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

FORM 10-K

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

For the fiscal year ended December 31, 2024

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

For the transition period from _____ to _____

Commission File Number 001-41705

Azitra, Inc.
(Exact name of registrant as specified in its charter)

Delaware	**46-4478536**
(State or other jurisdiction of incorporation or organization)	(IRS Employer Identification No.)

21 Business Park Drive
Branford, CT 06405
(Address of principal executive offices and zip code)

(203)-646-6446
(Registrant's telephone number, including area code)

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

Title of each class	**Trading Symbol(s)**	**Name of each exchange on which registered**
Common stock: Par value $0.0001	AZTR	NYSE American, LLC

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

None

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

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or 15(d) of the Exchange Act. Yes ☐ No ☒

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 (Section 232.405 of this chapter) during the preceding 12 months (or 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, a smaller reporting company or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company," and "emerging growth company" in Rule 12b-2 of the Exchange Act:

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

If an emerging growth company, 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. ☐

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 whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). Yes ☐ No ☒

State the aggregate market value of voting and non-voting common equity held by non-affiliates computed by reference to the price at which the common equity was last sold, or the average bid and asked price of such common equity, as of the last business day of the registrant's most recently completed second fiscal quarter: $1,954,147.

The number of shares of the registrant's common stock outstanding as of February 24, 2025 was 14,979,354.

DOCUMENTS INCORPORATED BY REFERENCE

None

AZITRA, INC.

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CAUTIONARY NOTICE

This annual report on Form 10-K contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. Those forward-looking statements include our expectations, beliefs, intentions and strategies regarding the future.

These and other factors that may affect our financial results are discussed more fully in "Risk Factors" and "Management's Discussion and Analysis of Financial Condition and Results of Operations" included in this report. Moreover, we operate in a very competitive and rapidly changing environment, and new risks emerge from time to time. It is not possible for us to predict all risks, nor can we assess the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in any forward-looking statements we may make. In light of these risks, uncertainties and assumptions, the forward-looking events and circumstances discussed in this report may not occur and actual results could differ materially and adversely from those anticipated or implied in our forward-looking statements. Although we believe that the expectations reflected in our forward-looking statements are reasonable, we cannot guarantee that the future results, levels of activity, performance or events and circumstances described in the forward-looking statements will be achieved or occur. Moreover, neither we nor any other person assumes responsibility for the accuracy and completeness of the forward-looking statements. We caution readers not to place undue reliance on any forward-looking statements. We do not undertake, and specifically disclaim any obligation, to update or revise such statements to reflect new circumstances or unanticipated events as they occur, and we urge readers to review and consider disclosures we make in this and other reports that discuss factors germane to our business. See in particular our reports on Forms 10-K, 10-Q, and 8-K subsequently filed from time to time with the Securities and Exchange Commission.

Except as otherwise indicated, all share and share price in this report gives effect to a forward stock split effected on May 17, 2023 at a ratio of one for 7.1 for one and a reverse stock split effected on July 1, 2024 at a ratio of one for 30.

INDUSTRY AND MARKET DATA

This report, particularly the section "Business," contains observations, statistical data, estimates, and forecasts that are based on independent industry, government and non-government organization publications or other publicly available information, as well as other information based on our internal sources. Although we believe that the third-party sources referred to in this report are reliable, estimates as they relate to projections involve numerous assumptions, are subject to risks and uncertainties, and are subject to change based on various factors, including those discussed under the section titled "Risk Factors" and elsewhere in this report. These and other factors could cause results to differ materially from those expressed in the estimates made by the independent parties and by us.

