€ -	€ 31,138,166
Share-based compensation	-	739,884	-	-	739,884
Capital increase ATM program	100	531	-	-	531
Other comprehensive income	-	-	(32,011)	231,142	199,131
Net loss	-	-	(11,645,455)	-	(11,645,455)
Balance at December 31, 2023	18,216,958	€ 67,344,140	€ (47,143,025)	€ 231,142	€ 20,432,257
Share-based compensation	-	847,255	-	-	847,255
Capital increase ATM program	72,908	270,885	-	-	270,885
Other comprehensive loss	-	-	-	(142,196)	(142,196)
Net loss	-	-	(8,912,495)	-	(8,912,495)
Balance at December 31, 2024	18,289,866	€ 68,462,280	€ (56,055,520)	€ 88,946	€ 12,495,706

The accompanying notes are an integral part of these consolidated financial statements.

Genenta Science S.p.A.
Consolidated Statements of Cash Flows

	At December 31,		
	2024	**2023**	**2022**
		(in Euros)	
Cash flows from operating activities			
Net loss	€ (8,912,495)	€ (11,645,455)	€ (8,477,763)
Adjustments to reconcile net loss to net cash used in operating activities:			
Foreign exchange adjustment	-	-	32,011
Depreciation and amortization expense	44,523	42,453	6,140
Retirement benefit obligation	63,112	75,692	58,344
Share-based compensation	847,255	739,884	722,735
Changes in operating assets and liabilities			
Prepaid expenses and other current assets	667,328	(554,042)	(407,489)
Other non-current assets	699,816	596,943	(427,906)
Accounts payable	22,855	(747,079)	877,235
Accounts payable - related party	9,228	18,900	126,941
Accrued expenses	79,171	(49,253)	(509,924)
Accrued expenses - related party	169,767	372,371	357,066
Other current liabilities	82,702	(42,813)	197,156
Other non-current liabilities	(13,436)	(12,624)	27,218
Net cash used in operating activities	(6,240,174)	(11,205,023)	(7,418,236)
Cash flows from investing activities			
Purchases of marketable securities	(16,380,363)	(14,878,875)	-
Proceeds from maturities of marketable securities	23,267,895	-	-
Purchases of fixed assets	(4,468)	(13,791)	(27,070)
Net cash (used in)/produced by investing activities	6,883,064	(14,892,666)	(27,070)
Cash flows from financing activities			
Proceeds from ATM	270,885	531	-
Net cash provided by financing activities	270,885	531	-
Effect of exchange rate changes	(23,446)	(6,278)	-
Net increase (decrease) in cash and cash equivalents	890,329	(26,103,436)	(7,445,306)
Cash and cash equivalents at beginning of period	3,691,420	29,794,856	37,240,162
Cash and cash equivalents at end of period	€ 4,581,749	€ 3,691,420	€ 29,794,856

The accompanying notes are an integral part of these consolidated financial statements.

1. **Nature of business and history**

Genenta Science S.p.A. (the "Company" or "Genenta") was founded in Milan, Italy by San Raffaele Hospital ("OSR"), Pierluigi Paracchi, Luigi Naldini, and Bernhard Gentner, and was incorporated in July 2014. The registered office (or headquarters) is located in Milan, Italy. The Company's reporting currency is Euros ("EUR" or "€"). The Company formed a wholly owned, Delaware incorporated subsidiary, Genenta Science, Inc., intended for future operations in the U.S. ("U.S. Subsidiary"). The U.S. Subsidiary operates in U.S. Dollars ("USD" or "$").

The Company stock has been publicly traded on The NASDAQ Capital Market since December 15, 2021.

Genenta is an early-stage company developing first-in-class cell and gene therapies to address unmet medical needs in cancerous solid tumors. The Company is initially developing its clinical leading product, Temferon™, to treat glioblastoma multiforme ("GBM"), a solid tumor affecting the brain. The Company intends to continue its clinical trials in Italy and eventually start a clinical trial in Europe and the U.S. to study Temferon™ in other cancers. In June 2023, the Company's Board of Directors selected metastatic Renal Cell Cancer ("mRCC") as the second solid tumor indication for Temferon. The Company is currently enrolling patients for a Phase 1 trial in mRCC. The Company has recently completed its Phase 1 trial in GBM and its Phase 2a trial in GBM is ongoing.

The Company is subject to risks and uncertainties common to early-stage clinical companies in the life-science and biotechnology industries, including but not limited to, risks associated with completing preclinical studies and clinical trials, receiving regulatory approvals for product candidates, development by competitors of new competing products, dependence on key personnel, protection of proprietary technology, compliance with government regulations and the ability to secure additional capital to fund operations. The clinical product candidates currently under development will require significant additional research and development efforts, including regulatory approval and clinical testing before commercialization. These efforts require additional capital, adequate personnel and infrastructure, and extensive compliance-reporting capabilities. Even if the Company's product development efforts are successful, it is uncertain when, if ever, the Company will realize revenue from product sales and profit from operations.

In June 2023, the Company's stockholders reduced the number of directors from seven (7) to five (5).

Liquidity and risks

The Company has incurred losses since its inception, including a net loss of €8.9 million, €11.6 million, and €8.5 million for the years ended December 31, 2024, December 31, 2023, and December 31, 2022, respectively. In addition, as of December 31, 2024, the Company had an accumulated deficit of €56.1 million. The Company has primarily funded these losses through the proceeds from sales of convertible debt and equity. Although the Company has incurred recurring losses and expects to continue to incur losses for the foreseeable future, the Company expects that its existing cash and cash equivalents and marketable securities on hand as of December 31, 2024 of €12.7 million, will be sufficient to fund current planned operations and capital expenditure requirements for at least the next twelve months from the filing date of these consolidated financial statements. However, the future viability of the Company is dependent on its ability to raise additional capital to finance its operations. The Company's inability to raise capital as and when needed could have a negative impact on its financial condition and ability to pursue its business strategies. There can be no assurance that the current operating plan will be achieved or that additional funding will be available on terms acceptable to the Company, or at all.

The Company has evaluated whether there are conditions and events considered in the aggregate that raise substantial doubt about the Company's ability to continue as a going concern. The Company's business model, typical of biotechnology companies developing new therapeutic products that have not reached a balanced income and financial position, features negative cash flows. This is because, at this stage, costs must be borne in relation to services and personnel, directly connected to research and development activities, and return for these activities is not certain and, in any case, it is expected in future years. Based on the accounting policies adopted, requiring full recognition of research and development costs in the Statement of Operations and Comprehensive Loss in the year they are incurred, the Company has reported a loss since its inception and expects to continue to incur significant costs for research and development in the foreseeable future. There is no certainty that the Company will become profitable in the future.

The Company will require additional capital to meet its long-term operating requirements. It expects to raise additional capital through, among other things, the sale of equity or debt securities, which may include sales of ADSs pursuant to the Sales Agreement (as defined below). If adequate funds are not available in the future, the Company may be forced to delay, reorganize, or cancel research and development programs, or to enter into financing, licensing or collaboration agreements with unfavorable conditions or waive rights to certain products which otherwise it would not have waived, resulting in negative effects on the activity and on the economic, patrimonial and /or financial situation of the Company.

The Company's ability to raise additional capital may be adversely impacted by the potential worsening of global economic and political conditions and volatility in the credit and financial markets in the U.S. and worldwide. This could be exacerbated by, among other factors, inflation, fluctuating interest rates, tariffs and geopolitical conflicts. The Company's failure to raise capital as and when needed or on acceptable terms could have a negative impact on the Company's financial condition and its ability to pursue its business strategy and the Company may have to delay, reduce the scope of, suspend or eliminate one or more of its research-stage programs, clinical trials, or future commercialization efforts.

Shelf Registration Statement and Sales Agreement

On May 12, 2023, the Company filed with the Securities and Exchange Commission (the "SEC") a shelf registration statement on Form F-3 that was subsequently declared effective on May 24, 2023 (the "Shelf Registration Statement"). The Shelf Registration Statement permits the Company to sell from time-to-time ordinary shares, including ordinary shares represented by ADSs, or rights to subscribe for ordinary shares or ordinary shares represented by ADSs in one or more offerings in amounts, at prices, and on the terms that the Company will determine at the time of offering for aggregate gross sale proceeds of up to $100.0 million.

In July 2023, the Company issued 100 ADSs for gross proceeds of €531 (or $582), increasing the total number of shares outstanding to 18,216,958, pursuant to a Controlled Equity Offering Sales Agreement, dated May 12, 2023 (the "Sales Agreement"), between the Company and Cantor Fitzgerald & Co. ("Cantor"), as agent, subject to the terms and conditions described in the Sales Agreement and SEC rules and regulations (the "ATM Offering").

In March 2024, the Company issued 72,908 ADSs for net proceeds of approximately €271,000 (or approximately $293,000), bringing the total number of ordinary shares outstanding to 18,289,866, pursuant to the Sales Agreement. On March 28, 2024, the Company and Cantor mutually agreed to terminate the Sales Agreement.

On April 26, 2024, the Company entered into an ATM Sales Agreement (the "Original Sales Agreement") with Capital One Securities, Inc. and Virtu Americas LLC (the "Sales Agents"), pursuant to which the Company may offer and sell ADSs, for an aggregate offering price of up to $16,362,816 from time to time through or to the Sales Agents, acting as sales agents or principals, subject to the terms and conditions described in the Original Sales Agreement and SEC rules and regulations (the "Original ATM Offering").

In May 2024, the Company's shareholders approved an amendment of article 9 of the Company's Bylaws, increasing voting rights to certain stockholders by introducing a mechanism whereby each ordinary share owned by either an entity or an individual for a continuous period of not less than twenty-four months entitles the holder to a double vote and therefore to an increase from one to two votes per share. In addition, a further vote is attributed at the end of each twelve-months, following the first vesting period of twenty-four months, in which the ordinary share belonged to the same entity or individual, up to a total maximum of 10 votes per ordinary share. The amendment applies to only ordinary shares, not ADSs.

On December 20, 2024, the Company entered into an amendment to the Original Sales Agreement (the "Sales Agreement Amendment" and the Original Sales Agreement, as amended by the Sales Agreement Amendment, the "Sales Agreement") to replace Capital One Securities with Rodman & Renshaw LLC ("Rodman & Renshaw" and, together with Virtu, each a "Sales Agent" and, collectively, the "Sales Agents") as a Sales Agent and party to the Original Sales Agreement. The Sales Agreement provides to: (i) increase the aggregate dollar amount of ADSs that the Company may sell pursuant to the Sales Agreement; and, (ii) replace Capital One Securities with Rodman & Renshaw as a Sales Agent under the Sales Agreement.

The Original Sales Agreement authorized the Company to offer and sell ADSs having an aggregate offering price of up to $16,362,816. As of December 20, 2024, the Company sold ADSs pursuant to the Sales Agreement for gross proceeds of €271,416 (or $303,001). The Sales Agreement Amendment increased the dollar amount of ADSs available to be sold from time-to-time under the Sales Agreement to $29,696,999, which consists of $16,059,815 remaining as originally authorized under the Original Sales Agreement and an additional $13,637,184, from December 20, 2024.

Sales of ADSs, under the Sales Agreement, may be made by any method that is deemed to be an "at the market offering" as defined in Rule 415(a)(4) under the Securities Act of 1933, as amended (the "Securities Act"). The Sales Agents are not required to sell any specific number or dollar amount of ADSs but will act as our sales agents and use commercially reasonable efforts consistent with their normal trading and sales practices, on mutually agreed terms between the Sales Agents and the Company. There is no arrangement for funds to be received in any escrow, trust, or similar arrangement.

The Sales Agents will receive from the Company a commission of up to 3.0% of the gross proceeds of any ADSs sold through them under the Sales Agreement. In connection with the sale of ADSs on behalf of the Company, each of the Sales Agents will be deemed to be an "underwriter" within the meaning of the Securities Act and the compensation of the Sales Agents may be deemed to be underwriting commissions or discounts. The Company has also agreed to provide indemnification and contribution to the Sales Agents with respect to certain liabilities, including liabilities under the Securities Act.

Quantitative and qualitative disclosure about market risk

The Company is exposed to market risks in the ordinary course of its business. Market risk represents the risk of loss that may impact the Company's financial position due to adverse changes in financial market prices and rates. The Company's current investment policy is conservative due to the need to support operations. The Company maintains bank accounts with reputable banks and financial institutions and invests available cash in Italian and U.S. government bonds and treasury notes with short-term maturities and a minimum credit rating of "BBB". A minority of the Company's cash and cash equivalents and marketable securities are held in deposits that bear a small amount of interest. The Company's market risk exposure is primarily a result of foreign currency exchange rates, which is discussed in detail in the following paragraph.

The Company is an early-stage cell and gene therapy company commercializing technology licensed from OSR. The Company intends to continue to conduct its operations so that neither it nor its subsidiary is required to register as an investment company under the Investment Company Act of 1940, as amended, and the rules and regulations promulgated thereunder (the "40 Act"). To ensure that the Company does not become subject to regulation under the '40 Act, the Company may be limited in the type of assets that it may own or acquire. If the Company were to become inadvertently subject to the '40 Act, any violation of the '40 Act could subject the Company to material adverse consequences.

Foreign currency exchange risk

The Company's results of operations and cash flow may be subject to fluctuations due to changes in foreign currency exchange rates. The Company's liquid assets and expenses are denominated in EUR and USD. At December 31, 2024, the Company maintained €4.6 million in cash and cash equivalents and €8.1 million in marketable securities. Changes in the USD/EUR exchange rate could increase/decrease the Company's operating expenses, especially as more costs are incurred in the U.S. or, as USD are exchanged for EUR to cover European operating costs. As the Company continues to grow its business, the Company's results of operations and cash flows might be subject to significant fluctuations due to changes in foreign currency exchange rates, which could adversely impact the Company's results of operations.

Currently, the Company has recorded an unrealized net gain from exchange rates of approximately €0.2 million. The Company does not currently hedge its foreign currency exchange risk. In the future, the Company may enter formal currency hedging transactions to decrease the risk of financial exposure from fluctuations in the exchange rates of its principal operating currencies. These measures, however, may not adequately protect the Company from the material adverse effects of such fluctuations.

2. Summary of significant accounting policies

Basis of presentation

The accompanying consolidated financial statements have been prepared in accordance with accounting principles generally accepted in the United States of America ("US GAAP") for consolidated financial information and with the instructions to Form 20-F and Article 10 of Regulation S-X promulgated by the Securities and Exchange Commission ("SEC"). Any reference in these notes to applicable guidance is meant to refer to the authoritative US GAAP guidance as found in the Accounting Standards Codification ("ASC") and Accounting Standards Update ("ASU") of the Financial Accounting Standards Board ("FASB") unless otherwise stated.

A summary of the significant accounting policies applied in the preparation of these consolidated financial statements is presented below, only for the categories and headings now applicable and that might be applicable in the future based on the Company's business. These policies have been consistently applied unless otherwise stated.

Principles of consolidation

The accompanying consolidated financial statements include the accounts of the Company and its wholly owned subsidiary. All significant intercompany accounts and transactions have been eliminated in consolidation.

Use of estimates

The preparation of consolidated financial statements in conformity with US GAAP requires management to make estimates and assumptions that affect the reported amounts reported in the consolidated financial statements and the disclosures made in the accompanying notes. Estimates and assumptions reflected in these consolidated financial statements include but are not limited to, the accrual for research and development expenses and related milestone payments, share-based compensation expense, valuation of Research & Development ("R&D") tax credits, the valuation of equity and the recoverability of the Company's net deferred tax assets and related valuation allowance. Estimates are periodically reviewed considering changes in circumstances, facts, and experience. Actual results may differ from these estimates under different assumptions or conditions. Changes in estimates are recorded in the period in which they become known. The areas involving a higher degree of judgment or complexity, or areas where assumptions and estimates are significant to the consolidated financial statements are disclosed below.

Cash and cash equivalents

The Company considers all highly liquid investments purchased with original maturities of 90 days or less at acquisition to be cash equivalents, which amounts may at times exceed insured limits. The Company has not experienced any losses on such accounts and does not believe it is exposed to any significant credit risk. In the consolidated Cash Flow Statements, cash and cash equivalents include: cash on hand, deposits held with banks, and other short-term highly liquid investments. In the consolidated balance sheets, bank overdrafts, if any, are shown in current liabilities. Cash and cash equivalents are detailed as follows:

	At December 31,		
	2024	2023	2022
		(Euro)	
Cash in bank	€ 2,530,549	€ 3,687,402	€ 29,790,838
Cash in short-term marketable securities	2,047,200	-	-
Cash in hand & prepaid cards	4,000	4,018	4,018
Total cash and cash equivalents	€ 4,581,749	€ 3,691,420	€ 29,794,856

Marketable securities

	December 31, 2024			
	Amortized Cost	Fair Value	Unrealized Gain (Loss)	Allowance for Credit Losses
Available-for-sale (AFS)	€ 7,992,891	€ 8,078,002	€ 96,234	€ -
Total Debt Securities	**€ 7,992,891**	**€ 8,078,002**	**€ 96,234**	**€ -**

	December 31, 2023			
	Amortized Cost	Fair Value	Unrealized Gain (Loss)	Allowance for Credit Losses
Available-for-sale (AFS)	€ 15,123,831	€ 15,084,284	€ 214,984	€ -
Total Debt Securities	**€ 15,123,831**	**€ 15,084,284**	**€ 214,984**	**€ -**

There were no marketable securities in 2022.

The Company invests available liquid assets, (i.e., not used or are expected to be needed in short/very short-term operations), in marketable securities consisting of highly rated domestic and foreign government debt securities, specifically U.S. Treasury Bills and Notes, and Italian Government Bonds. Since the Company's intent was not to sell the securities immediately, but the Company was uncertain if the securities would be held until maturity, it was determined that debt securities were to be classified as available for sale marketable securities ("AFS").

Investments with a remaining maturity of greater than three (3) months at the time of purchase are classified as AFS marketable securities.

AFS marketable securities with a remaining maturity date greater than one year are classified as non-current assets.

Measurement is made at fair value and change in value is made with the unrealized gains and losses included in other comprehensive income (loss) as a component of shareholders' equity until realized. Any premium arising at purchase is amortized to the earliest call date and any discount arising at purchase is accreted to maturity. Amortization and accretion of premiums and discounts are recorded in interest income, net. Realized gains and losses on AFS debt securities are determined using the specific identification method and are included in other income (expense), net.

The Company assesses its available-for-sale debt securities under the AFS debt security impairment model in ASC 326 as of each reporting date in order to determine if a portion of any decline in fair value below carrying value recognized on its AFS debt securities is the result of a credit loss. The Company records credit losses in the Consolidated Statements of Operations and Comprehensive Loss as credit loss expense within other income (expense), net, which is limited to the difference between the fair value and the amortized cost of the security. To date, the Company has not recorded any credit losses on its AFS debt securities.