Certain information in the text of this report is contained in independent industry government and non-governmental organizational publications. The sources of these publications are provided below:

- Stacy and Belkaid Study, Apollo Stacy and Yasmine Belkaid, Microbial Guardians of Skin Health. Science, 2019 Jan 18;363(6424):227-228. Doi: 10.1126/science.aat4326. PMID: 30655428

- Oh Study, Zhou W, Spoto M, Hardy R, Guan C, Fleming E, Larson PJ, Brown JS, Oh J. Host-Specific Evolutionary and Transmission Dynamics Shape the Functional Diversification of Staphylococcus epidermidis in Human Skin. Cell. 2020 Feb 6;180(3):454-470.e18. doi: 10.1016/j.cell.2020.01.006. Epub 2020 Jan 30. PMID: 32004459; PMCID

- Satoh Study, Satoh TK, Mellett M, Meier-Schiesser B, Fenini G, Otsuka A, Beer HD, Rordorf T, Maul JT, Hafner J, Navarini AA, Contassot E, French LE. IL-36γ drives skin toxicity induced by EGFR/MEK inhibition and commensal Cutibacterium acnes. J Clin Invest. 2020 Mar 2;130(3):1417-1430. doi: 10.1172/JCI128678. PMID: 31805013; PMCID: PMC7269569

- Barbati Study, Netherton Syndrome in Children: Management and Future Perspectives, Federica Barbati, Mattia Giovannini Teresa Oranges, Lorenzo Lodi, Simona Barni, Elio Novembre, Ermanno Baldo, Mario Cristofolini, Stefano Stagi, Silvia Ricci, Francesca Mori, Cesare Filippeschi, Chiara Azzari and Giuseppe Indol; Frontiers in Pediatrics, May 2021

- Sun Study, Netherton syndrome: A case report and review of the literature, Joannie D. Sun, MD, and Kenneth G. Linden, PhD, MD, International Journal of Dermatology 2006

- Orphanet, Netherton Syndrome, Orphanet: Netherton syndrome

RISK FACTOR SUMMARY

Our business is subject to numerous risks and uncertainties, including those described in "Risk Factors" in this Annual Report on Form 10-K. These risks include, but are not limited to the following:

- We are an early-stage clinical biopharmaceutical company with limited operating history;
- We have a history of significant operating losses and anticipate continued operating losses for the foreseeable future;
- Our Joint Development Agreement, or JDA, with Bayer includes an option for Bayer to acquire an exclusive royalty bearing license for up to six strains. There can be no assurance we will be able to conclude a licensing agreement;
- We expect we will need additional financing to execute our business plan and fund operations, which additional financing may not be available on reasonable terms, or at all;
- The clinical and commercial utility of our microbial library and genetic engineering platform is uncertain and may never be realized;
- Our product candidates are in early stages of development, and therefore they will require extensive additional preclinical and clinical testing;
- We will need to grow the size of our organization, and we may experience difficulties in managing this growth;
- We currently have no sales and marketing organization;
- We will be completely dependent for the foreseeable future on third parties to manufacture our product candidates for commercial sale;
- Our business model includes the potential out-licensing of strains from our proprietary microbial library or our product candidates to other pharmaceutical companies; however, technology licensing in the pharmaceutical industry is a lengthy process and subject to several risks and factors outside of our control;
- Our business may suffer with the loss of key personnel;
- If product liability lawsuits are brought against us, we may incur substantial liabilities and may be required to limit commercialization of our product candidates;
- Our business operations could suffer in the event of information technology systems' failures or security breaches;
- We face significant competition from other biotechnology and pharmaceutical companies targeting medical dermatological indications;
- Our success is entirely dependent on our ability to obtain the marketing approval for our product candidates by the FDA and the regulatory authorities in foreign jurisdictions in which we intend to market our product candidates, of which there can be no assurance;
- Our clinical trials may fail to demonstrate substantial evidence of the safety and efficacy of our product candidates or any future product candidates;
- Results of preclinical studies of our product candidates may not be predictive of the results of future preclinical studies or clinical trials;
- Even if we receive regulatory approval for any of our product candidates, we may not be able to successfully commercialize the product and the revenue that we generate from its sales, if any, may be limited;

- Current and future legislation may increase the difficulty and cost for us to obtain marketing approval of and commercialize our product candidates and affect the prices we may obtain;
- It is difficult and costly to protect our intellectual property rights, and we cannot ensure the protection of these rights;
- Our product candidates may infringe the intellectual property rights of others, which could increase our costs and delay or prevent our development and commercialization efforts;
- An active, liquid and orderly trading market for our shares may not develop;
- Future capital raises may dilute your ownership and have other adverse effects on our operations;
- The market price of our shares may be subject to fluctuation and volatility;
- Our failure to meet the continued listing requirements of the NYSE American could result in a delisting of our common stock;
- If we fail to maintain an effective system of internal control over financial reporting, we may not be able to accurately report our financial results or prevent fraud;
- We ratified certain corporate actions pursuant to Section 204 of the Delaware General Corporate Law, or DGCL; however, there can be no assurance that claims will not be made to challenge the validity of the ratification or the related corporate actions; and
- Our charter documents and Delaware law may inhibit a takeover that stockholders consider favorable.

PART I

Item 1. Business

Background

Azitra, Inc. was formed as a Delaware corporation on January 2, 2014 for the purpose of developing innovative therapies for precision dermatology using engineered proteins and topical live biotherapeutic products. Since our formation, we have built a proprietary platform that includes a microbial library comprised of approximately 1,500 unique bacterial strains that can be screened for unique therapeutic characteristics. The platform is augmented by an artificial intelligence and machine learning technology that analyzes, predicts and helps screen our library of strains for drug like molecules. The platform also utilizes a licensed genetic engineering technology, which can enable the transformation of previously genetically intractable strains. We have not commenced commercial operations. Unless otherwise indicated, the terms "Azitra," Company," "we," "us," and "our" refer to Azitra, Inc. and its wholly-owned subsidiaries.

Overview

We are an early-stage clinical biopharmaceutical company focused on developing innovative therapies for precision dermatology using engineered proteins and topical live biotherapeutic products. We have built a proprietary platform that includes a microbial library comprised of approximately 1,500 unique bacterial strains that can be screened for unique therapeutic characteristics. The platform is augmented by an artificial intelligence and machine learning technology that analyzes, predicts and helps screen our library of strains for druglike molecules. The platform also utilizes a licensed genetic engineering technology, which can enable the transformation of previously genetically intractable strains. Our initial focus is on the development of genetically engineered strains of *Staphylococcus epidermidis*, or *S. epidermidis,* which we consider to be an optimal therapeutic candidate species for engineering of dermatologic therapies. The particular species demonstrates a number of well-described properties in the skin. As of the date of this report, we have identified, among our microbial library, over 60 distinct bacterial species that we believe are capable of being engineered to create living organisms or engineered proteins with significant therapeutic effect.

We are a pioneer in genetically engineering bacteria for therapeutic use in dermatology. Our goal is to leverage our platforms and internal microbial library bacterial strains to create new therapeutics that are either engineered living organisms or engineered proteins or peptides to treat skin diseases. Our initial focus is on the development of our current product candidates, including:

- **ATR-12**, a genetically modified strain of *S. epidermidis* for treating the orphan disease, Netherton syndrome, a chronic and sometimes fatal disease of the skin estimated to affect approximately one to nine in every 100,000, but its prevalence may be underestimated due to misdiagnosis caused by similarities to other skin diseases. We received Pediatric Rare Disease Designation for ATR-12 by the United States Food and Drug Administration, or FDA, in 2019. In December 2022, we submitted an investigational new drug application, or IND, for a Phase 1b clinical trial of ATR-12 in adult Netherton syndrome patients, and on January 27, 2023 we received notification from the FDA that the "study may proceed" with respect to the proposed Phase 1b clinical trial. After submitting post-IND manufacturing reports, we have commenced operating activities for our Phase 1b clinical trial in December 2023, and we have dosed our first patient in August 2024. We expect to report initial safety results in the first half of 2025.