Accrued interest receivable related to the Company's AFS debt securities is presented within prepaids and other current assets on the Company's Consolidated Balance Sheets. The Company excludes accrued interest receivable from both the fair value and the amortized cost basis of AFS debt securities for the purposes of identifying and measuring any impairment. The Company writes-off accrued interest receivable once it has determined that the asset is not realizable. Any write-offs of accrued interest receivable are recorded by reversing interest income, recognizing credit loss expense, or a combination of both. To date, the Company has not written off any accrued interest receivables associated with its marketable securities.

The unrealized gain recognized during the reporting period on marketable securities still held at the report date was approximately €96,000, while there was no unrealized loss recognized during the reporting period on marketable securities still held at the report date.

Net loss and comprehensive income (loss)

Comprehensive loss is defined as the change in equity during a period from transactions and other events and circumstances from non-owner sources. ASC 220 Comprehensive Income requires that an entity records all components of comprehensive income (loss), net of their related tax effects, in its financial statements in the period in which they are recognized.

For the year ended December 31, 2024, net loss was approximately €8.9 million with other comprehensive loss being approximately €142,196 and total comprehensive loss was approximately €9.1 million.

For the year ended December 31, 2023, net loss was €11.6 million with other comprehensive income being approximately €199,131 and total comprehensive loss was €11.4 million.

For 2022, the comprehensive loss was equal to the net loss.

Net loss per share

Net loss per share ("EPS") is computed in accordance with US GAAP. Basic EPS is computed by dividing net loss by the weighted average number of common shares outstanding during the period. Diluted EPS reflects potential dilution and is computed by dividing net loss by the weighted average number of common shares outstanding during the period, increased by the number of additional common shares that would have been outstanding if all potential common shares had been issued and were dilutive.

The EPS calculation was applied at the Company conversion to S.p.A. in June 2021, after the increase in capital to €50,000 was required to be an S.p.A. by Italian law. The Company's shareholders authorized 59.7 million ordinary common shares.

In July 2023, following the ATM Offering exercise, 100 new ADS were issued.

In March 2024, 72,908 additional ADSs were issued pursuant to the Sales Agreement.

At December 31, 2024, the Company had 18,289,866 common shares issued and outstanding with 1.8 million common shares reserved for the Company's Equity Incentive Plan 2021–2035.

At December 31, 2024, the Company had 889,658 outstanding options and 23,502 common share equivalents, in the form of underwriters' common share warrants. Diluted EPS was not relevant at December 31, 2024, 2023, or 2022, as the effect of common share equivalents, in the form of 889,658 stock options and of 23,502 underwriters' common share warrants, would have been anti-dilutive. (See Note 11. Shareholders' equity and Note 12. Share-based compensation.)

Foreign currency translation

The reporting and functional currency of the Company is Euros. All amounts are presented in Euros unless otherwise stated. All amounts disclosed in the consolidated financial statements and notes have been rounded to the nearest Euro unless otherwise stated. Foreign currency transactions, if any, are translated into Euros using the exchange rates prevailing at the date(s) of the transaction(s) or valuation where items are re-measured. Foreign exchange gains and losses resulting from the settlement of such transactions and the translation at period-end exchange rates of monetary assets and liabilities denominated in foreign currencies are recognized in the consolidated Statements of Operations. For financial reporting purposes, the assets and liabilities of the U.S. Subsidiary are translated into EUR using exchange rates in effect at the balance sheet date. The net income/(loss) of the U.S. Subsidiary is translated into EUR using average exchange rates in effect during the reporting period. The resulting currency translation impact is recorded in Shareholders' equity as a cumulative translation adjustment.

For the year ended 2024, the currency translation impact was approximately €23,400. During the period ended December 31, 2024, foreign exchange gains and losses were a net gain of approximately €0.2 million.

For the year ended 2023, the currency translation impact was approximately €15,800. During the period ended December 31, 2023, foreign exchange gains and losses were a net loss of approximately €0.2 million.

For the year ended 2022, the net exchange gain was approximately €2.3 million, and was related mainly to: i) approximately €1.6 million in net exchange rate gains realized on the conversion of $12.0 million of IPO proceeds obtained in December 2021 to Euros; ii) approximately €0.4 million in net exchange rate gain realized on USD$ trade payables; and iii) approximately €0.3 million in exchange gain unrealized on USD$ time deposits.

Any change in the net foreign exchange rate effect is due to the fluctuation in the USD exchange rate with the Euro.

Emerging growth company status

The Company is an "emerging growth company," as defined in the U.S. Jumpstart Our Business Startups Act, or U.S. JOBS Act, and may take advantage of certain exemptions from various reporting requirements that are applicable to other public companies that are not emerging growth companies. The Company may take advantage of these exemptions until the Company is no longer an "emerging growth company." Section 107 of the U.S. JOBS Act provides that an "emerging growth company" can take advantage of the extended transition period afforded by the U.S. JOBS Act for the implementation of new or revised accounting standards. The Company has elected to use the extended transition period for complying with new or revised accounting standards and, because of this election, its consolidated financial statements may not be comparable to companies that comply with public company effective dates. The Company may take advantage of these exemptions up until the last day of the fiscal year following the fifth anniversary of its initial public offering ("IPO") or such earlier time that it is no longer an "emerging growth company."

Fair value measurements

Certain assets and liabilities of the Company are carried at fair value under US GAAP. Fair value is defined as the exchange price that would be received for an asset or paid to transfer a liability (an exit price) in the principal or most advantageous market for the asset or liability in an orderly transaction between market participants on the measurement date. Valuation techniques used to measure fair value must maximize the use of observable inputs and minimize the use of unobservable inputs. Financial assets and liabilities carried at fair value are to be classified and disclosed in one of the following three levels of the fair value hierarchy, of which the first two are considered observable and the last is considered unobservable:

- Level 1 — Quoted prices in active markets for identical assets or liabilities.

- Level 2 — Observable inputs (other than Level 1 quoted prices), such as quoted prices in active markets for similar assets or liabilities, quoted prices in markets that are not active for identical or similar assets or liabilities, or other inputs that are observable or can be corroborated by observable market data.

- Level 3 — Unobservable inputs that are supported by little or no market activity that are significant to determining the fair value of the assets or liabilities, including pricing models, discounted cash flow methodologies and similar techniques.

To the extent that the valuation is based on models or inputs that are less observable or unobservable in the market, the determination of fair value requires more judgment. Accordingly, the degree of judgment exercised by the Company in determining fair value is greatest for instruments categorized in Level 3. A financial instrument's level within the fair value hierarchy is based on the lowest level of any input that is significant to the fair value measurement.

The carrying values of the Company's R&D tax credits, VAT credits, accounts payable, accrued expenses and other current liabilities were evaluated and determined to approximate their fair values due to the short-term nature of these assets and liabilities.

	December 31, 2024			
	Total	**Level 1**	**Level 2**	**Level 3**
Cash and cash equivalents	€ 4,581,749	4,581,749	€ -	€ -
Marketable Securities	8,078,002	8,078,002	-	-
Total financial assets	**€ 12,659,751**	**€ 12,659,751**	**€ -**	**€ -**

	December 31, 2023			
	Total	**Level 1**	**Level 2**	**Level 3**
Cash and cash equivalents	3,691,420	3,691,420		
Marketable Securities	€ 15,084,284	15,084,284	€ -	€ -
Total financial assets	**€ 18,775,704**	**€ 18,775,704**	**€ -**	**€ -**

	December 31, 2022			
	Total	**Level 1**	**Level 2**	**Level 3**
Cash and cash equivalents	€ 29,794,856	29,794,856	€ -	€ -
Total financial assets	**€ 29,794,856**	**€ 29,794,856**	**€ -**	**€ -**

Segment information

Operating segments are identified as components of an enterprise for which separate discrete financial information is available for evaluation by the chief operating decision-maker in making decisions regarding resource allocation and assessing performance. The Company and its chief operating decision-maker view the Company's operations and manages its business in one operating segment, which is the research and development in the pharmaceutical sector with a focus on developing novel therapeutics to treat cancer.

Tax credit on investments in research and development

In line with the legislation in force at December 31, 2024, 2023 and 2022, companies in Italy that invest in eligible research and development activities, regardless of the legal form and economic sector in which they operate, can benefit from a tax credit which can be used to reduce most taxes payable, including income tax or regional tax on productive activities, as well as social security contributions and payroll withholding taxes.

For eligible research and development activities, the tax credit was equal to 20% in fiscal year 2022 ("FY 2022") of the eligible costs incurred, with a maximum annual amount of €4.0 million. Starting with the fiscal year 2023 ("FY 2023") the law extended the measure up to the tax period ended December 31, 2031; however, the tax credit rate was decreased to 10% of the eligible expenses, and the annual ceiling of the credit increased to €5.0 million.

The eligible activities consist of fundamental research, industrial research, and experimental development as defined in letters m), q) and j) of point 15, par. 1.3 of the Communication no. 198/2014 of the European Commission. To determine the cost basis of the benefit, the following expenses are eligible:

- Personnel costs;
- Depreciation charges, costs of the financial or simple lease and other expenses related to movable tangible assets and software used in research and development projects;

- Expenses for extra-euro research contracts concerning the direct execution of eligible research and development activities by the provider;
- Depreciation charges;
- Expenses for consulting services and equivalent services related to eligible research and development activities; and,
- Expenses for materials, supplies, and other similar products used in research and development projects.

The receivable is recognized when there is reasonable assurance that: (1) the recipient will comply with the relevant conditions; and (2) the grant will be received. The Company has elected to present it net of the related expenditure on the Consolidated Statements of Operations and Comprehensive Loss.

While these tax credits can be carried forward indefinitely, the Company recognized an amount which reflects management's best estimate of the amount that is reasonably assured to be realized or utilized in the foreseeable future based on historical benefits realized, adjusted for expected changes, as applicable. The tax credits are recorded as an offset to research and development expenses in the Consolidated Statements of Operations and Comprehensive Loss.

Share-based compensation

To reward the efforts of employees, officers, directors, and certain consultants, and to promote the Company's growth and development, the Board may approve, upon occasion, various share-based awards. The Company's stock option plan (the "Equity Incentive Plan 2021–2025" or the "Plan"), under which stock options are granted, was originally approved on May 20, 2021.

In June 2023, the Company's shareholders modified the Plan to extend the final deadline for the issuance of the ordinary shares until December 31, 2035, to allow that all stock options granted during the term of the Plan could provide for an exercise period of 10 years starting from the date of grant. (See Note 12. Share-based compensation.)

Currently, the Company has authorized options on 1,828,986 ordinary shares (i.e., approximately 10% of the number of shares outstanding, which are currently 18,289,866 ordinary shares outstanding); however, as provided by the Plan, the Company may increase the authorized shares under the Plan up to a maximum of 2,700,000 ordinary shares without further shareholder approval. Therefore, as the Company raises additional capital, the Board has the authority to issue options on 1,828,986 to 2,700,000 ordinary shares, as the number of issued and outstanding ordinary shares grows, i.e., the Company does not have to obtain further authorization from shareholders to increase the number of ordinary shares available for equity grants until the outstanding ordinary shares exceed 27,000,000.

The Company measures its stock option awards granted to employees, officers, directors, and consultants under the Plan based on their fair value on the date of the grant and recognizes compensation expense for those awards over the requisite service period, which is normally the vesting period of the respective award. Forfeitures are accounted for as they occur. The measurement date for option awards is the date of the grant. The Company classifies stock-based compensation expense in its Consolidated Statement of Operations and Comprehensive Loss in the same manner in which the award recipient's payroll costs are classified or in which the award recipient's service payments are classified.

The Company chose the Black-Scholes-Merton model because it is considered easier to apply and also it is a defined equation and incorporates only one set of inputs. As a result, it is the model most commonly in use.

Representative warrants

The Company agreed to issue warrants to the underwriters of the IPO ("Warrants") to purchase 23,502 ADSs. The Warrants are exercisable at a per share exercise price of $14.375 per ADS. The Warrants are exercisable at any time and from time to time, in whole or in part, during the four and one-half-year period commencing June 13, 2022.

The Warrants will provide for adjustment in the number and price of the Warrants and the ADSs underlying such Warrants in the event of recapitalization, merger, stock split or other structural transactions, or a future financing undertaken by the Company. The Warrants were evaluated under applicable guidance and accordingly classified as equity in the consolidated financial statements.

Non-current assets right of use (ROU)

Upon commencement of a contract containing a lease, the Company classifies leases other than short-term leases as either an operating lease or a finance lease according to the criteria prescribed by ASC 842. The Company recognizes both lease liabilities and right-of-use assets on the balance sheet for all leases, except for short-term leases (those with a lease term of 12 months or less). Lease liabilities are initially measured at the present value of the future lease payments over the lease term, discounted at the rate implicit in the lease or, if that rate is not readily determinable, the Company's incremental borrowing rate. The right-of-use assets represent the lessee's right to use the underlying asset for the lease term and are initially measured at the same amount as the corresponding lease liability. For finance leases, the Company recognizes interest expense on the lease liability and amortization expense on the right-of-use asset. For operating leases, lease expense is recognized on a straight-line basis over the lease term.

Fixed Assets

Fixed assets are stated at cost, including any accessory and direct costs that are necessary to make the assets fit for use, and adjusted by the corresponding accumulated depreciation. Depreciation is systematically recorded in the consolidated financial statements taking into consideration the use, purpose, and financial-technical duration of the assets, based on their estimated useful economic lives. Leasehold improvements depreciation is recorded based on the shorter of the life of the leasehold improvement or the remaining term of the lease.

Ordinary maintenance costs are expensed to the Consolidated Statements of Operations and Comprehensive Loss in the year in which they are incurred. Extraordinary maintenance costs, the purpose of which is to extend the useful economic life of the asset, to technologically upgrade it and/or to increase its productivity or safety for the purpose of economic productivity of the Company, are attributed to the asset to which they refer and depreciated on the basis of its estimated useful economic life. Amortization of leasehold improvements is computed using the straight-line method based upon the terms of the applicable lease or estimated useful life of the improvements, whichever is less.

Impairment of long-lived assets

In accordance with ASC Topic 360-10-20, "Property, Plant and Equipment," the Company performs an impairment test whenever events or circumstances indicate that the carrying value of long-lived assets with finite lives may be impaired. Impairment is measured by comparing the carrying value of the long-lived assets to the estimated undiscounted pre-tax cash flows expected to result from the use of such assets and their ultimate disposition. In circumstances where impairment is determined to exist, the Company will write down the asset to its fair value based on the present value of estimated cash flows. To date, no impairments have been identified for the years ended December 31, 2024, 2023, and 2022.

Deferred offering costs

Deferred public offering costs, which primarily consist of direct, incremental legal and accounting fees relating to fundraising activities (e.g., an IPO), were capitalized within prepaid expenses and other current assets prior to the IPO and netted or offset with the IPO proceeds upon closing of the IPO.

For the year ended December 31, 2024, the Company incurred approximately €0.2 million of costs in connection with its sales of ADSs pursuant to the Sales Agreement that were fully expensed in the Consolidated Statement of Operations and Comprehensive Loss and approximately €0.2 million of deferred due diligence and other preliminary activities connected to a financing transaction expected to be completed in the following period.

For the year ended December 31, 2023, the Company incurred approximately €0.3 million of ATM Offering costs that were fully expensed in the Consolidated Statement of Operations and Comprehensive Loss.

For the year ended December 31, 2022, the Company did not incur offering costs.

Recently issued accounting pronouncements

In November 2023, FASB issued ASU 2023-07, which amends ASC 280 to improve the information that a public entity discloses about its reportable segments and to address investor requests for more information about reportable segment expenses by requiring incremental disclosures for segment reporting. The effective date for ASU 2023-07 is for fiscal years beginning after December 15, 2023, and interim periods with fiscal years beginning after December 15, 2024. The amendment requires companies to disclose more information about their reportable segments, including: (1) significant segment expenses, (2) 'other' segment items, (3) the title and position of the chief operating decision maker ("CODM"), (4) how the CODM uses the reported measure(s) of segment profit or loss and (5) annual disclosures about a reportable segment's profit or loss and assets. The Company believes that this ASU does not have a material impact on its consolidated financial statements and related disclosures.

In December 2023, the FASB issued ASU 2023-09, Income Taxes (Topic 740): Improvements to Income Tax Disclosures, which modifies the rules on income tax disclosures to require disaggregated information about a reporting entity's effective tax rate reconciliation as well as information on income taxes paid. The standard is intended to benefit investors by providing more detailed income tax disclosures that would be useful in making capital allocation decisions. The guidance is effective for annual periods beginning after December 15, 2024, with early adoption permitted. ASU 2023-09 should be applied on a prospective basis, but retrospective application is permitted. The Company believes that this ASU does not have a material impact on its consolidated financial statements and related disclosures.

In March 2024, FASB issued ASU 2024-01, Scope Application of Profits Interest and Similar Awards, which clarifies how an entity determines whether a profits interest or similar award (hereafter a "profits interest award") is (1) within the scope of Accounting Standards Codification (ASC) 718, Compensation — Stock Compensation, or (2) not a share-based payment arrangement and therefore within the scope of other guidance. For public business entities, ASU 2024-01 is effective for annual periods beginning after December 15, 2024, and interim periods within those annual periods. For all other entities, the amendments are effective for annual periods beginning after December 15, 2025, and interim periods within those annual periods. The Company believes that this ASU does not have a material impact on its consolidated financial statements and related disclosures.

In November 2024, FASB issued ASU 2024-04, Debt – Debt with conversion and other options (subtopic 470-20): Induced conversions of convertible debt instruments which provides guidance on accounting for induced conversions of convertible debt instruments. For public business entities, ASU 2024-04 is effective for annual reporting periods beginning after December 15, 2025, and interim reporting periods within those annual periods. The Company is still evaluating the impact.

3. Research and development

Research and development costs are expensed as incurred. Research and development expenses consist of costs incurred in performing research and development activities, including salaries, share-based compensation and benefits, facilities costs, third-party license fees, and external costs of outside vendors and consultants engaged to conduct clinical development activities and clinical trials, (e.g., contract research organizations, or CROs), as well as costs to develop a manufacturing processes, perform analytical testing and manufacture clinical trial materials, (e.g., contract manufacturing organizations, or CMOs). Non-refundable prepayments for goods or services that will be used or rendered for future research and development activities are recorded as prepaid expenses. Such amounts are recognized as an expense as the goods are delivered or the related services are performed, or until it is no longer expected that the goods will be delivered, or the services rendered. In addition, funding from research grants, if any, is recognized as an offset to research and development expense based on costs incurred on the research program.