- **ATR-04**, a genetically modified strain of *S. epidermidis* for treating the papulopustular rash experienced by cancer patients undergoing epidermal growth factor receptor inhibitor, or EGFRi, targeted therapy. In August 2024, we obtained IND clearance from the FDA to commence a Phase 1/2 clinical trial in certain cancer patients undergoing EGFRi targeted therapy. In September 2024, we obtained Fast Track designation by the FDA in this indication. We expect to dose the first patient in the Phase 1/2 clinical trial in the first half of 2025.

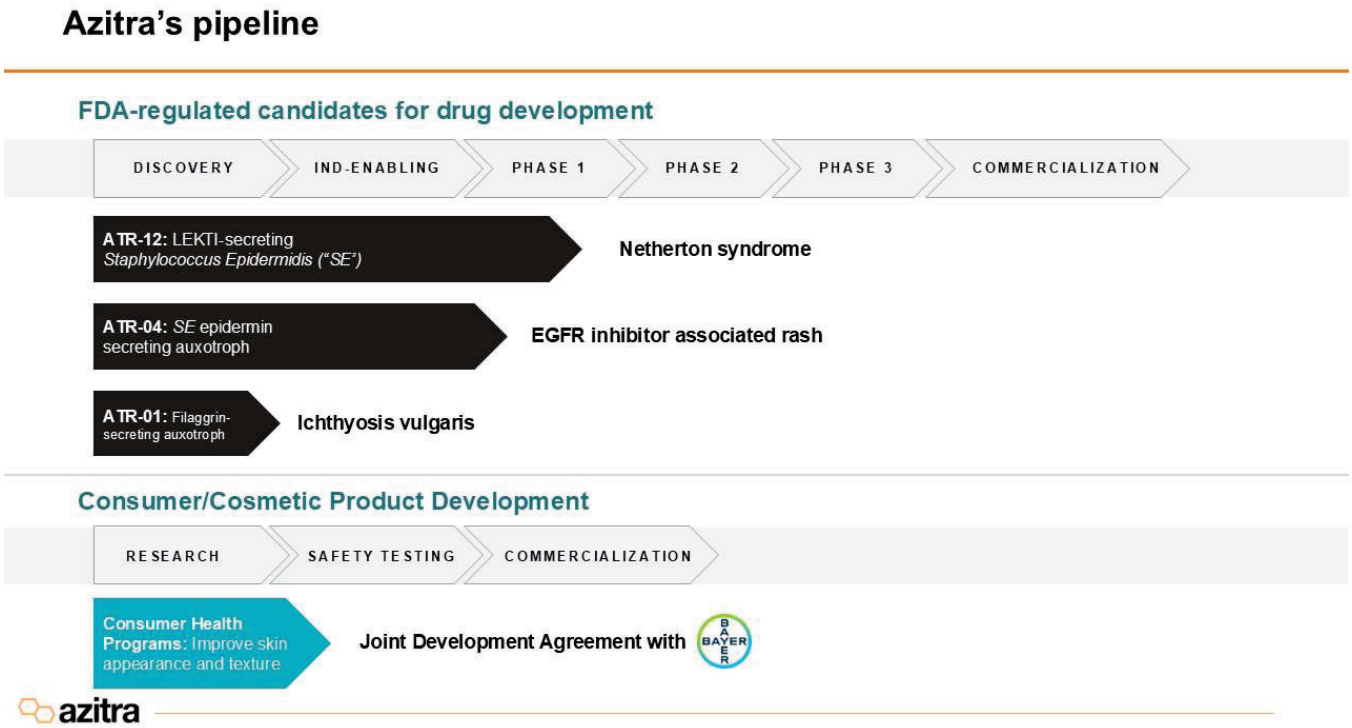
- **ATR-01**, a genetically modified strain of *S. epidermidis* that expresses an engineered recombinant human filaggrin protein for treating ichthyosis vulgaris, a chronic, xerotic (abnormally dry), scaly skin disease with an estimated incidence and prevalence of 1 in 250, which suggests a total patient population of 1.3 million in the United States. We are planning to perform lead optimization and IND-enabling studies in 2025 to support an IND filing.