The Company annually incurs a significant amount of research costs to meet its business objectives. The Company has various research and development contracts, and the related costs are recorded as research and development expenses as incurred. When billing terms under these contracts do not coincide with the timing of when the work is performed, the Company is required to make estimates of outstanding obligations at period end to those third parties. Any accrual estimates are based on several factors, including the Company's knowledge of the progress towards completion of the research and development activities, invoicing to date under the contracts, communication from the research institution or other companies of any actual costs incurred during the period that have not yet been invoiced, and the costs included in the contracts. Significant judgments and estimates may be made in determining the accrued balances at the end of any reporting period. Actual results could differ from the estimates made by the Company. The historical accrual estimates made by the Company have not been materially different from the actual costs. For further details, please refer to the Related Parties disclosures in Note 13 below.

4. General and administrative

General and administrative costs consist primarily of salaries, share-based compensation, benefits and other related costs for personnel and consultants in the Company's executive and finance functions, professional fees for legal, finance, accounting, auditing, tax and consulting services, travel expenses and facility-related expenses, which include rent and maintenance of facilities and other operating costs not otherwise included in research and development expense.

5. Income taxes

The Company is subject to taxation in Italy, and with the addition of the Company's wholly owned subsidiary in the U.S., the Company is subject to taxation in the U.S. Taxation in Italy includes the standard corporate income tax and a regional business tax. Taxation in the U.S. includes federal corporate income tax ("IRS"), as well as state and local taxes. Taxes are recorded on an accrual basis. They therefore represent the allowances for taxes paid or to be paid for the year, calculated according to the current enacted rates and applicable laws. In the future, the Company may be taxed in various other countries where it may have permanent establishments, as applicable.

For the years ending December 31, 2024, due to the tax loss position reported, no income taxes were due in Italy, while in the U.S. there was no material tax charge.

For the years ending December 31, 2023 and 2022, due to the tax loss position reported, no income taxes were due in Italy or the U.S., although the U.S. subsidiary had taxable income in 2022. In addition, the subsidiary in the U.S. had an immaterial amount of other state taxes.

The Company uses the asset and liability method of accounting for deferred income taxes. Under this method, deferred tax assets and liabilities are recognized for the expected future tax consequences of temporary differences between the carrying amounts and the tax basis of assets and liabilities, measured at tax rates expected to be enacted at the time of their reversals. These temporary differences primarily relate to net operating losses carried forward available to offset future taxable income.

At each reporting date, the Company considers existing evidence, both positive and negative, that could impact its view with regards to future realization of deferred tax assets. In consideration of the start-up status of the Company, a valuation allowance has been established to offset the deferred tax assets, as the related realization is currently uncertain. In the future, should the Company conclude that it is more likely than not that the deferred tax assets are partially or fully realizable, the valuation allowance will be reduced to the extent of such expected realization, and the corresponding amount will be recognized as income tax benefit in the Company's Consolidated Statements of Operations and Comprehensive Loss.

The Company recognizes tax liabilities from an uncertain tax position if it is more likely than not that the tax position will not be sustained upon examination by the taxing authorities, based on the technical merits of the tax position. There are no uncertain tax positions that have been recognized in the accompanying consolidated financial statements. For the Company, the prior five years of tax returns (2020-2024) are potentially subject to audit, and for the Company's U.S. subsidiary, Genenta Science, Inc., the open years for tax examination are 2022, 2023, and 2024.

The Company files tax returns as prescribed by the tax laws of the jurisdictions in which it operates. A reconciliation of the Company's effective tax rate is summarized as follows:

	At December 31,		
	2024	2023	2022
	(in Euros)		
Income taxes at Italy statutory rate	€ (2,037,277)	€ (2,794,909)	€ (2,034,663)
Permanent differences	(39,935)	309,512	(160,133)
Other	71,627	(171,032)	715
Federal Income tax for Genenta INC	(62,825)	(89,910)	(31,993)
Change in valuation allowance	2,068,410	2,746,339	2,226,074
Total provision expense for income taxes	€ -	€ -	€ -

Significant components of the Company's net deferred tax assets are summarized as follows:

	At December 31,		
	2024	2023	2022
	(in Euros)		
Deferred tax assets			
Net operating loss carryforwards	€ 13,876,117	€ 11,772,870	€ 9,197,563
Other temporary differences	130,131	150,347	52,996
Allowance for corporate equity	481,071	495,692	422,011
Total deferred tax assets	14,487,319	12,418,909	9,672,570
Valuation allowance	(14,487,319)	(12,418,909)	(9,672,570)
Net deferred tax assets	€ -	€ -	€ -

At December 31, 2024, 2023, and 2022, the Company believes there are no significant differences with regard to its deferred tax assets and its relevant components, compared to the computations of the preceding periods.

In 2011, the Italian tax authorities issued rules that modified the previous treatment of tax loss carryforwards. According to the applicable law, all existing tax loss carry forwards will never expire but they can off-set 80% of the taxable income of the year. The rules do not affect the tax loss carryforward that refer to the start-up period, defined as the first three years of operations starting from the inception of the Company.

The following table shows the amount of deferred tax assets that can be carried forward indefinitely and used without limitation or with the limit of 80% of taxable income generated in Italy, as provided by Legislative Decree 98/2011:

	At December 31,		
	2024	2023	2022
	(in Euros)		
No expiration date	€ 5,487,085	€ 5,487,085	5,487,085
No expiration date - DL 98/2011	51,680,567	43,191,915	33,054,966
Total	€ 57,167,652	€ 48,679,000	38,542,051

The Company has analyzed its tax position by determining the amount of tax losses that can be carried forward indefinitely and has decided to accrue an allowance for related deferred tax assets as the Company is in a situation of pre-revenues that is destined to remain in the long run and there is no certainty of the future recoverability of such tax losses through tax relevant incomes. Future taxable profits for the Company depend on the manufacture of marketable drugs following the successful completion of the clinical trial. Since the clinical trial is still in an early phase, the time frame and uncertainties regarding the outcome of the completion justify the full allowance of deferred tax assets.

6. Prepaid expenses and other current assets

Prepaid expenses and other current assets consist of the following:

	At December 31,		
	2024	2023	2022
		(in Euros)	
Value Added Tax (VAT)	€ 698,735	€ 1,170,634	€ 912,423
Research and development tax credit	749,676	833,000	650,000
Advances payments to suppliers	35,991	34,108	41,149
Other current assets	210,830	64,664	219,400
Other prepaids	117,994	378,148	103,540
Total	€ 1,813,226	€ 2,480,554	€ 1,926,512

Value Added Tax (VAT) receivables are linked to purchases. Italian VAT (*Imposta sul Valore Aggiunto*) applies to the supply of goods and services carried out in Italy by entrepreneurs, professionals, or artists and on imports carried out by anyone. Intra-Community acquisitions are also subject to VAT under certain situations. The Italian standard VAT rate for 2024, 2023, and 2022 was 22%. Reduced rates are provided for specifically listed supplies of goods and services. It is carried forward indefinitely and does not expire.

Tax credits on research and development represent a special tax relief offered to Italian companies operating in the research and development sector and can be used to offset most taxes payable. The Company has a total research and development tax credit available to be used of approximately €3.8 million at December 31, 2024, €4.1 million at December 31, 2023, and approximately €4.4 million at December 31, 2022, which can be carried forward indefinitely and do not expire. However, given the start-up status of the Company, and the fact that it will not be profitable in the foreseeable future (which limits the utilization of the credit), the Company recognized a receivable balance that represents the Company's best estimate of the amount of tax credit that can be used in offsetting taxes payable for approximately 12 months after December 31, 2024.

During the 12-month period ended December 31, 2024, and 2023, the Company utilized approximately €750,000 and €732,000, respectively, to offset certain social contributions and taxes payable, while during the financial year 2022, the Company utilized approximately €600,000. The benefit recorded for the 12-months ended December 31, 2024, 2023, and 2022, to offset research and development expenses was approximately €499,000, €430,000, and €698,000, respectively.

Advance payments to suppliers at December 31, 2024, 2023, and 2022 mainly relate to R&D operating services.

Other current assets at December 31, 2024 mainly relate to interest maturing on investment in marketable securities and the allowance for corporate equity ("ACE") of approximately €180,000 reclassified from long-term assets since, based on the latest updates received from the Italian Revenue Agency. It will be recovered in the short term.

Other current assets at December 31, 2023 mainly relate to interests maturing on investment in marketable securities, while Other current assets at December 31, 2022 mainly relate to the allowance for corporate equity of approximately €180,000 and the quota of accruing financial interest income on time deposits of approximately €38,000.

At December 31, 2024, Other prepaids mainly include expenses for various services, already financially incurred but attributable to the following year.

At December 31, 2023, Other prepaid expenses mainly relate to the directors and officers ("D&O") insurance policy paid in December 2023 of approximately €0.2 million, while at December 31, 2022, Other prepaids mainly include expenses for various services, already financially incurred but attributable to the following year.

7. Fixed assets, net

Fixed assets consist of the following:

	At December 31,		
	2024	**2023**	**2022**
	(In Euros)		
Software (ERP Implementation)	€ 87,800	€ 87,800	€ 87,800
Computer	37,841	35,971	31,307
Furniture and fixtures	15,604	13,005	4,676
Total fixed assets	141,245	136,776	123,783
Less: accumulated depreciation and amotization	(98,323)	(53,799)	(12,144)
Fixed assets, net	€ 42,922	€ 82,977	€ 111,639

Fixed assets include software mainly related to customization and development of the information technology security infrastructure, and the new ERP system; computers, furniture, and fixtures of our office space in Milan, Italy.

There were no significant purchases, disposals, nor impairments during the periods.

Depreciation and amortization have been calculated by taking into consideration the use, purpose, and financial-technical duration of the assets, based on their estimated economic lives.

8. Non-current assets right of use (ROU)

In February 2022, the Company entered into a four-year (i.e., 48-month) lease of an automobile, with an ending date of January 2026. The "base" annual lease payment is €13,967 payable monthly in the amount of €1,164. The lease payment will remain fixed for the four (4) years. The automobile lease was identified and accounted for as a finance type lease.

For the initial measurement, the calculation of the net present value of the right of use asset and liability was made by using the discounted rate of 6.25% and was determined to be approximately €49,320. Lessee initial direct costs were deemed not material. Other non-lease component costs for lease insurance were accounted for separately from the lease.

At December 31, 2024, the net present value of the ROU asset and liability amounted to approximately €14,600. The liability was determined to be €13,400 as a current liability and €1,200 as a long-term liability.

9. Other non-current assets

Other non-current assets consist of the long-term portion of the VAT receivable and R&D tax credit, as follows:

	At December 31,		
	2024	2023	2022
		(in Euros)	
Value Added Tax (VAT)	€ 290,150	€ 630,342	€ 912,424
Research and development tax credit	-	167,000	650,000
Other non-current assets	14,594	207,218	39,079
Total other non-current assets	€ 304,744	€ 1,004,560	€ 1,601,503

During the year ended December 31, 2024, the portion of the VAT credit classified as long-term as of December 31, 2023, was refunded in the amount of approximately €0.4 million, which explains the change in the balance.

With regards to the R&D tax credit, the conservative estimate of its utilization as of December 31, 2024, pertains only to the short-term portion; therefore, no R&D tax credit is accrued as a long-term asset.

As for the Other non-current assets, these are composed of minor, immaterial amounts, while the reason for the change in the balance relates to the reclassification of the ACE tax credit from long-term to short-term is due to an improved reimbursement forecast.

In addition, Other non-current assets - related party includes a security deposit of €3,350 paid to OSR - San Raffaele Hospital as a security guarantee for the office lease contract. (See Note 14. Commitments and contingencies).

10. Retirement benefit obligation

Employees in Italy are entitled to Trattamento di Fine Rapporto ("TFR"), commonly referred to as an employee leaving indemnity, which represents deferred compensation for employees in the private sector. Under Italian law, an entity is obligated to accrue for TFR on an individual employee basis payable to each individual upon termination of employment (including both voluntary and involuntary dismissal). The annual accrual is approximately 7% of total pay, with no ceiling, and is revalued each year by applying a pre-established rate of return of 1.50%, plus 75% of the Consumer Price Index, and is recorded by a book reserve. TFR is an unfunded plan. The costs of the retirement benefit obligation are accounted for under the provisions of ASC 715, *Compensation – Retirement Benefits*.

The amount of the obligation at December 31, 2024, 2023, and 2022 was €227,767, €164,655, and €88,963, respectively. The increase was mainly due to the increase in the Company's organizational structure.

11. Shareholders' equity

The number of the Company's outstanding ordinary shares on December 31, 2022, was 18,216,858, no par value. All ordinary shares outstanding are held in ledger form with some of the ordinary shares represented by ADSs.

For the year ended December 31, 2022, the Company accrued €722,735 as the fair value of stock options granted as per the Equity Incentive Plan 2021-2025. (See Note 12. Share-based compensation for more details.)

In July 2023, 100 new ADSs were issued in an ATM Offering, and the Company recorded an increase in the ordinary shares, no par value of €531.

For the year ended December 31, 2023, the Company accrued €739,884 as the fair value of stock options granted as per the Equity Incentive Plan 2021-2025. (See Note 12. Share-based compensation for more details.)

At December 31, 2023, the Company had 18,216,958 ordinary shares issued and outstanding with approximately 1.8 million ordinary shares reserved for the Plan.

In March 2024, 72,908 new ADSs were issued pursuant to the Sales Agreement and the Company recorded an increase in the ordinary shares, no par value of €270,885.

For the year ended December 31, 2024, the Company accrued €847,255 as the fair value of stock options granted as per the Plan. (See Note 12. Share-based compensation for more details.)

At December 31, 2024, the Company had 18,289,866 ordinary shares issued and outstanding with approximately 1.8 million ordinary shares reserved for the Plan.

Weighted average shares

The calculation was performed by taking the number of shares outstanding during a given period and weighting them for the number of days that number of shares were outstanding. For the year ended December 31, 2024, 2023, and 2022, there was a weighted average of 18,273,490, 18,216,907 and 18,216,858 shares, respectively, of the Company's ordinary shares, no par value.

12. Share-based compensation

To reward the efforts of employees, officers, directors, and certain consultants, and to promote the Company's growth and development, the Board may approve, upon occasion, various share-based awards.

The Plan was originally approved on May 20, 2021, and was subsequently modified, in June 2023, to extend the final deadline for the issuance of the ordinary shares until December 31, 2035, to allow that all stock options granted during the term of the Plan could provide for an exercise period of 10 years starting from the date of grant.

In April 2022, the Company's board of directors, as administrator of the Plan, awarded a nonqualified stock option ("NSO") on 147,783 shares to its (former) Chairman according to the terms of a Sub-Plan called "2021-2025 Chairman Sub-Plan" (the "Sub-Plan") attached to the Plan. The exercise price of the NSO was €6.38 per share, as pre-determined in the Sub-Plan. The NSO was fully vested upon grant and carried a two (2) year exercise term, therefore the options expired on April 2024 unexercised, and were returned to the stock options pool.

In July 2022, the Company's board of directors, as administrator of the Plan, awarded NSOs on 392,740 shares to certain of the Company's directors, officers and employees. The director NSOs vested monthly over a one-year period with a 10-year term. The officer and employee NSOs vested monthly over a four (4) year period with a 10-year term; however, the vesting of the officer NSOs were adjusted based on hire date per their employment contracts. All NSOs were priced based on a 30-day volume weighted average formula, adjusted by Black-Scholes, which was determined to be $4.76 per share.

At December 31, 2022, there were 540,523 granted stock options and 1,281,162 stock options remaining available for grant.

In March 2023, the Board, as administrator of the Plan, awarded NSOs on 46,400 shares to the Company's directors. The NSOs vested monthly over a one (1) year period with a 10-year term. All NSOs were priced based on a 30-day volume weighted average formula, adjusted by Black-Scholes, which was determined to be $5.62 per share.

At December 31, 2023, there were 586,923 granted stock options and 1,234,772 stock options remaining available for grant.

In July 2024, the Company's board of directors, as administrator of the Plan, awarded NSOs on 587,650 shares to certain of the Company's officers and employees. The NSOs vested monthly over a three-year period with a 10-year term, expiring on July 1, 2034. A cliff vesting period is provided for those employees with less than one (1) year of service at the time of grant, until the first anniversary of employment is completed. The exercise price of the NSOs is $3.083 per share, corresponding to the market price at the date of grant. In addition, each new Board member received equity compensation in the form of an initial stock option equity grant of $50,000 (based on the Black Scholes model) that vest immediately but are held for distribution for one year.

In the second half of 2024, two employees and a consultant left the Company. As per the applicable rules, the options already granted to the aforementioned employees and consultant, but not yet vested as of the termination date of their respective employment or consultancy contracts, have been returned to the stock option pool for a total of 56,482. Combined with those already returned to the pool on April 2024, a total of 204,265 options were returned to the pool in 2024.

At December 31, 2024, there were 970,308 granted stock options and 858,678 stock options remaining available for grant.

	Number of Options	Weighted Average Exercise Price	Weighted Average Remaining Contractual Term (Years)	Aggregate Intrinsic Value
Outstanding as of January 1, 2022	-	-	-	-
Granted	540,523	€ 4.99	7.3	€ -
Vested and exercised	-	-	-	-
Cancelled or forfeited	-	-	-	-
Outstanding as of December 31, 2022	540,523	€ 4.99	7.3	€ 272,480
Exercisable as of December 31, 2022	237,129	€ 5.66	4.42	€ 61,988
Outstanding, expected to vest as of December 31, 2022	**303,394**	**€ 4.67**	**9.55**	**€ 210,492**
Outstanding as of January 1, 2023	540,523	€ 4.99	7.3	€ 272,480
Granted	46,400	5.30	9.17	-
Vested and exercised	-	-	-	-
Cancelled or forfeited	-	-	-	-
Outstanding as of December 31, 2023	586,923	€ 4.84	6.53	€ 67,596
Exercisable as of December 31, 2023	382,785	€ 5.11	5.44	€ 33,796
Outstanding, expected to vest as of December 31, 2023	**204,138**	**€ 4.34**	**8.58**	**€ 33,800**
Outstanding as of January 1, 2024	586,923	€ 4.84	6.53	€ 67,596
Granted	587,650	2.87	9.50	-
Vested and exercised	-	-	-	-
Cancelled or forfeited	(204,265)	5.94	-	-
Outstanding as of December 31, 2024	970,308	€ 3.65	8.75	€ 706,366
Exercisable as of December 31, 2024	514,210	€ 4.13	8.23	€ 199,667
Outstanding, expected to vest as of December 31, 2024	**456,098**	**€ 3.10**	**9.33**	**€ 506,699**

The Company calculates the fair value of stock option awards granted to employees and non-employees using the Black-Scholes option-pricing method. If the Company determines that other methods are more reasonable, or other methods for calculating these assumptions are prescribed by regulators, the fair value calculated for the Company's stock options could change significantly. Higher volatility and longer expected lives would result in an increase to share-based compensation expense to non-employees determined at the date of grant. Share-based compensation expense to non-employees affects the Company's general and administrative expenses, and the Company's research and development expenses, depending on the non-employee's function.

The Company calculated the share compensation expense for the options granted by utilizing the Black Scholes method with the following inputs for each of the stock grants in March 2023, July 2022, and April 2022:

- The option's exercise price.
- The option's expected term.
- The underlying share's current price.
- The underlying share's expected price volatility during the option's expected (or in certain cases, contractual) term, or in cases where calculated value is used, the historical volatility of an appropriate industry sector index.
- The underlying shares' expected dividends during the option's expected (or in certain cases, contractual) term, except cases such as when dividend protection is provided; and
- The risk-free interest rate during the option's expected (or in certain cases, contractual) term.

The Company's share-based compensation expense for the years ended December 31, 2024, 2023, and 2022 is represented by the following table:

	Year ended December 31		
	2024	**2023**	**2022**
(in Euros)			
Research & development expense	€ 116,532	€ 73,392	€ 35,164
Research & development expense - related party	39,800	-	-
General & administrative expense	436,877	505,828	486,962
General & administrative expense - related party	254,046	160,664	200,609
Total	€ 847,255	€ 739,884	€ 722,735
Unrecognized expense	€ 1,404,415	€ 907,683	€ 1,639,082

For the years ended December 31, 2024, 2023, and 2022, the Company recorded €847,255, €739,884, and €722,735, respectively, as the fair value of the stock options granted.

The amount of unrecognized expense at December 31, 2024, 2023, and 2022 was €1,404,415, €907,683, and €1,639,082 respectively.

The weighted average fair value of the options granted during the period ended December 31, 2024, 2023 and 2022 was €2.87, €5.30 and €4.99 per share respectively.

13. Accumulated other comprehensive income

	Changes in Accumulated Other Comprehensive Income For the year ended December 31, 2024		
	Unrealized gains and losses on available-for-sale debt securities	Foreign Currency Translation Adjustments	Total
Beginning Balance	€ 214,984	€ 16,158	€ 231,142
Adjustment for net (gain) loss on marketable securities	(214,984)	-	(214,984)
Change in fair value of marketable securities	96,234	-	96,234
Cumulative translation adjustment	-	(23,446)	(23,446)
Total	€ 96,234	€ (7,288)	€ 88,946

Accumulated Other Comprehensive Income relates to marketable securities fair value measurement reserve and cumulative translation adjustment reserve as reported in the above table.

The net realized gain for the year ended December 31, 2024, from the Company's investing activity was approximately €0.4 million. The unrealized net gain on marketable securities not matured at December 31, 2024, was approximately €0.1 million.

The cumulative translation adjustments reserve was not material, and it mainly included the effect of the translation of U.S. dollars held by the U.S. Subsidiary into Euros as the consolidated financial statements currency.

14. Related parties

The Company's research and development expenses are a combination of third-party expenses, and related party expenses, as detailed below:

	For the Year Ended December 31, 2024		
	Third Parties	Related Parties	Total
(In Euros)			
Consultants & other third parties	€ 262,229	€ 753,679	€ 1,015,908
Materials & supplies	2,301,038	-	2,301,038
Compensation (including share-based)	744,959	695,764	1,440,723
Travel & entertainment	29,137	-	29,137
Other	26,048	-	26,048
Total	€ 3,363,410	€ 1,449,443	€ 4,812,854

	For the Year Ended December 31, 2023		
	Third Parties	Related Parties	Total
(in Euros)			
Consultants & other third parties	€ 305,289	€ 1,331,166	€ 1,636,455
Materials & supplies	3,639,920	-	3,639,920
Compensation (including share-based)	467,557	645,932	1,113,489
Travel & entertainment	44,243	-	44,243
Other	39,965	369	40,334
Total	€ 4,496,974	€ 1,977,467	€ 6,474,441

	For the Year Ended December 31, 2022		
	Third Parties	Related Parties	Total
		(in Euros)	
Consultants & other third parties	€ 804,341	€ 726,082	€ 1,530,423
Materials & supplies	2,790,982	-	2,790,982
Compensation (including share-based)	412,085	580,196	992,281
Other	25,276	-	25,276
Total	€ 4,032,684	€ 1,306,278	€ 5,338,962

Related party R&D expenses for consultants & other third parties refer mainly to the costs of preclinical and clinical activities charged by OSR. R&D costs for materials & supplies relate mainly to manufacturing costs charged by the Company's main manufacturing vendor, AGC Biologics. Compensation costs relate to R&D personnel wages, salaries, and share-based compensation including social contribution and other related personnel costs. Travel & entertainment expenses relate mainly to business trips and scientific conferences. Other R&D expenses relate to minor general operating costs.

The Company recorded research and development expenses of approximately €4.8 million in 2024, €6.5 million in 2023, and €5.3 million in 2022. The tax credit compensation effect was approximately €0.5 million in 2024, €0.4 million in 2023, and €0.7 million in 2022. Net of tax credit compensation effect, during 2024, the Company had a decrease in research and development expenses of approximately €1.7 million.

The decrease in R&D expenses of approximately €1.7 million was mainly due to several factors as explained above under the section *Results of Operations Comparison of Year Ended December 31, 2024 to Year Ended December 31, 2023.*

The increase in research and development expenses related parties for the year ended December 31, 2023, compared to the year ended December 31, 2022, was due to the increase in the number of treated patients and related clinical trial activities. Furthermore, the increase was also determined by the reduction in the offsetting effect of research and development tax credits as a consequence of the reduction from 20% to 10% of the calculation percentage to apply to the relevant research and development expenses.

The Company's general and administrative expenses are also a combination of third-party and related party expenses, as detailed below:

	For the Year Ended December 31, 2024		
	Third Parties	Related Parties	Total
(In Euros)			
Compensation (including share-based)	€ 1,019,056	€ 1,459,302	€ 2,478,358
Accounting, legal & other professional	828,592	-	828,592
Communication & IT related Facility	188,951		188,951
Facility & insurance related	3,348	14,795	18,143
Consultants & other third parties	561,458	-	561,458
Other	874,165	1,789	875,954
Total	€ 3,475,570	€ 1,475,886	€ 4,951,456

	For the Year Ended December 31, 2023		
	Third Parties	Related Parties	Total
(In Euros)			
Compensation (including share-based)	€ 1,218,299	€ 1,317,068	€ 2,535,367
Accounting, legal & other professional	1,026,534	-	1,026,534
Communication & IT related Facility	166,416		166,416
Facility & insurance related	6,180	15,731	21,911
Consultants & other third parties	610,103	-	610,103
Other	896,018	2,152	898,170
Total	€ 3,923,550	€ 1,334,951	€ 5,258,501

	For the Year Ended December 31, 2022		
	Third Parties	Related Parties	Total
		(in Euros)	
Compensation (including share-based)	€ 1,293,880	€ 1,268,974	€ 2,562,854
Accounting, legal & other professional	781,817	-	781,817
Communication & IT related	171,380	-	171,380
Facility & insurance related	1,241,692	14,815	1,256,507
Consultants & other third parties	593,788	-	593,788
Other	331,824	6,860	338,684
Total	€ 4,414,381	€ 1,290,649	€ 5,705,030

General and administrative expenses were approximately €5.0 million for the year ended December 31, 2024, as compared to approximately €5.3 million for the year ended December 31, 2023. The decrease of approximately €0.3 million was primarily due to the combined effect of:

1) a net decrease in accounting, legal and other professional (approximately €62,000) as the combined effect of the following main changes in the costs category: a decrease in external audit expenses due to the change of the audit company in the second half of 2023 (approximately €167,000); an increase in legal fees due to the amendment of the Sales Agent Agreement related to the ATM Offering program (approximately €130,000), and other minor costs decrease (approximately €25,000);

2) an increase in communication and IT related costs (approximately €23,000) mainly due to the cybersecurity system implementation;

3) a net decrease in consultants and other third party costs (approximately €26,000) as result of the combined effect of the reclassification of Board of Director cost from payroll expense to consultant expense (approximately €60,000), and the termination of some consultancy agreements (approximately €86,000); and,

4) a net decrease in other general and administrative costs (approximately €22,000) as a combined effect of: a decrease in the limited liability ("D&O") insurance cost (approximately €259,000); an increase in patent maintenance costs (approximately €134,000), and several other cumulative change (approximately €100,000).

There were no significant changes in general and administrative expenses related parties during the year ended December 31, 2023, compared to the year ended December 31, 2022. General and administrative expenses, other than related party, decreased mainly because of the decrease in the Company's limited liability insurance cost, aka director and officer ("D&O") insurance.

The Company's accounts payable to related parties are comprised as follows:

	At December 31,		
	2024	2023	2022
		(in Euros)	
San Raffaele Hospital (OSR)	€ 180,116	€ 170,888	€ 150,206
Carlo Russo	-	-	198
Richard Slansky	-	-	1,584
Total	€ 180,116	€ 170,888	€ 151,988

The Company's accrued expenses to related parties are comprised as follows:

	At December 31,		
	2024	2023	2022
		(in Euros)	
San Raffaele Hospital (OSR)	€ 128,188	€ 413,935	€ 176,559
Pierluigi Paracchi	336,000	175,254	112,501
Richard Slansky	243,101	116,738	81,369
Carlo Russo	324,055	155,651	118,778
Total	€ 1,031,345	€ 861,578	€ 489,207

The Company has identified the following related parties:

- Pierluigi Paracchi (director and co-founder of the Company);
- Luigi Naldini (co-founder of the Company and chair of the scientific advisory board);
- Bernhard Rudolph Gentner (co- founder of the Company and member of the scientific advisory board);
- Carlo Russo (former XDG Biomed - chief medical officer); and,
- Richard Slansky (chief financial officer);
- OSR - San Raffaele Hospital (co-founder of the Company, shareholder, main service provider for clinical activity and licensor of brands of any product that can be obtained through research).

The following is a description of the nature of the transactions between the Company and these related parties:

Pierluigi Paracchi

Mr. Pierluigi Paracchi is the Chief Executive Officer, Chairman and co-founder of the Company. Prior to the Company's conversion, he was the Chief Executive Officer, Vice-Chairman, and co-founder. His current employment arrangement with the Company provides an annual gross salary of €420,000 plus a 40% annual bonus subject to Board approval. Mr. Paracchi also has use of a Company car, for which the Company entered an operating lease agreement in February 2022.

For the year ended December 31, 2024, 2023, and 2022, the Company expensed approximately €688,000 €692,000, and €624,000, respectively, related to compensation for Mr. Paracchi. In July 2024, Mr. Paracchi received options on 120,000 shares of GNTA stock.

At December 31, 2024 and 2023, the Company accrued €168,000 for Mr. Paracchi's bonus to reward the activity performed respectively in 2024 and 2023. Mr. Paracchi's bonus for 2024 and 2023 remained unpaid at December 31, 2024 so that the bonus outstanding payment at December 31, 2024 amount to €336,000. At December 31, 2022, the Company accrued €112,501 for Mr. Paracchi's bonus from July to December. Mr. Paracchi's bonus for 2022 was paid in March 2023.

In April 2022, Mr. Paracchi received a bonus of €60,000 (gross amount), of which €23,000 related to the activity performed in the second half of 2021 and €37,000 for the activity performed following the IPO in the first few months of 2022. In July 2022, the Board approved an increase in Mr. Paracchi's bonus from 20% to 40% to begin effective January 1, 2023.

Luigi Naldini/Bernhard Rudolph Gentner

Drs. Naldini and Gentner are co-founders of Genenta and part of the SAB – Scientific Advisory Board, with Dr. Naldini as Chairman, and Dr. Gentner as a member. Dr. Naldini has an advisory agreement approved by the Board of Directors and performs pre-clinical studies for the Company. In particular, the pre-clinical experiments are in solid tumor indications. The last consulting agreement with Dr. Naldini was signed on June 20, 2022, which included an annual fee of €100,000 starting July 1, 2022.

At December 31, 2024 and 2023, Dr. Naldini billed €100,000, respectively, and all the issued invoices were paid before December 31st of each year.

Dr. Gentner, like Dr. Naldini, oversees pre-clinical research related to the Company's platform technology. In addition, he analyzes clinical biological data. The last agreement with Dr. Gentner started on July 1, 2022, and provided fees in the amount of €45,000 per year.

At December 31, 2024 and 2023, Dr. Gentner billed €45,000, respectively, and all the issued invoices were paid before December 31st of each year. In addition, during 2024, Dr. Gentner billed €5,000 for other consultancy activities and those invoices were paid in the same year.

Carlo Russo – former XDG Biomed LLC

XDG Biomed (XDG) is Dr. Carlo Russo's LLC. Dr. Russo had a contract with XDG, and the Company's Board of Directors approved the agreement along with multiple amendments. Dr. Russo, via XDG, served as the Company's Chief Medical Officer and Head of Development. Dr. Russo is responsible for the clinical development of Temferon™, the Company's gene therapy platform. The applicable recurring fees under XDG were €300,000 per year, plus a performance bonus of €50,000 for the period July-June of each year and payable after Board of Directors approval. This agreement continued until the Company's IPO. Since the IPO date, December 15, 2021, Dr. Russo has been employed by Genenta Science, Inc. with the same role and responsibilities under an employment agreement. The annual gross salary of Dr. Russo, as an employee, is $500,000 per year plus a 30% annual bonus subject to Board of Director approval.

For the year ended December 31, 2024, 2023, and 2022, the Company expensed approximately €611,000, €592,000 and €580,000, respectively, related to compensation for Dr. Russo. In July 2024 Mr. Russo received options on 100,000 shares of GNTA stock.

At December 31, 2024 and 2023, the Company accrued approximately € 145,000 and €156,000, respectively, for Dr. Russo's bonus to reward the activity performed in 2024 and 2023. Dr. Russo's bonus for 2024 and 2023 remained unpaid at December 31, 2024. At December 31, 2022, the Company accrued approximately €112,000 for Dr. Russo's bonus to reward the activity performed in 2022, which bonus was paid in March 2023.

Richard Slansky

Mr. Slansky is the Chief Financial Officer of the Company. Prior the IPO, he was engaged by the Company to assist with financial, accounting, and audit support under an advisory agreement until the end of October 2021. On November 1, 2021, he joined the Company full-time and has been employed as Chief Financial Officer. Under his employment agreement, Mr. Slansky was entitled to receive a gross annual compensation of $300,000 per year plus a 30% annual bonus subject to Board of Director approval. Beginning January 1, 2023, his gross annual compensation was increased to $375,000 plus a 30% annual bonus subject to Board of Director approval.

For the years ended December 31, 2024, 2023, and 2022, the Company expensed approximately €458,000, €456,000, and €445,000, respectively, related to compensation for Mr. Slansky. At December 31, 2024 and 2023, the Company accrued approximately €108,000 and €116,000, respectively, for Mr. Slansky's bonus to reward the activity performed in 2024 and 2023. Mr. Slansky's bonus for 2024 and 2023 remained unpaid at December 31, 2024. At December 31, 2022, the Company accrued approximately €77,000 for Mr. Slansky's bonus to reward the activity performed in 2022, which bonus was paid in March 2023. In July 2024 Mr. Slansky received options on 100,000 shares of GNTA stock.

In July 2022, Mr. Slansky was awarded a stock option grant and part of it was immediately vested, with value accrued into the Company's Consolidated Statements of Operations and Comprehensive Loss of approximately €201,000.

OSR – San Raffaele Hospital

OSR - San Raffaele Hospital is a co-founder of the Company, and the Company is a corporate and research spin-off of OSR. OSR is one of the leading biomedical research institutions in Italy and Europe, with a 45-year history of developing innovative therapies and procedures. The Company has agreements to license technology, to perform research, pre-clinical and clinical activities, as well as to lease facilities and obtain certain other support functions. The Company's headquarters is currently in an OSR facility.

Amended and Restated OSR License Agreement

The Company entered into an Amended and Restated License Agreement (the "ARLA") with OSR in March 2023. The ARLA replaced the Company's original license agreement originally entered into with OSR on December 15, 2014, as subsequently amended on March 16, 2017, February 1, 2019, December 23, 2020, September 28, 2021, January 22, 2022, September 29, 2022, and December 22, 2022 (the "Original OSR License Agreement").

The effectiveness of the ARLA was subject to Italy's Law Decree No. 21 of March 15, 2012 (i.e., the Italian Golden Power regulations), as subsequently amended and supplemented, and would not become effective until the applicable Italian governmental authority consented to the ARLA. On April 20, 2023, such consent was received and the ARLA became effective.

Pursuant to the terms of the ARLA, OSR has granted the Company an exclusive, royalty-bearing, non-transferrable (except with the prior written consent of OSR), sublicensable, worldwide license, subject to certain retained rights, to (1) certain patents, patent applications and existing know-how for the use in the field(s) of Interferon ("IFN") gene therapy by lentiviral based-hematopoietic stem and progenitor cells ("HSPC") gene transfer with respect to any solid cancer indication (including glioblastoma and solid liver cancer) and/or (b) any lympho-hematopoietic indication for which the Company exercises an option (described below); and (2) certain gene therapy products (subject to certain specified exceptions related to replication competent viruses) developed during the license term for use in the aforementioned field(s) consisting of any lentivirals or other viral vectors regulated by miR126 and/or miR130 and/or other miRs with the same expression pattern as miR126 and miR130 in hematopoietic cells for the expression of IFN under the control of a Tie2 promoter. Lympho-hematopoietic indication means any indication related to lympho-hematopoietic malignancies and solid cancer indication means any solid cancer indication (e.g., without limitation, breast, pancreas, colon cancer), with each affected human organ counting as a specific solid cancer indication.

The rights retained by OSR, and extending to its affiliates, include the right to use the licensed technology for internal research within the field(s) of use, the right to use the licensed technology within the field(s) of use other than in relation to the licensed products, and the right to use the licensed technology for any use outside the field(s) of use, but subject to the options described below. In addition, the Company granted OSR a perpetual, worldwide, royalty-free, non-exclusive license to any improvement generated by the Company with respect to the licensed technology, to conduct internal research within the field(s) of use directly, or in or with the collaboration third parties; and, for any use outside the field(s) of use, in which case the license is sublicensable by OSR. Finally, the world-wide rights for the field(s) of use granted to the Company regarding the Lentigen know-how are non-exclusive and cannot be sublicensed due to a pre-existing nonexclusive sublicense to these rights between OSR and GlaxoSmithKline Intellectual Property Development Limited.

Pursuant to the ARLA, the Company has an exclusive option exercisable until April 20, 2026 to any OSR product improvements at no additional cost, which could be useful for the development and/or commercialization of licensed products in the field of use. The Company also has an exclusive option exercisable until April 20, 2026 (the "LHI Option Period") to any lympho-hematopoietic indication(s) to be included as part of the field of use, on an indication-by-indication basis, subject to the payment of specified option fees and milestone payments:

- €1.0 million for the first lympho-hematopoietic indication;
- €0.5 million for the second lympho-hematopoietic indication; and
- €0.3 million for the third lympho-hematopoietic indication.

No option fee is due for the fourth lympho-hematopoietic indication and any subsequent lympho-hematopoietic indications.

The Company has the right to extend the LHI Option Period twice for additional 12-month periods, subject to the payment of specified extension fees.

Prior to the effective date of the ARLA, the Company paid OSR an upfront fee in amount equal to €250,000 pursuant to the Original OSR License Agreement.

Pursuant to the ARLA, as consideration, the Company agreed to pay OSR additional license fees equal to up to €875,000 in total, which are payable on April 20, 2023, December 31, 2023, and upon our entering into a sublicense agreement with a third party sublicensee (pursuant to which the Company is entitled to receive an upfront payment in an amount exceeding a specified threshold from such sublicensee) during the period between September 30, 2022 and April 20, 2028 (with most of these additional license fees being triggered upon our entering into such a sublicense agreement). In addition, the Company has agreed to pay OSR royalties and on a single digit percentage of the net sales of each licensed product. The royalty may be reduced upon the introduction of generic competition or patent stacking, but in no event would the royalty be less than half of what it would have otherwise been, but for the generic competition or patent stacking. The Company also agreed to pay OSR a royalty of our net sublicensing income for each licensed product and to pay OSR certain milestone payments upon the achievement of certain milestone events, such as the initiation of different phases of clinical trials of a licensed product, market authorization application ("MAA") approval by a major market country, MAA approval in the United States, the first commercial sale of a licensed product in the United States and certain E.U. countries, and achievement of certain net sales levels.

As part of the ARLA, the Company has agreed to use reasonable efforts to involve OSR in Phase I clinical trials for licensed products in the field of use, subject to OSR maintaining any required quality standards and providing its services on customary and reasonable terms and consistent with then-applicable market standards. We are also obligated to carry out our development activities using qualified and experienced professionals and sufficient level of resources. In particular, consistent with the terms of the Original OSR License Agreement, the ARLA continues to require us to invest (a) at least €5,425,000 with respect to the development of the licensed products, and (b) at least €2,420,000 with respect to the manufacturing of such licensed products (subject to certain adjustments). (See Note 14. Commitments and contingencies.)

OSR maintains control of the preparation, prosecution and maintenance of the patents licensed. The Company is obligated to pay those costs unless additional licensees benefit from these rights, in which case the cost will be shared *pro rata*. OSR controls enforcement of the patents and know-how rights, at its own expense. In the event that OSR fails to file suit to enforce such rights after notice from the Company, the Company has the right to enforce the licensed technology within the field of use. Both the Company and OSR must consent to settlement of any such litigation, and all monies recovered will be shared, after reimbursement for costs, in relation to the damages suffered by each party, or failing a bona fide agreement between the Company and OSR, on a 50% - 50% basis.

The ARLA expires upon the expiry of the "Royalty Term" for all licensed products and all countries, unless terminated earlier. The Royalty Term begins on the first commercial sale of a licensed product in each country, on a country by country basis, and ends upon the later of the (a) expiration of the commercial exclusivity for such product in that country (wherein the commercial exclusivity refers to any remaining valid licensed patent claims covering such licensed product, any remaining regulatory exclusivity to market and sell such licensed product or any remaining regulatory data exclusivity for such licensed product), and (b) 10 years from the first commercial sale of such licensed product in such country.

The parties may terminate the agreement in the event the other party breaches its obligations therein, which termination shall become effective 60 business days following written notice thereof to the breaching party. The breaching party shall have the right to cure such breach or default during such 60 business days. OSR may terminate the agreement for failure to pay in the event that the Company fail to pay any of the upfront payment, additional license fees, sublicensing income or milestone payments within 30 days of due dates for each. In addition, OSR may terminate (with a 60-business-day prior written notice) the Company's rights as to certain fields of use for the Company's failure to achieve certain development milestones for specified licensed products within certain time periods, which may be subject to extension. In addition, OSR may terminate the agreement in the event that commercialization of a licensed product is not started within 24 months from the grant of both (i) the MAA approval and (ii) the pricing approval of such licensed product, provided that such termination will relate solely to such licensed product and to such country or region to which both such MAA approval and pricing approval were granted.

Amendment to OSR Amended and Restated License Agreement

On September 28, 2023, the Company and OSR entered into an amendment to the ARLA, whereby the Company and OSR agreed that the Company had fulfilled the obligations as set forth in the ARLA specific to Candidate Products 1 pursuant to the CP1 SRA. Furthermore, the amendment provides that the Company and OSR have no further obligations to negotiate and execute a sponsored research agreement for the performance of feasibility studies related to certain gene therapy products consisting of any lentiviral vectors regulated by miR126 and/or miR130 and/or other miRs with the same expression pattern as miR126 and miR130 in hematopoietic cells for the expression of cytokines and their variants (other than IFN or in addition to IFN) under the control of a Tie2 promoter, either alone or in combination with any immunotherapy ("Candidate Products 2"). Notwithstanding the removal of the obligation to enter into a sponsored research agreement with regards to Candidate Products 2, OSR granted the Company an exclusive option, to be exercised by sending written notice to OSR on or before September 30, 2025, to include certain intellectual property related to Candidate Products 2 and Candidate Products 2 as part of the licensed patents and licensed products under the ARLA. The option fee and the Company's fee to extend the option period, if necessary, remain consistent with the prior fees to those costs reflected in the ARLA specific to Candidate Products 2. OSR will also have the right to prepare, file and prosecute patents and patent applications with respect to the results of Candidate Products 2. The amendment provides that the costs of the foregoing activities will be borne by the Company.

At December 31, 2024, the cumulative total amount of expense for the OSR clinical trial activity from inception amounted to approximately €11.5 million and including the cost for the exercise of the first and the second solid cancer indication option fee of €1.0 million, as well as the cost for ARLA fees of approximately €0.4 million.

At December 31, 2024, there were no pending activities with OSR related to any agreement in place prior to the ARLA effective date, except for the project called "TEM-MM unspent budget reallocated to the TEM-GBM study", for which the last tranche of activities corresponding to the 20% of the total project of approximately €0.2 million still pending completion.

OSR Sponsored Research Agreement

On August 1, 2023, the Company entered into a Sponsored Research Agreement ("CP1 SRA"), which was contemplated under the ARLA, pursuant to which the Company will fund feasibility studies for certain gene therapy products consisting of any lentiviral vectors regulated by miR126 and/or miR130 and/or other miRs with the same expression pattern as miR126 and miR130 in hematopoietic cells for the expression of IFN under the control of a Tie2 promoter, in combination with any immunotherapy ("Candidate Products 1"), along with three additional research projects, to be conducted at OSR. If OSR determines that additional funds are needed, OSR will inform the Company and provide an estimate for completing the research.

During the period from the date of execution from the CP1 SRA until six months from the last report delivered to the Company under the CP1 SRA (the "CP1 Option Period"), the Company has the exclusive option to include certain intellectual property related to Candidate Products 1 and Candidate Products 1 as part of the licensed patents and licensed products under the ARLA. To exercise this option, the Company must pay an option exercise fee. The Company also has the right to extend the CP1 Option Period twice for additional 24-month periods. The extension requires payment of an extension fee for each 24-month extension.

As of December 31, 2024, the Company recorded and paid approximately €0.4 million for the CP1 SRA studies.

Operating leases

The Company entered into a non-cancelable lease agreement for office space in December 2020 (see Note 15 Commitments and contingencies below).

15. Commitments and contingencies

The Company exercises considerable judgment in determining the exposure to risks and recognizing provisions or providing disclosure for contingent liabilities related to pending litigations or other outstanding claims and liabilities. Judgment is necessary in assessing the likelihood that a pending claim will succeed, or a liability will arise, and to quantify the possible range of the final settlement. Provisions are recorded for liabilities when losses are considered probable and can be reasonably estimated. Because of the inherent uncertainties in making such judgments, actual losses may be different from the originally estimated provision. Estimates are subject to change as new information becomes available, primarily with the support of internal specialists or outside consultants, such as actuaries or legal counsel. Adjustments to provisions may significantly affect future operating results.

The following table summarizes the Company obligations by contractual maturity at December 31, 2024:

	Payments by Period				
(in Euros)	Total	Less than a year	1 to 3 years	4 to 5 years	More than 5 years
OSR office rent, and parking	€ 16,012	€ 16,012	€ -	€ -	€ -
OSR- ARLA	83,400	83,400	-	-	-
AGC manufacturing	4,036,518	2,414,851	1,621,667	-	-
Insurance policies	7,597	6,996	600	-	-
Total	€ 4,143,527	€ 2,521,260	€ 1,622,267	€ -	€ -

The commitments with OSR relate to the office rent agreement and the ARLA while the commitments with AGC Biologics ("AGC") relate to product manufacturing.

Insurance on operating leases is related to the non-lease insurance component of the Company's auto lease agreement, which was entered into in February 2022 and has a term of four (4) years.

The Company has not included future milestone and royalty payments in the table above because the payment obligations under these agreements are contingent upon future events, such as the Company's achievement of specified milestones or generating product sales, and the amount, timing and likelihood of such payments are unknown and are not yet considered probable.

CMOs and CROs agreements

The Company enters into contracts in the normal course of business with CMOs, CROs, and other third parties for exploratory studies, manufacturing, clinical trials, testing, and services (shipments, travel logistics, etc.). These contracts do not contain minimum purchase commitments and, except as discussed below, are cancelable by the Company upon prior written notice. Payments due upon cancellation consist only of payments for services provided or expenses incurred, including non- cancelable obligations of the Company's vendors or third-party service providers, up to the date of cancellation. These payments are not included in the table above as the amount and timing of such payments are not known.

OSR - San Raffaele Hospital

As part of the ARLA, the Company is obligated to carry out development activities using qualified and experienced professionals and sufficient level of resources. In particular, consistent with the terms of the Original OSR License Agreement, the ARLA continues to require the Company to invest (a) at least €5,425,000 with respect to the development of the licensed products, and (b) at least €2,420,000 with respect to the manufacturing of such licensed products (subject to certain adjustments).

The Company incurred €1.8 million, €2.5 million, and €1.3 million of expenses during the period ended December 31, 2024, 2023, and 2022, respectively. The cumulative expense to date is approximately €10.0 million, therefore, there is no residual commitment for the Company at December 31, 2024.

The Company has agreed to pay OSR royalties for four percent (4%) of the net sales of each licensed product. The royalty may be reduced upon the introduction of generic competition or patent stacking, but in no event would the royalty be less than half of what it would have otherwise been, but for the generic competition or patent stacking. The Company also agreed to pay OSR a royalty of the Company's net sublicensing income for each licensed product and to pay OSR certain milestone payments upon the achievement of certain milestone events, such as the initiation of different phases of clinical trials of a licensed product, market authorization application ("MAA") approval by a major market country, MAA approval in the United States, the first commercial sale of a licensed product in the United States and certain E.U. countries, and achievement of certain net sales levels.

No events have occurred or have been achieved (and none are considered probable) to trigger any contingent payments under the ARLA during the period ended December 31, 2024. For information relating to the contingency payments or future milestones for these indications, please refer to Note 14 - Commitments and Contingencies.

AGC Biologics

The AGC agreement is non-cancelable, except in the case of breach of contract, and includes a potential milestone of €0.3 million if a phase 3 study is approved by the relevant authority, as well as potential royalty fees between 0.5% and 1.0% depending on the volume of annual net sales of the first commercial and named patient sale of the product. In the AGC Agreement, the Company entrusts AGC with certain development activities that will allow the Company to carry out activities related to its clinical research and manufacturing. The AGC agreement also includes a technology transfer fee of €0.5 million related to the transfer of the manufacturing know-how and €1.0 million related to the marketability approval by regulatory authorities. The agreement is a "pay-as-you-go" type arrangement with all services expensed in the period the services were performed.

In March 2022, the Company entered into Side Letter to the Framework Service Agreement with ACG Biologics to perform the manufacture of one (1) additional GMP batch of 24L INFa LV vector (TIA-126 LV) completed in November 2022, for €311,280.

In October 2022, the Company entered into Side Letter to the Master Service Agreement dated March 6, 2019 to negotiate a technology transfer agreement regarding the transfer and implementation of the manufacturing process in the AGC facility located in Bresso, Italy, including timeline, budget and the technology transfer protocol (the "Tech Transfer") and AGC agreed with the Company to procure raw materials to be use under the Tech Transfer. At December 31, 2024, the project was completed.

In December 2022, the Company signed respectively: (i) the Amendment No. 1 to the Master Service Agreement dated March 6, 2019 mainly to update the definition of raw materials; and (ii) a Process Transfer Agreement to agree on producing the raw materials necessary for the performance of the services related to the Tech Transfer for a total commitment of €405,000 for raw materials, € 40,500 for handling and €24,000 for the stability timepoints. At December 31, 2024, the project was completed.

In January 2023, the Company entered into a new Development and Manufacturing Service Agreement providing the framework under which AGC will provide services pursuant to one or more work statements to be entered into from time to time during the agreement term. Based on this agreement AGC will reserve slots in its facility on the basis of Genenta requirements for the product manufacturing. Each party retains sole ownership of any intellectual property owned or controlled by that party (i) as of the effective date or before the commencement of the services; or (ii) as a consequence of any activities of that party or its affiliates which are unconnected with the services performed hereunder ("Pre-Existing IPR"). The agreement may be terminated on the later of (a) the date that all stages under all work statements have been completed and (b) ten (10) years from the effective date, unless sooner terminated in case of material breach, in case of liquidation or default of any party. Genenta may also terminate the agreement or any stage of the services at any time before completion of the services or stage by giving no less than sixty (60) days' notice in writing to AGC detailing the stages of the services that are to be terminated. In case of early termination payments are due to AGC for services performed up to and including the day of termination for all completed stages and for partially completed stages in an amount calculated on a pro-rata basis. Cancellation fees for any batch scheduled for manufacture are provided to the extent of 30% or 50% of the relevant work statement.

Under this Manufacturing Service Agreement, work statements WS01, WS02, and WS03 have been issued for a total production value of approximately €4.8 million, of which, as of December 31, 2024, around €0.9 million still remains to be executed.

In December 2023, the Company entered into purchase orders n. 41 and 42 under the Master Service Agreement dated March 6, 2019 as amended in December 2022, for a total amount of approximately €0.2 million. At December 31, 2024 the production activity was completed.

During 2024, Genenta and AGC reached an agreement to renew the Master Service Agreement (MSA) originally signed in March 2019. Initially, the same agreement was temporarily extended until June 2025 to allow for better definition of the scope and terms of the new MSA, which was signed with effect from December 24, 2024.

The new MSA is an open-ended agreement with no specific expiration date, as its term is tied to the completion of any service phase, or work statement ("WS"), starting with WS01.

The service provided by AGC includes activities of manufacturing, testing, and release of Cell Therapy Drug Product using an Exclusive GMP Suite ("EGS") and a dedicated team ("EGS Team"). The service is remunerated through monthly fees that primarily cover the costs of the suite and the dedicated team, in addition to direct production costs for materials and other accessories if applicable. AGC retains control over both the logistical and organizational aspects of the service, as well as the operational aspects related to the hiring, training, and coordination of personnel. AGC also remains solely responsible for fulfilling any remuneration and social security obligations toward its personnel.

WS01 includes two main phases:

1. An initial Ramp-Up Phase with an estimated duration of 6 months, starting on February 1, 2025 (start of activities) and ending on August 1, 2025.

2. A Routine Phase, which is scheduled to begin on the first day of the subsequent month after the completion of the Ramp-Up Phase (specifically, after the receipt of authorization from the Regulatory Agency ("AIFA") to use the Exclusive Suite and the successful completion of the training of personnel assigned to the dedicated team).

The Company may terminate this schedule or work statement by providing twelve (12) months' prior written notice to AGC. However, such notice cannot be issued before the sixth (6th) month anniversary of the Ramp-Up Phase commencement date (for clarity, the notice must not be sent before August 1, 2025).

As a result of these contractual provisions, as of December 31, 2024, the Company has a commitment of approximately €3.5 million, and since the agreement was signed in December 2024, the commencement date of this agreement is February 2025. The Company is determining if the agreement qualifies as an operating lease under ASC 842.

Operating leases

On December 1, 2019, the Company began a six-year non-cancelable (and renewable for further six (6) years until December 1, 2026) lease agreement for office space with OSR. Withdrawal is allowed from the fourth year with a notice of 12 months. After the initial expiration date, the contract is automatically renewed for an additional six (6) years. As of December 31, 2024, neither party has communicated any termination of the lease agreement, which is therefore considered renewed until December 2031, subject to any potential earlier resignation.

Since the annual rent amounts to approximately €15,000, at December 31, 2024, outstanding minimum payments amount to approximately €15,000 until December 1, 2025.

Legal proceedings

The Company is not currently party to any material legal proceedings. At each reporting date, the Company evaluates whether a potential loss or a potential range of loss is probable and reasonably estimable under the provisions of ASC 450, Contingencies.

16. Subsequent events.

AGC Biologics Agreement

On February 18, 2025, the Company and AGC Biologics S.p.A. ("AGC") entered into a Project Change Order ("PCO") n. 6 for Work Statement 02 ("WS02"), project number 1486-04, under the Master Service Agreement ("MSA") dated January 20, 2023 and WS02 dated February 2, 2023. The change order consists of changes in the addition of one 24CF/48 L GMP LVV Manufacturing and Release process. The batch will be executed according to AGC platform process with an estimated timeline of six (6) months for completion, including reporting results. The activity is expected to be completed by June 2025, and the order is not cancellable. The cost of the service under this PCO, including the manufacturing and release of one additional batch, as well as materials, external testing, and other external costs, is estimated at approximately €0.6 million.

Mandatory Convertible Bond Financing

On March 12, 2025, the Company and Fondazione Enea Tech e Biomedical ("Enea"), a private law foundation subject to the supervision of the Ministry of Enterprises and Made in Italy, entered into a Subscription Agreement (the "Subscription Agreement") providing for the subscription of a mandatory convertible bond loan denominated "MANDATORY CONVERTIBLE LOAN GENENTA 2025-2028" (the "Mandatory Convertible Bond") by Enea, with an aggregate nominal value of up to €20 million and consisting of up to a total of 2,000 bonds (the "Convertible Bonds"), each with a nominal value of €10,000 (the "Nominal Value"), to be issued in two tranches by the Company at an issue price per unit equal to €10,000 for 100% of the Nominal Value. The Subscription Agreement contains certain representations and warranties and covenants of the parties and conditions precedent to the issuance of the Convertible Bonds, and the terms and conditions of the Mandatory Convertible Bond are governed by the Regulation of the Mandatory Convertible Bond Loan Denominated "Mandatory Convertible Loan Genenta 2025-2028" (the "Bond Regulation").

The Convertible Bonds consist of two tranches: an initial tranche in the amount of €7,500,000 (the "First Tranche") issued on March 19, 2025 (the "First Tranche Issue Date") and a subsequent tranche in the amount of €12,500,000 (the "Second Tranche") to be issued by September 19, 2026 (the "Second Tranche Issue Date" and, together with the First Tranche Issue Date, each an "Issue Date"). The issuance of the Second Tranche on the Second Tranche Issue Date is subject to a number of conditions precedent, including: (i) the Company's achievement of safety and tolerability on the project on research and creation of new therapeutic products for the prevention and treatment of oncological pathologies and, in particular, for the development of Temferon cell and gene therapy for the clinical indication of renal cancer in a phase 1 and phase 2 clinical trial in the so-called Renal Cell Cancer Trial by using gene-based cytokine delivery to activate the immune system within the tumor (the "Project"), which is considered to have been achieved following verification and certification by an independent scientific advisor appointed by Enea (the "Scientific Advisor"), (ii) the approval by the Italian Medicines Agency (Agenzia Italiana del Farmaco) ("AIFA") of the phase 2 clinical trial referred to in the Project and (iii) the completion of investment transactions in the Company's share capital through the issuance of shares, convertible bonds, warrants or similar instruments for a total aggregate amount of €32,500,000.

The Convertible Bonds will automatically convert into ordinary shares of the Company (the "Conversion Shares") on the earlier of (i) the occurrence of either (x) a Change of Control, which is defined as an acquisition by a person or group of persons not currently controlling the Company of more than 50% of the Company's issued share capital with voting rights or a takeover bid and/or exchange offer launched on all of the Company's outstanding ordinary shares and American depositary shares ("ADSs") or (y) the completion of an Investment Round, which is defined as any further investment transactions in the Company's share capital through the issuance of shares, convertible bonds, warrants or similar instruments for a total aggregate amount of €50,000,000 (the "Early Conversion Date" and, together with the Maturity Date, each a "Conversion Date") and (ii) three years after the First Tranche Issue Date (the "Maturity Date").

The Convertible Bonds will bear interest at a fixed annual nominal rate calculated on the Nominal Value before withholding tax, to be paid in arrears in a lump-sum amount no later than five business days after either the Early Conversion Date or the Maturity Date, with the Company having the option to pay Enea in (i) ordinary shares of the Company calculated at an interest rate equivalent to 6% on the Nominal Value or (ii) cash at an interest rate equivalent to 4% calculated on the Nominal Value.

Upon conversion of the Convertible Bonds at the Maturity Date, the conversion price (the "Ordinary Conversion Price") will be determined as follows: (i) 55% of the Ordinary Conversion Price will be represented by the weighted average of the official prices of the Company's ADSs recorded on the Nasdaq Capital Market in the 90 days preceding the Maturity Date; and (ii) 45% of the Ordinary Conversion Price will be represented by the fair market value of the Company's ordinary shares determined by an independent financial advisor appointed by Enea (the "Advisor"), according to criteria used internationally for the valuation of companies comparable to the Company and, in particular, the criteria of the so-called "Free Cash Flow Method" and "Venture Capital Method" and, in any case, in compliance with the relevant provisions of Art. 2441(6) of the Italian Civil Code ("Fair Market Value"). A discount will be applied to the Ordinary Conversion Price equal to (i) 6% of the Ordinary Conversion Price, if the Ordinary Conversion Price is equal to or greater than 50% of the weighted average of the official prices of the ADSs recorded on the Nasdaq Capital Market during the 90 days preceding the First Tranche Issue Date; and (ii) 3% of the Ordinary Conversion Price, if the Ordinary Conversion Price is less than 50% of the weighted average of the official prices of the ADSs recorded on the Nasdaq Capital Market in the 90 days preceding the First Tranche Issue Date.

Upon conversion of the Convertible Bonds at the Early Conversion Date, the conversion price (the "Early Conversion Price" and, together with the Ordinary Conversion Price, each a "Conversion Price") will be determined as follows: (a) in the event of a Change of Control: (i) 55% of the Early Conversion Price will be represented by the weighted average of the official prices of the Company's ADSs recorded on the Nasdaq Capital Market in the 90 days preceding the Early Conversion Date; and (ii) 45% of the Early Conversion Price will be represented by the official price of the takeover and/or exchange offer; and (b) in the event that, from the First Tranche Issue Date and prior to the Conversion Date, an Investment Round occurs, a discount equal to 10% of the price of the shares actually applied in the subscription and payment of the portion of the capital increase relating to the Investment Round which resulted in the aggregate amount of the Investment Round of €50,000,000 being reached or exceeded will be applied to the Early Conversion Price. In no event will the Conversion Price exceed $17.64 per ordinary share of the Company.

The number of Conversion Shares that will be issued upon conversion of the Convertible Bonds (the "Conversion Ratio") will be calculated by dividing the sum of the Nominal Value of and, if the Company decides to pay interest in ordinary shares as describe above, the accrued interest on the Convertible Bonds, divided by the Conversion Price. The Conversion Ratio is subject to adjustment upon certain extraordinary transactions as set forth in the Bond Regulation. Further, in no event will the application of the Conversion Ratio result in the allotment of a number of Conversion Shares representing an interest in the Company's share capital on the Conversion Date in excess of 29%. In addition, the Bond Regulation provides that the Conversion Shares will be subject to a lock-up period of two years following the Conversion Date (the "Lock-Up Period").

The Subscription Agreement provides that the Company and Enea will establish a project committee for the purpose of monitoring and overseeing the Company's research and development project for new therapeutic products for the prevention and treatment of renal cell cancer by using gene-based cytokine delivery to activate the immune system within the tumor, which will remain in effect until the completion of the activities related to the phase 2 trial of the Project. In addition, upon Enea receiving the Conversion Shares, the Subscription Agreement provides that Enea will have the right, but not the obligation, to appoint an observer to the Company's Board of Directors (the "Observer") at any time for the duration of the Lock-Up Period. The Observer will have the right to attend and participate at the Company's meetings of its Board of Directors, and access documents presented and exchanged at such meetings, but will not have any voting rights.

The Bond Regulation contains certain events of default that entitle Enea to demand the early redemption of the Convertible Bonds for a cash amount equal to 100% of the total amount thereof. These events of default include the Company's failure to complete an investment of up to €7,500,000 in accordance with the Company's operating plan (the "Plan") for the Project, certain suspensions or interruptions of the Project, certain failures of the Company to comply with the Plan, certain failures of the Company to comply with its reporting obligations to Enea, the delisting of the Company's ADSs, if the Company's auditor expresses an adverse opinion or states that it cannot express an opinion on the Company's financial statements, certain cross defaults in excess of €1,500,000 and certain material adverse changes in relation to the continuation of the Project.

The Convertible Bonds and the Conversion Shares have been and will be issued in offshore transactions exempt for registration pursuant to Regulation S under the Securities Act.

Proceeds from ATM

On March 20, 2025, the Company issued 856,602 ADSs for net proceeds of approximately €2,977,100 (or approximately $3,222,900), bringing the total number of ordinary shares outstanding to 19,146,468, pursuant to the Sales Agreement in place with Rodman & Renshaw and Virtu Capital.

Exhibit 2.4

DESCRIPTION OF SECURITIES REGISTERED UNDER SECTION 12 OF THE EXCHANGE ACT

As of December 31, 2024, Genenta Science S.p.A. (the "Company," "we," "us," and "our") had the following classes of securities registered pursuant to Section 12(b) of the Exchange Act:

#	Title of each class	Trading symbol	Name of each exchange on which registered
I.	Ordinary Shares, with no par value *		The Nasdaq Stock Market LLC
II.	American Depositary Shares, or ADSs,** each representing one Ordinary Share	GNTA	The Nasdaq Stock Market LLC

* *Not for trading, but only in connection with registration of ADSs.*
** Evidenced by American Depositary Receipts, or ADRs.

Capitalized terms used but not defined herein have the meanings given to them in our annual report on Form 20-F for the fiscal year ended December 31, 2024 (our "annual report"), unless otherwise indicated herein.

I. ORDINARY SHARES

The following description of our share capital and certain material provisions of our corporate rules is a summary and does not purport to be complete. It is subject to, and qualified in its entirety by, our Amended and Restated By-laws (*statuto*) (our "By-laws") and Italian corporate law.

A copy of our By-laws is attached to our annual report as Exhibit 3.2. We encourage you to read our By-laws and the applicable sections of our annual report for additional information.

Share Capital

Our capital stock is composed of Ordinary Shares with no par value. As of December 31, 2024, our issued share capital consisted of 18,273,490 Ordinary Shares. All issued shares are fully paid, non-assessable and in registered form.

Form and Transfer of Shares

Our Ordinary Shares are not represented by share certificates (*certificati azionari)* as they are *dematerialised (azioni dematerializzate*). The ownership of the shares, their transfer, the related rights and restrictions on the shares (if any) results from the electronical register managed by an intermediary (banks and other financial institutions). The entitlement to exercise the rights attached to the shares is then proven by the exhibition of certifications or communications to the issuer made by the intermediary, pursuant to its own accounting records, in favor of the subject entitled to the right.

There are no limitations on the right to own or vote our Ordinary Shares, which applies to non-Italian residents and foreign residents. There are no provisions in our articles of association or bylaws that would have the effect of delaying, deferring or preventing a change of control of our Company and that would operate only with respect to a merger, acquisition or corporate restructuring involving our Company. There are no provisions in our bylaws governing the ownership threshold which shareholder ownership must be disclosed. There are no provisions discriminating against any existing or prospective holder of our Ordinary Shares as a result of such shareholder owning a substantial number of our shares. There are no sinking fund provisions or provisions providing for liability for further capital calls by our Company.

Dividend Rights

Payment by the Company of any annual dividend is proposed by the board of directors and is subject to the approval of the shareholders at the annual shareholders' meeting. Before dividends may be paid out of the Company's unconsolidated net income in any year, an amount at least equal to 5% of such net income must be allocated to the Company's legal reserve until such reserve is at least equal to one-fifth of the par value of the Company's issued share capital. If the Company's share capital is reduced as a result of accumulated losses, no dividends may be paid until the capital is reconstituted or reduced by the amount of such losses. The Company may pay dividends out of available retained earnings from prior years, provided that, after such payment, the Company will have a legal reserve at least equal to the legally required minimum. No interim dividends may be approved or paid.

Dividends will be paid in the manner and on the date specified in the shareholders' resolution approving their payment (usually within 30 days from their annual general meeting). Dividends that are not collected within five years of the date on which they become payable are forfeited to the benefit of the Company. Holders of ADSs will be entitled to receive payments in respect of dividends on the underlying shares through BNY, as Depositary, in accordance with the Deposit Agreement.

Voting Rights

In general, registered holders of the Company's Ordinary Shares are entitled to one vote *per* Ordinary Share.

In addition, at our 2024 Ordinary and Extraordinary Shareholders' Meeting, our shareholders approved an amendment to our By-laws that established a loyalty share program. Under the loyalty share program, each Ordinary Share held in registered form entitles the shareholder to a double vote (i.e. two votes for each Ordinary Share) if the Ordinary Share has been held by the same shareholder for a continuous period of not less than twenty-four months from the date of its registration in the special list maintained by us, and an additional vote is also granted upon the expiration of each 12-month period, following the expiration of the period referred to above, in which such Ordinary Share has been held by the shareholder, up to a total maximum of ten votes per Ordinary Share.

To effect the loyalty share program, a special list (the "Special List") is maintained by us. To be added to the Special List, the registered shareholder would need to submit a specific application, enclosing a communication certifying the Ordinary Share ownership – which may also concern only part of the Ordinary Shares held by the registered shareholder – issued by the intermediary with whom the Ordinary Shares are deposited pursuant to the laws in force. In the case of entities other than individuals, the application would need to specify whether the entity is subject to direct or indirect control by third parties and the identification data of the controlling entity, if any. The Special List is updated by us. Cancellation from the Special List results from the following cases: renunciation of the interested party; communication of the interested party or of the intermediary proving the loss of the prerequisites for the increase of the voting right or the loss of the ownership of the right; ex officio, when we are informed of the occurrence of facts that entail the loss of the prerequisites for the increase of the voting right or the loss of the ownership of the right.

As a registered shareholder, the Depositary (or its nominee) will be entitled to vote the Ordinary Shares underlying the ADSs. The Deposit Agreement requires the Depositary (or its nominee) to accept voting instructions from holders of ADSs and to execute such instructions to the extent permitted by law. However, only shareholders who own their shares in registered form are entitled to take advantage of the loyalty share program and ADS holders are not entitled to additional voting rights. Neither Italian law nor the Company's By-laws limit the right of non-resident or foreign owners of the Company's Ordinary Shares to hold or vote shares of the Company.

Pre-emptive Rights

Pursuant to Italian law, holders of outstanding ordinary shares and convertible debentures are entitled to subscribe for newly issued ordinary shares or convertible debentures in proportion to their holdings at the time that the shareholders authorize the capital increase for those issuances, unless those issuances are for non-cash considerations. Those who exercise their preemptive rights, provided they make such request simultaneously, have a pre-emption right on the purchase of shares and debentures convertible into shares that have not been subscribed. Preemptive rights may be excluded or limited by resolution of the shareholders at an extraordinary shareholders' meeting, or by the board of directors if the bylaws delegate such power to the board of directors (including the power to exclude or limit the preemptive right), and provided that such exclusion or limitation is in the interest of the Company, or if the shares are to be paid by means of contributions in kind. According to Italian law proposals to increase share capital with exclusion or limitation of preemptive rights must be accompanied by a report of the board of directors setting forth the reasons for the exclusion or limitation of pre-emptive rights, or, if the exclusion derives from a contribution in kind, the reasons for such contribution in kind, and the report must in all cases set forth the criteria adopted for determining the issue price. The report must be communicated by the board of directors to the board of statutory auditors and to the external auditor at least 30 days prior to the date set for the shareholders' meeting. Within 15 days, the board of statutory auditors must express its opinion on the fairness of the issue price of the shares. The opinion of the board of statutory auditors and, only in the case of contributions in kind, the sworn report of an expert appointed by a competent court or documentation provided by Italian law, must remain deposited at the Company's registered office during the 15 days prior to the shareholders' meeting and until the latter has passed a resolution. The resolution shall determine the issue price of the shares on the basis of shareholders' equity, taking into account, in the case of shares listed on regulated markets, also the trend in prices over the last six months. The foregoing procedure shall apply also in case of capital increase delegated to the board of directors.

Liquidation Rights

Pursuant to Italian law and subject to the satisfaction of the claims of all creditors, our shareholders are entitled to a distribution in liquidation that is equal to an amount resulting from the division of the positive liquidation balance by the number of shares (to the extent available out of our net assets). Preferred shareholders and holders of "participating certificates", if any, typically do not participate in the distribution of assets of a dissolved corporation beyond their established contractual preferences. Once the rights of preferred shareholders and holders of participating certificates and the claims of all creditors have been fully satisfied, holders of ordinary shares are entitled to the distribution of any remaining assets.

II. AMERICAN DEPOSITARY SHARES

The following description of the ADSs and certain material provisions of our corporate rules is a summary and does not purport to be complete. It is subject to, and qualified in its entirety by the Deposit Agreement (as defined below), the form of ADS, which contain the terms of the ADSs, and any applicable law, as amended from time to time. In the following description, an "Owner" is the person in whose name an ADS is registered on the books of the Depositary (as defined below).

A copy of the Deposit Agreement is attached to our annual report as Exhibit 4.1. Copies of the Deposit Agreement are also available for inspection at the offices of our Depositary.

We encourage you to read the Deposit Agreement, the ADS form and the applicable sections of our annual report for additional information.

General

In the U.S., we trade ADSs representing our Ordinary Shares, which are evidenced by ADRs. Our ADSs, each representing one Ordinary Share, are traded on the Nasdaq Capital Market, under the ticker symbol GNTA.

The Bank of New York Mellon acts as depositary for our ADSs (the "Depositary"). In its capacity, the Depositary will register and deliver the ADSs, each representing an ownership interest in one Ordinary Share deposited with the custodian, as agent of the Depositary, under the deposit agreement dated December 17, 2021, between us, the Depositary, and Owners and beneficial owners from time to time of the ADSs (the "Deposit Agreement"), and (ii) any other securities, cash or other property which may be held by the Depositary.

The principal executive office of the Depositary and the office at which the ADSs will be administered is currently located at 240 Greenwich Street, New York, New York 10286, United States.

Voting

ADS holders may instruct the depositary how to vote the number of deposited shares their ADSs represent. If we request the depositary to solicit your voting instructions (and we are not required to do so), the depositary will notify you of a shareholders' meeting and send or make voting materials available to you. Those materials will describe the matters to be voted on and explain how ADS holders may instruct the depositary how to vote. For instructions to be valid, they must reach the depositary by a date set by the depositary. The depositary will try, as far as practical, subject to the laws of Italy and the provisions of our articles of association or similar documents, to vote or to have its agents vote the shares or other deposited securities as instructed by ADS holders. If we do not request the depositary to solicit your voting instructions, you can still send voting instructions, and, in that case, the depositary may try to vote as you instruct, but it is not required to do so.

Except by instructing the depositary as described above, you will not be able to exercise voting rights unless you surrender the ADSs and withdraw the shares. However, you may not know about the meeting enough in advance to withdraw the shares. In any event, the depositary will not exercise any discretion in voting deposited securities and it will only vote or attempt to vote as instructed.

We cannot assure you that you will receive the voting materials in time to ensure that you can instruct the depositary to vote your shares. In addition, the depositary and its agents are not responsible for failing to carry out voting instructions or for the manner of carrying out voting instructions. This means that you may not be able to exercise voting rights and there may be nothing you can do if your shares are not voted as you requested.

In order to give you a reasonable opportunity to instruct the depositary as to the exercise of voting rights relating to Deposited Securities, if we request the Depositary to act, we agree to give the depositary notice of any such meeting and details concerning the matters to be voted upon at least 45 days in advance of the meeting date.

As noted above, only shareholders who own their shares in registered form are entitled to take advantage of the loyalty share program and ADS holders are not entitled to additional voting rights.

Share Dividends and Other Distributions

The depositary has agreed to pay or distribute to ADS holders the cash dividends or other distributions it or the custodian receives on shares or other deposited securities, upon payment or deduction of its fees and expenses. You will receive these distributions in proportion to the number of shares the ADSs represent.

Cash. The depositary will convert any cash dividend or other cash distribution we pay on the shares into U.S. dollars, if it can do so on a reasonable basis and can transfer the U.S. dollars to the United States. If that is not possible or if any government approval is needed and cannot be obtained, the deposit agreement allows the depositary to distribute the foreign currency only to those ADS holders to whom it is possible to do so. It will hold the foreign currency it cannot convert for the account of the ADS holders who have not been paid. It will not invest the foreign currency and it will not be liable for any interest.

Before making a distribution, any withholding taxes, or other governmental charges that must be paid will be deducted. The depositary will distribute only whole U.S. dollars and cents and will round fractional cents to the nearest whole cent. If the exchange rates fluctuate during a time when the depositary cannot convert the foreign currency, you may lose some of the value of the distribution.

Shares. The depositary may distribute additional ADSs representing any shares we distribute as a dividend or free distribution. The depositary will only distribute whole ADSs. It will sell shares which would require it to deliver a fraction of an ADS (or ADSs representing those shares) and distribute the net proceeds in the same way as it does with cash. If the depositary does not distribute additional ADSs, the outstanding ADSs will also represent the new shares. The depositary may sell a portion of the distributed shares (or ADSs representing those shares) sufficient to pay its fees and expenses in connection with that distribution.

Rights to purchase additional shares. If we offer holders of our securities any rights to subscribe for additional shares or any other rights, the depositary may (i) exercise those rights on behalf of ADS holders, (ii) distribute those rights to ADS holders or (iii) sell those rights and distribute the net proceeds to ADS holders, in each case after deduction or upon payment of its fees and expenses. To the extent the depositary does not do any of those things, it will allow the rights to lapse. In that case, you will receive no value for them. The depositary will exercise or distribute rights only if we ask it to and provide satisfactory assurances to the depositary that it is legal to do so. If the depositary will exercise rights, it will purchase the securities to which the rights relate and distribute those securities or, in the case of shares, new ADSs representing the new shares, to subscribing ADS holders, but only if ADS holders have paid the exercise price to the depositary. U.S. securities laws may restrict the ability of the depositary to distribute rights or ADSs or other securities issued on exercise of rights to all or certain ADS holders, and the securities distributed may be subject to restrictions on transfer.

Other Distributions. The depositary will send to ADS holders anything else we distribute on deposited securities by any means it thinks is legal, fair and practical. If it cannot make the distribution in that way, the depositary has a choice. It may decide to sell what we distributed and distribute the net proceeds, in the same way as it does with cash. Or, it may decide to hold what we distributed, in which case ADSs will also represent the newly distributed property. However, the depositary is not required to distribute any securities (other than ADSs) to ADS holders unless it receives satisfactory evidence from us that it is legal to make that distribution. The depositary may sell a portion of the distributed securities or property sufficient to pay its fees and expenses in connection with that distribution. U.S. securities laws may restrict the ability of the depositary to distribute securities to all or certain ADS holders, and the securities distributed may be subject to restrictions on transfer.

The depositary is not responsible if it decides that it is unlawful or impractical to make a distribution available to any ADS holders. We have no obligation to register ADSs, shares, rights or other securities under the Securities Act. We also have no obligation to take any other action to permit the distribution of ADSs, shares, rights or anything else to ADS holders. This means that you may not receive the distributions we make on our shares or any value for them if it is illegal or impractical for us to make them available to you.

Procedures for Transmitting Notices, Reports and Proxy Soliciting Material

The depositary will make available for your inspection at its office all communications that it receives from us as a holder of deposited securities that we make generally available to holders of deposited securities. The depositary will send you copies of those communications or otherwise make those communications available to you if we ask it to. You have a right to inspect the register of holders of ADSs, but not for the purpose of contacting those holders about a matter unrelated to our business or the ADSs.

Amendment and Termination

We may agree with the depositary to amend the deposit agreement and the ADRs without your consent for any reason. If an amendment adds or increases fees or charges, except for taxes and other governmental charges or expenses of the depositary for registration fees, facsimile costs, delivery charges or similar items, or prejudices a substantial right of ADS holders, it will not become effective for outstanding ADSs until 30 days after the depositary notifies ADS holders of the amendment. At the time an amendment becomes effective, you are considered, by continuing to hold the ADSs, to agree to the amendment and to be bound by the ADRs and the deposit agreement as amended.

The depositary will initiate termination of the deposit agreement if we instruct it to do so. The depositary may initiate termination of the deposit agreement if

- 60 days have passed since the depositary told us it wants to resign but a successor depositary has not been appointed and accepted its appointment;
- we delist the ADSs from an exchange in the United States on which they were listed and do not list the ADSs on another exchange in the United States or make arrangements for trading of ADSs on the U.S. over-the-counter market;
- we delist our shares from an exchange outside the United States on which they were listed and do not list the shares on another exchange outside the United States;
- the depositary has reason to believe the ADSs have become, or will become, ineligible for registration on Form F-6 under the Securities Act of 1933;
- we appear to be insolvent or enter insolvency proceedings;
- all or substantially all the value of the deposited securities has been distributed either in cash or in the form of securities;
- there are no deposited securities underlying the ADSs or the underlying deposited securities have become apparently worthless; or
- there has been a replacement of deposited securities.

If the deposit agreement will terminate, the depositary will notify ADS holders at least 90 days before the termination date. At any time after the termination date, the depositary may sell the deposited securities. After that, the depositary will hold the money it received on the sale, as well as any other cash it is holding under the deposit agreement, unsegregated and without liability for interest, for the pro rata benefit of the ADS holders that have not surrendered their ADSs. Normally, the depositary will sell as soon as practicable after the termination date.

After the termination date and before the depositary sells, ADS holders can still surrender their ADSs and receive delivery of deposited securities, except that the depositary may refuse to accept a surrender for the purpose of withdrawing deposited securities or reverse previously accepted surrenders of that kind that have not settled if it would interfere with the selling process. The depositary may refuse to accept a surrender for the purpose of withdrawing sale proceeds until all the deposited securities have been sold. The depositary will continue to collect distributions on deposited securities, but, after the termination date, the depositary is not required to register any transfer of ADSs or distribute any dividends or other distributions on deposited securities to the ADSs holder (until they surrender their ADSs) or give any notices or perform any other duties under the deposit agreement except as described in this paragraph.

Withdrawal and Cancellation

You may surrender the ADSs to the depositary for the purpose of withdrawal. Upon payment of its fees and expenses and of any taxes or charges, such as stamp taxes or stock transfer taxes or fees, the depositary will deliver the shares and any other deposited securities underlying the ADSs to the ADS holder or a person the ADS holder designates at the office of the custodian. Or, at your request, risk and expense, the depositary will deliver the deposited securities at its office, if feasible. However, the depositary is not required to accept surrender of ADSs to the extent it would require delivery of a fraction of a deposited share or other security. The depositary may charge you a fee and its expenses for instructing the custodian regarding delivery of deposited securities.

You may surrender your ADR to the depositary for the purpose of exchanging your ADR for uncertificated ADSs. The depositary will cancel that ADR and will send to the ADS holder a statement confirming that the ADS holder is the registered holder of uncertificated ADSs. Upon receipt by the depositary of a proper instruction from a registered holder of uncertificated ADSs requesting the exchange of uncertificated ADSs for certificated ADSs, the depositary will execute and deliver to the ADS holder an ADR evidencing those ADSs.

Limitations on Obligations and Liability of the Company and Depositary

The deposit agreement expressly limits our obligations and the obligations of the depositary. It also limits our liability and the liability of the depositary. We and the depositary:

- are only obligated to take the actions specifically set forth in the deposit agreement without negligence or bad faith, and the depositary will not be a fiduciary or have any fiduciary duty to holders of ADSs;
- are not liable if we are or it is prevented or delayed by law or by events or circumstances beyond our or its ability to prevent or counteract with reasonable care or effort from performing our or its obligations under the deposit agreement;
- are not liable if we or it exercises discretion permitted under the deposit agreement;
- are not liable for the inability of any holder of ADSs to benefit from any distribution on deposited securities that is not made available to holders of ADSs under the terms of the deposit agreement, or for any special, consequential or punitive damages for any breach of the terms of the deposit agreement;

- have no obligation to become involved in a lawsuit or other proceeding related to the ADSs or the deposit agreement on your behalf or on behalf of any other person;
- may rely upon any documents we believe or it believes in good faith to be genuine and to have been signed or presented by the proper person;
- are not liable for the acts or omissions of any securities depository, clearing agency or settlement system; and
- the depositary has no duty to make any determination or provide any information as to our tax status, or any liability for any tax consequences that may be incurred by ADS holders as a result of owning or holding ADSs or be liable for the inability or failure of an ADS holder to obtain the benefit of a foreign tax credit, reduced rate of withholding or refund of amounts withheld in respect of tax or any other tax benefit.

In the deposit agreement, we and the depositary agree to indemnify each other under certain circumstances.

Exhibit 8.1

Subsidiaries of Genenta Science S.p.A.

Subsidiary	Place of Incorporation
Genenta Science, Inc.	Delaware

POLICY

GEN-POL-009 v2.0

TITLE

INSIDER TRADING

Supersedes:	Not Applicable	Effective Date:	February 27, 2023
Author:	Richard Slansky, CFO	*/s/ Richard Slansky*	Signature/Date
Reviewed by	Pierluigi Paracchi, CFO	*/s/ Pierluigi Paracchi*	Signature/Date
Approved by	Mark Sirgo, Chairman	*/s/ Mark Sirgo*	Signature/Date

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1. PURPOSE

This Insider Trading Policy (this "***Policy***") provides guidelines with respect to transactions in the securities of Genenta Science S.p.A. (the "***Company***") and the handling of confidential information about the Company and the companies with which the Company does business. The Company's Board of Directors has adopted this Policy to promote compliance with U.S. federal, state and foreign securities laws that prohibit certain persons who are aware of material nonpublic information about a company from: (i) trading in securities of that company; or (ii) providing material nonpublic information to other persons who may trade on the basis of that information.

2. SCOPE

2.1 Persons subject to the policy

This Policy applies to all officers of the Company and its subsidiaries, all members of the Company's Board of Directors and all employees of the Company and its subsidiaries. The Company may also determine that other persons should be subject to this Policy, such as contractors or consultants who have access to material nonpublic information. This Policy also applies to family members, other members of a person's household and entities controlled by a person covered by this Policy, as described below.

2.2 Transactions subject to the policy

This Policy applies to transactions in the Company's securities (collectively referred to in this Policy as "***Company Securities***"), including the Company's ordinary shares (including ordinary shares represented by American Depositary Shares ("***ADSs***")), options to purchase ordinary shares, and any other type of securities that the Company may issue, including (but not limited to) preference shares, convertible debentures and warrants, as well as derivative securities that are not issued by the Company, such as exchange-traded put or call options or swaps relating to the Company Securities.

3. DEFINITIONS

3.1 Definition of material nonpublic information

3.1.2 Material Information.

Information is considered "***material***" if a reasonable investor would consider that information important in making a decision to buy, hold or sell securities. Any information that could be expected to affect the Company's share price, whether it is positive or negative, should be considered material. There is no bright-line standard for assessing materiality; rather, materiality is based on an assessment of all of the facts and circumstances, and is often evaluated by enforcement authorities with the benefit of hindsight. While it is not possible to define all categories of material information, some examples of information that ordinarily would be regarded as material are:

- Projections of future earnings or losses, or other earnings guidance (especially cash balance, burn and runway);
- Changes to previously announced earnings guidance, or the decision to suspend earnings guidance;

- A pending or proposed merger, acquisition or tender offer;
- A pending or proposed acquisition or disposition of a significant asset; A pending or proposed joint venture;
- A Company restructuring;
- Significant related party transactions;
- A change in dividend policy, the declaration of a share split, or an offering of additional securities;
- Bank borrowings or other financing transactions out of the ordinary course;
- The establishment of a repurchase program for Company Securities;
- A change in the Company's pricing or cost structure;
- Major marketing changes; A change in management;
- A change in auditors or notification that the auditor's reports may no longer be relied upon;
- Development of a significant new product, process, or service;
- Timing and achievement of major development milestones;
- Results of clinical trials;
- Unusual gains or losses in major operations;
- Pending or threatened significant litigation, or the resolution of such litigation;
- Impending bankruptcy or the existence of severe liquidity problems;
- The gain or loss of a significant customer or supplier;
- The imposition of a ban on trading in Company Securities or the securities of another company.

3.1.3 When Information is Considered Public.

Information that has not been disclosed to the public is generally considered to be "***nonpublic***" information. In order to establish that the information has been disclosed to the public, it may be necessary to demonstrate that the information has been widely disseminated. Information generally would be considered widely disseminated if it has been disclosed through the Dow Jones "broad tape," newswire services, a broadcast on widely-available radio or television programs, publication in a widely-available newspaper, magazine or news website, or public disclosure documents filed with or furnished to the U.S. Securities and Exchange Commission (the "***SEC***") that are available on the SEC's website. By contrast, information would likely not be considered widely disseminated if it is available only to the Company's employees, or if it is only available to a select group of analysts, brokers and institutional investors.

Once information is widely disseminated, it is still necessary to afford the investing public with sufficient time to absorb the information. As a general rule, information should not be considered fully absorbed by the marketplace until after the second business day after the day on which the information is released. If, for example, the Company were to make an announcement on a Monday, you should not trade in Company Securities until Thursday. Depending on the particular circumstances, the Company may determine that a longer or shorter period should apply to the release of specific material nonpublic information.

4. ROLES AND RESPONSIBILITY

4.1 Individual responsibility

Persons subject to this Policy have ethical and legal obligations to maintain the confidentiality of information about the Company and to not engage in transactions in Company Securities while in possession of material nonpublic information. Each individual is responsible for making sure that he or she complies with this Policy, and that any family member, household member or entity whose transactions are subject to this Policy, as discussed below, also comply with this Policy. In all cases, the responsibility for determining whether an individual is in possession of material nonpublic information rests with that individual, and any action on the part of the Company, the Compliance Officer or any other employee or director pursuant to this Policy (or otherwise) does not in any way constitute legal advice or insulate an individual from liability under applicable securities laws. You could be subject to severe legal penalties and disciplinary action by the Company for any conduct prohibited by this Policy or applicable securities laws, as described below in more detail under the heading "Consequences of Violations."

4.1 Administration of the policy

The Chief Financial Officer or the Finance Director shall serve as the Compliance Officer for the purposes of this Policy, and in his or her absence, the Chief Executive Officer or another employee designated by the Compliance Officer shall be responsible for administration of this Policy. All determinations and interpretations by the Compliance Officer shall be final and not subject to further review.

5. STATEMENT OF POLICY

It is the policy of the Company that no director, officer, or other employee of the Company (or any other person designated by this Policy or by the Compliance Officer as subject to this Policy) who is aware of material nonpublic information relating to the Company may, directly, or indirectly through family members or other persons or entities:

- Engage in transactions in Company Securities, except as otherwise specified in this Policy under the headings "Transactions Under Company Plans" and "Rule 10b5-1 Plans;"
- Recommend the purchase or sale of any Company Securities;
- Disclose material nonpublic information to persons within the Company whose jobs do not require them to have that information, or outside of the Company to other persons, including, but not limited to, family, friends, business associates, investors and expert consulting firms, unless any such disclosure is made in accordance with the Company's policies regarding the protection or authorized external disclosure of information regarding the Company; or
- Assist anyone engaged in the above activities.

In addition, it is the policy of the Company that no director, officer or other employee of the Company (or any other person designated as subject to this Policy) who, in the course of working for the Company, learns of material nonpublic information about a company with which the Company does business, including a customer or supplier of the Company, may trade in that company's securities until the information becomes public or is no longer material.

There are no exceptions to this Policy, except as specifically noted herein. Transactions that may be necessary or justifiable for independent reasons (such as the need to raise money for an emergency expenditure), or small transactions, are not excepted from this Policy. The securities laws do not recognize any mitigating circumstances, and, in any event, even the appearance of an improper transaction must be avoided to preserve the Company's reputation for adhering to the highest standards of conduct.

6. POLICY

6.1 Transactions by family members and others

This Policy applies to your family members who reside with you (including a spouse, a child, a child away at college, stepchildren, grandchildren, parents, stepparents, grandparents, siblings and in-laws), anyone else who lives in your household, and any family members who do not live in your household but whose transactions in Company Securities are directed by you or are subject to your influence or control, such as parents or children who consult with you before they trade in Company Securities (collectively referred to as "***Family Membe***rs"). You are responsible for the transactions of these other persons and therefore should make them aware of the need to confer with you before they trade in Company Securities, and you should treat all such transactions for the purposes of this Policy and applicable securities laws as if the transactions were for your own account. This Policy does not, however, apply to personal securities transactions of Family Members where the purchase or sale decision is made by a third party not controlled by, influenced by or related to you or your Family Members.

6.2 Transactions by entities that you influence or control

This Policy applies to any entities that you influence or control, including any corporations, partnerships, or trusts (collectively referred to as "***Controlled Entities***"), and transactions by these Controlled Entities should be treated for the purposes of this Policy and applicable securities laws as if they were for your own account.

6.3 Transactions under company plans

This Policy does not apply in the case of the following transactions, except as specifically noted.

6.3.1 Stock Option Exercises.

This Policy does not apply to the exercise of an employee share option acquired pursuant to the Company's equity incentive plans, or to the exercise of a tax withholding right pursuant to which a person has elected to have the Company withhold shares subject to an option to satisfy tax withholding requirements. This Policy does apply, however, to any sale of ordinary shares (including ordinary shares in the form of ADSs) as part of a broker-assisted cashless exercise of an option, or any other market sale for the purpose of generating the cash needed to pay the exercise price of an option.

6.3.2 Restricted Stock Awards.

This Policy does not apply to the vesting of restricted shares, or the exercise of a tax withholding right pursuant to which you elect to have the Company withhold ordinary shares to satisfy tax withholding requirements upon the vesting of any restricted shares. This Policy does apply, however, to any market sale of restricted shares (including ordinary shares in the form of ADSs).

6.3.3 Plan.

This Policy does not apply to purchases of Company Securities in the Company's 401(k) plan resulting from your periodic contribution of money to the plan pursuant to your payroll deduction election. This Policy does apply, however, to certain elections you may make under the 401(k) plan, including: (a) an election to increase or decrease the percentage of your periodic contributions that will be allocated to the Company stock fund; (b) an election to make an intra-plan transfer of an existing account balance into or out of the Company stock fund; (c) an election to borrow money against your 401(k) plan account if the loan will result in a liquidation of some or all of your Company stock fund balance; and (d) an election to pre-pay a plan loan if the pre-payment will result in allocation of loan proceeds to the Company stock fund.

6.3.4 Employee Stock Purchase Plan.

The Company may in the future establish one or more employee share purchase plans in order to enable eligible employees to purchase ordinary shares with accumulated payroll deductions. This Policy does not apply to purchases of Company Securities in any such employee share purchase plan resulting from your periodic contribution of money to such plan pursuant to the election you made at the time of your enrollment in such plan. This Policy also does not apply to purchases of Company Securities resulting from lump sum contributions to any such plan, provided that you elected to participate by lump sum payment at the beginning of the applicable enrollment period. This Policy does apply, however, to your election to participate in any such plan for any enrollment period, and to your sales of Company Securities purchased pursuant to such plan.

6.3.5 Dividend Reinvestment Plan.

The Company may in the future establish one or more dividend reinvestment plans in order to enable eligible shareholders to purchase ordinary shares with the Company's ordinary share dividends. This Policy does not apply to purchases of Company Securities under any such dividend reinvestment plan resulting from your reinvestment of dividends paid on Company Securities. This Policy does apply, however, to voluntary purchases of Company Securities resulting from additional contributions you choose to make under any such dividend reinvestment plan, and to your election to participate in such plan or increase your level of participation in such plan. This Policy also applies to your sale of any Company Securities purchased pursuant to such plan.

6.3.6 Other Similar Transactions.

Any other purchase of Company Securities from the Company or sales of Company Securities to the Company are not subject to this Policy.

6.4 Transactions not involving a purchase or sale

Bona fide gifts of Company Securities are subject to this Policy. Unless approved in advance by the Compliance Officer, a person subject to this Policy may not make a gift, charitable contribution or other transfer without consideration of Company Securities during a period when such person cannot trade.

6.5 Special and prohibited transactions

The Company has determined that there is a heightened legal risk and/or the appearance of improper or inappropriate conduct if the persons subject to this Policy engage in certain types of transactions. It therefore is the Company's policy that any persons covered by this Policy may not engage in any of the following transactions, or should otherwise consider the Company's preferences as described below.

6.5.1 Short-Term Trading.

Short-term trading of Company Securities may be distracting to the person and may unduly focus the person on the Company's short-term stock market performance instead of the Company's long-term business objectives. For these reasons, any director, officer or other employee of the Company who purchases Company Securities in the open market may not sell any Company Securities of the same class during the six months following the purchase (or vice versa).

6.5.2 Short Sales.

Short sales of Company Securities (i.e., the sale of a security that the seller does not own) may evidence an expectation on the part of the seller that the securities will decline in value, and therefore have the potential to signal to the market that the seller lacks confidence in the Company's prospects. In addition, short sales may reduce a seller's incentive to seek to improve the Company's performance. For these reasons, short sales of Company Securities are prohibited. (Short sales arising from certain types of hedging transactions are governed by the paragraph below captioned "Hedging Transactions.")

6.5.3 Publicly-Traded Options.

Given the relatively short term of publicly traded options, transactions in options may create the appearance that a director, officer or employee is trading based on material nonpublic information and focus a director's, officer's or other employee's attention on short-term performance at the expense of the Company's long-term objectives. Accordingly, transactions in put options, call options or other derivative securities, on an exchange or in any other organized market, are prohibited by this Policy. (Option positions arising from certain types of hedging transactions are governed by the next paragraph below.)

6.5.4 Hedging Transactions.

Hedging or monetization transactions can be accomplished through a number of possible mechanisms, including through the use of financial instruments such as prepaid variable forwards, equity swaps, collars and exchange funds. Such hedging transactions may permit a director, officer or employee to continue to own Company Securities obtained through employee benefit plans or otherwise, but without the full risks and rewards of ownership. When that occurs, the director, officer or employee may no longer have the same objectives as the Company's other shareholders. Therefore, the Company strongly discourages you from engaging in such transactions. Any person wishing to enter into such an arrangement must first submit the proposed transaction for approval by the Compliance Officer. Any request for pre-clearance of a hedging or similar arrangement must be submitted to the Compliance Officer at least two weeks prior to the proposed execution of documents evidencing the proposed transaction and must set forth a justification for the proposed transaction.

6.5.5 Margin Accounts and Pledged Securities.

Securities held in a margin account as collateral for a margin loan may be sold by the broker without the customer's consent if the customer fails to meet a margin call. Similarly, securities pledged (or hypothecated) as collateral for a loan may be sold in foreclosure if the borrower defaults on the loan. Because a margin sale or foreclosure sale may occur at a time when the pledgor is aware of material nonpublic information or otherwise is not permitted to trade in Company Securities, directors, officers and other employees are prohibited from holding Company Securities in a margin account or otherwise pledging Company Securities as collateral for a loan. (Pledges of Company Securities arising from certain types of hedging transactions are governed by the paragraph above captioned "Hedging Transactions.")

6.5.6 Standing and Limit Orders.

Standing and limit orders (except standing and limit orders under approved Rule 10b5-1 Plans, as described below) create heightened risks for insider trading violations similar to the use of margin accounts. There is no control over the timing of purchases or sales that result from standing instructions to a broker, and as a result the broker could execute a transaction when a director, officer or other employee is in possession of material nonpublic information. The Company therefore discourages placing standing or limit orders on Company Securities. If a person subject to this Policy determines that they must use a standing order or limit order, the order should be limited to short duration and should otherwise comply with the restrictions and procedures outlined below under the heading "Additional Procedures."

7. ADDITIONAL PROCEDURES

The Company has established additional procedures in order to assist the Company in the administration of this Policy, to facilitate compliance with laws prohibiting insider trading while in possession of material nonpublic information, and to avoid the appearance of any impropriety. These additional procedures are applicable only to those individuals described below.

7.1 Pre-Clearance Procedures.

The persons designated by the Compliance Officer as being subject to these procedures, as well as the Family Members and Controlled Entities of such persons, may not engage in any transaction in Company Securities without first obtaining pre-clearance of the transaction from the Compliance Officer. A request for preclearance should be submitted to the Compliance Officer at least two business days in advance of the proposed transaction. The Compliance Officer is under no obligation to approve a transaction submitted for pre-clearance, and may determine not to permit the transaction. If a person seeks pre-clearance and permission to engage in the transaction is denied, then he or she should refrain from initiating any transaction in Company Securities, and should not inform any other person of the restriction.

When a request for pre-clearance is made, the requestor should carefully consider whether he or she may be aware of any material nonpublic information about the Company, and should describe fully those circumstances to the Compliance Officer. The requestor should also be prepared to comply with SEC Rule 144 and file a Form 144, if necessary, at the time of any sale.

7.2 Semi-Annual Trading Restrictions.

The persons designated by the Compliance Officer as subject to this restriction, as well as their Family Members or Controlled Entities, may not conduct any transactions involving the Company Securities (other than as specified by this Policy), during a "***Blackout Period***" beginning fifteen days prior to the end of each semi-annual fiscal period (i.e., June 15th and December 15th) and ending on the second business day following the date of the public release of the Company's earnings results for that period. In other words, these persons may only conduct transactions in Company Securities during the "***Window Period***" beginning on the second business day following the public release of the Company's earnings and ending fifteen days prior to the close of the next semi-annual fiscal period.

Under certain very limited circumstances, a person subject to this restriction may be permitted to trade during a Blackout Period, but only if the Compliance Officer concludes that the person does not in fact possess material nonpublic information. Persons wishing to trade during a Blackout Period must contact the Compliance Officer for approval at least two business days in advance of any proposed transaction involving Company Securities.

7.3 Event-Specific Trading Restriction Periods.

From time to time, an event may occur that is material to the Company and is known by only a few directors, officers and/or employees. So long as the event remains material and nonpublic, the persons designated by the Compliance Officer may not trade Company Securities. In addition, the Company's financial results may be sufficiently material in a particular fiscal quarter that, in the judgment of the Compliance Officer, designated persons should refrain from trading in Company Securities even sooner than the typical Blackout Period described above. In that situation, the Compliance Officer may notify these persons that they should not trade in the Company Securities, without disclosing the reason for the restriction. The existence of an event-specific trading restriction period or extension of a Blackout Period will not be announced to the Company as a whole, and should not be communicated to any other person. Even if the Compliance Officer has not designated you as a person who should not trade due to an event-specific restriction, you should not trade while aware of material nonpublic information. Exceptions will not be granted during an event-specific trading restriction period.

7.4 Exceptions.

The semi-annual trading restrictions and event-driven trading restrictions do not apply to those transactions to which this Policy does not apply, as described above under the headings "Transactions Under Company Plans." Further, the requirement for pre-clearance, the semi-annual trading restrictions and event driven trading restrictions do not apply to transactions conducted pursuant to approved Rule 10b5-1 plans, described under the heading "Rule 10b5-1 Plans."

7.5 Rule 10b5-1 plans

Rule 10b5-1 under the U.S. Securities Exchange Act of 1934, as amended (the "***Exchange Act***"), provides a defense from insider trading liability under Rule 10b-5 under the Exchange Act. In order to be eligible to rely on this defense, a person subject to this Policy must enter into a Rule 10b5-1 plan for transactions in Company Securities that meets certain conditions specified in the Rule (a "***Rule 10b5-1 Plan***"). If the plan meets the requirements of Rule 10b5-1, Company Securities may be purchased or sold without regard to certain insider trading restrictions.

In general, a Rule 10b5-1 Plan must be entered into at a time when the person entering into the plan is not aware of material nonpublic information. Once the plan is adopted, the person must not exercise any influence over the amount of securities to be traded, the price at which they are to be traded or the date of the trade. The plan must either specify the amount, pricing, and timing of transactions in advance or delegate discretion on these matters to an independent third party.

In order to enter into a Rule 10b5- 1 Plan pursuant to this Policy, the following requirements must be satisfied:

- The Rule 10b5-1 Plan must comply with the requirements of Rule 10b5-1 under the Exchange Act and this Policy.
- The Rule 10b5-1 Plan must be submitted to the Compliance Officer for approval and the person adopting the Rule 10b5- 1 Plan must certify to the Compliance Officer in writing, no earlier than five days prior to the date that the 10b5-1 Plan is formally adopted (and shall not have withdrawn such certification prior to such adoption), that as of such date and as of the adoption date of the 10b5-1 Plan, (i) such person is not and, to their knowledge, will not be, aware of material nonpublic information, (ii) all trades to be made pursuant to the 10b5-1 Plan will be in accordance with applicable SEC rules, (iii) such person is adopting the 10b5-1 Plan in good faith and not as part of a plan or scheme to evade the prohibitions of Section 10(b) of the Exchange Act and Rule 10b-5 of the Exchange Act, and (iv) such person will act in good faith with respect to the 10b5-1 Plan throughout its duration. Such person must notify the Compliance Officer promptly and withdraw the certification if any changes of circumstances prior to the adoption date of the 10b5-1 Plan have or will render such certification to be inaccurate as of that time.

- The first trade under the Rule 10b5- 1 Plan must not occur: (i) for directors and officers of the Company, until the later of (A) ninety (90) days after adoption of the 10b5-1 Plan and (B) two (2) business days following the disclosure of the Company's financial results in a Form 20-F or Form 6-K for the completed fiscal quarter in which the 10b5-1 Plan was adopted that discloses the Company's financial results (but not to exceed 120 days following the adoption of the 10b5-1 Plan); and (ii) for persons other than directors and officers of the Company, thirty (30) days after adoption of the 10b5-1 Plan, in each case, following the Compliance Officer's approval of the Rule 10b5- 1 Plan. These waiting periods are collectively referred to as the "***Cooling-Off Period***."

- The 10b5-1 Plan must not be a single-trade 10b5-1 Plan adopted during the 12-month period immediately following the person's adoption of another single-trade 10b5-1 Plan, subject to the exceptions noted in Rule 10b5-1.

- The Rule 10b5- 1 Plan must be adopted during a Trading Window and not during any Blackout Period.

- The person may have no more than one 10b5-1 Plan adopted at any point in time (i.e., multiple concurrent or overlapping plans are prohibited), subject to the exceptions noted in Rule 10b5-1.

Once a person has an approved 10b5-1 Plan in place, such person will need approval from the Compliance Officer to make certain changes to it. Modifying or changing the amount, price, or timing of the purchase or sale of Company Securities underlying the 10b5-1 Plan (or a modification or change to a written formula or algorithm, or computer program that affects the amount, price, or timing of the purchase or sale of such securities) (any such modification or change, a "***Plan Modification***") will be deemed to be the same as terminating the existing 10b5-1 Plan and entering into a new 10b5-1 Plan. As a result, the approval process for a Plan Modification is the same as the approval process for initially adopting a 10b5-1 Plan, including being subject to a new Cooling-Off Period.

Once a person has an approved 10b5-1 Plan in place, they will need approval from the Compliance Officer to terminate it.

Persons subject to this Policy may also enter into a "non-Rule 10b5-1 trading arrangement" (as defined in Regulation S-K Item 408(c)). The approval process for a non-Rule 10b5-1 trading arrangement will be subject to the same approval process as a 10b5-1 Plan except the non-Rule 10b5-1 trading arrangement is not subject to a Cooling-off Period.

7.6 Post-termination transactions

This Policy continues to apply to transactions in Company Securities even after termination of service to the Company. If an individual is in possession of material nonpublic information when his or her service terminates, that individual may not trade in Company Securities until that information has become public or is no longer material. The preclearance procedures specified under the heading "Additional Procedures" above, however, will cease to apply to transactions in Company Securities upon the expiration of any Blackout Period or other Company-imposed trading restrictions applicable at the time of the termination of service.

7.7 Consequences of violations

The purchase or sale of securities while aware of material nonpublic information, or the disclosure of material nonpublic information to others who then trade in the Company's

Securities, is prohibited by U.S. federal and state laws. Insider trading violations are pursued vigorously by the SEC, U.S. Attorneys and state enforcement authorities as well as the laws of foreign jurisdictions. Punishment for insider trading violations is severe, and could include significant fines and imprisonment. While the regulatory authorities concentrate their efforts on the individuals who trade, or who tip inside information to others who trade, the federal securities laws also impose potential liability on companies and other "controlling persons" if they fail to take reasonable steps to prevent insider trading by company personnel. In addition, an individual's failure to comply with this Policy may subject the individual to Company-imposed sanctions, including dismissal for cause, whether or not the employee's failure to comply results in a violation of law. Needless to say, a violation of law, or even an SEC investigation that does not result in prosecution, can tarnish a person's reputation and irreparably damage a career.

7.8 Company assistance

Any person who has a question about this Policy or its application to any proposed transaction may obtain additional guidance from the Compliance Officer.

7.9 Certification

All persons subject to this Policy must certify their understanding of, and intent to comply with, this Policy. See Annex 1.

8. REVIEW AND REVISIONS

This Policy will be reviewed periodically (at least every 3 years) and updated if necessary.

9. REASON FOR CHANGE

This Policy was amended effective as of February 27, 2022 as a result of the SEC's adoption of amendments to Rule 10b5-1 under the Exchange Act and new disclosure requirements to enhance investor protections against insider trading, as well as to incorporate ministerial and clarifying changes.

10. PREVIOUS HISTORY OF POLICY

This Policy was originally adopted effective as of July 21, 2021, and subsequently amended effective as of February 27, 2023.

ANNEX 1: CERTIFICATION FORMAT

I certify that:

1. I have read and understand the Company's Insider Trading Policy (the "Policy"). I understand that the Compliance Officer is available to answer any questions I have regarding the Policy.

2. Since December 15, 2021, or such shorter period of time that I have been an employee of the Company, I have complied with the Policy.

3. I will continue to comply with the Policy for as long as I am subject to the Policy.

Print name:

Signature:

Date:

Exhibit 12.1

Certification of the Chief Executive Officer (Principal Executive Officer) pursuant to Rule 13a-14(a) of the Securities Exchange Act, as amended

I, Pierluigi Paracchi, certify that:

1.I have reviewed this annual report on Form 20-F of Genenta Science S.p.A. (the "Company");

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the consolidated financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the company as of, and for, the periods presented in this report;

4. The Company's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the Company and have:

a. Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the Company, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

b. Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of consolidated financial statements for external purposes in accordance with generally accepted accounting principles;

c. Evaluated the effectiveness of the Company's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

d. Disclosed in this report any change in the Company's internal control over financial reporting that occurred during the Company's most recent fiscal quarter (the Company's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the Company's internal control over financial reporting; and

5. The Company's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the Company's auditors and the board of statutory auditors, acting as the audit committee of the Company's Board of Directors (or persons performing the equivalent functions):

a. All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the Company's ability to record, process, summarize and report financial information; and

b. Any fraud, whether or not material, that involves management or other employees who have a significant role in the Company's internal control over financial reporting.

Date: March 28, 2025

By: */s/ Pierluigi Paracchi*
Name: Pierluigi Paracchi
Title: Chief Executive Officer
(Principal Executive Officer)

Exhibit 12.2

Certification of the Financial Officer (Principal Financial Officer) pursuant to Rule 13a-14(a) of the Securities Exchange Act, as amended

I, Richard B. Slansky, certify that:

1. I have reviewed this annual report on Form 20-F of Genenta Science S.p.A. (the "Company");

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the consolidated financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the company as of, and for, the periods presented in this report;

4. The Company's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the Company and have:

a. Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the Company, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

b. Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of consolidated financial statements for external purposes in accordance with generally accepted accounting principles;

c. Evaluated the effectiveness of the Company's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

d. Disclosed in this report any change in the Company's internal control over financial reporting that occurred during the Company's most recent fiscal quarter (the Company's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the Company's internal control over financial reporting; and

5. The Company's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the Company's auditors and the board of statutory auditors, acting as the audit committee of the Company's Board of Directors (or persons performing the equivalent functions):

a. All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the Company's ability to record, process, summarize and report financial information; and

b. Any fraud, whether or not material, that involves management or other employees who have a significant role in the Company's internal control over financial reporting.

Date: March 28, 2025

By: */s/ Richard B. Slansky*
Name: Richard B. Slansky
Title: Chief Financial Officer
(Principal Financial and Accounting Officer)

Exhibit 13.1

Certification of the Chief Executive Officer and Chief Financial Officer pursuant to 18 U.S.C. 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002

Pursuant to U.S.C. Section 1350 of the Sarbanes-Oxley Act of 2002 (subsections (a) and (b) of Section 1350, Chapter 63 of Title 18, United States Code), as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, each of the undersigned officers of Genenta Science S.p.A. (the "Company"), does hereby certify, to such officer's knowledge, that:

(1) The Annual Report on Form 20-F for the year ended December 31, 2024 of the Company (the "Annual Report") fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended; and

(2) The information contained in the Annual Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

GENENTA SCIENCE S.P.A.

March 28, 2025

By: */s/ Pierluigi Paracchi*
Name: Pierluigi Paracchi
Title: Chief Executive Officer
(Principal Executive Officer)

March 28, 2025

By: */s/ Richard B. Slansky*
Name: Richard B. Slansky
Title: Chief Financial Officer
(Principal Financial and Accounting Officer)

Exhibit 23.1

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

March 28, 2025

We hereby consent to the incorporation by reference in the Registration Statement on Form F-3 (No. 333-271901) and in the Registration Statement on Form S-8 (No. 333-278392) of our report dated March 28, 2025, with respect to the consolidated financial statements of Genenta Science S.p.A included in this Form 20-F of Genenta Science S.p.A for the year ended December 31, 2024.

Dannible & McKee, LLP
Syracuse, New York