- Two separate strains of bacterial microbes are being investigated and developed by us and Bayer Consumer Care AG, the consumer products division of Bayer AG, or Bayer, the international life science company. We entered into a Joint Development Agreement, or JDA, with Bayer in December 2019. Under the terms of the JDA, we are responsible for testing our library of bacterial strains and their natural products for key preclinical properties. After screening through hundreds of strains, we and Bayer have selected two particular strains to move forward into further development. Bayer holds the exclusive option to license the patent rights to these strains.

We also have established partnerships with teams from Carnegie Mellon University and the Fred Hutchinson Cancer Center, or Fred Hutch, two of the premier academic centers in the United States. Our collaboration with the Carnegie Mellon based team takes advantage of the power of whole genome sequencing. This partnership is mining our proprietary library of bacterial strains for novel, drug like peptides and proteins. The artificial intelligence/machine learning technology developed by this team predicts the molecules made by microbes from their genetic sequences. The system then compares the predictions to the products actually made through tandem mass spectroscopy and/or nuclear magnetic resonance imaging to refine future predictions. The predictions can be compared to publicly available 2D and 3D protein databases to select drug like structures.

We hold an exclusive, worldwide license from Fred Hutch regarding the use of its patented SyMPL technologies for all fields of genetic engineering, including to discover, develop and commercialize engineered microbial therapies and microbial-derived peptides and proteins for skin diseases. To date, our team has successfully engineered our lead therapeutic candidates without the SyMPL technology. However, we believe that SyMPL will open up the ability to make genetic transformations of an expanded universe of microbial species, and we expect that some or all of our future product candidates will incorporate the SyMPL technology.

Beyond our three lead product candidates and collaboration with Bayer, our goal is to develop a broad portfolio of product candidates focused on expanding the application of our platforms for precision dermatology. We believe that we have established a unique position in advancing the development of biologics for precision dermatology.



We intend to create a broad portfolio of product candidates for precision dermatology through our development of genetically engineered proteins selected from our proprietary microbial library of approximately 1,500 unique bacterial strains. Our strategy is as follows:

- ***Build a sustainable precision dermatology company.*** Our goal is to build a leading precision dermatology company with a sustainable pipeline of product candidates. To that end, we are focused on rapidly advancing our current pipeline of live biotherapeutic candidates while actively developing additional product candidates. Each of our current product candidates are proprietary and subject to pending patent applications. We expect that most, if not all, genetically engineered product candidates we develop will be eligible for patent protection.

- ***Advance our lead product candidates, ATR-12 and ATR-04, through clinical trials.*** We expect to report initial safety results of our Phase 1b clinical trial for our ATR-12 in Netherton syndrome patients in the first half of 2025 and are currently planning to dose the first patient in a Phase 1/2b trial with ATR-04 in certain cancer patients undergoing EGFRi therapy in the first half of 2024. In August 2024, we obtained IND clearance from the FDA to commence a Phase 1/2 clinical trial, and in September 2024, we obtained Fast Track designation by the FDA for ATR-04.

- ***Broaden our platform by selectively exploring strategic partnerships that maximize the potential of our precision dermatology programs.*** We intend to maintain significant rights to all of our core technologies and product candidates. However, we will continue to evaluate partnering opportunities in which a strategic partner could help us to accelerate development of our technologies and product candidates, provide access to synergistic combinations, or provide expertise that could allow us to expand into the treatment of different types of skin diseases. We may also broaden the reach of our platform by selectively in-licensing technologies or product candidates. In addition, we will consider potentially out-licensing certain of our proprietary technologies for indications and industries that we are not ourselves pursuing. We believe our genetic engineering techniques and technologies have applicability outside of the field of medicine, including cosmetics and in the generation of clean fuels and bioremediation.

- ***Leverage our academic partnerships.*** We currently have partnerships with investigators at the Fred Hutchinson Cancer Center, Yale University, Duke University and Carnegie Mellon University. We have an exclusive license from the Fred Hutchinson Cancer Center covering DNA technologies, which enable the genetic transformation of strains that have previously been genetically intractable. Our collaboration with investigators at Carnegie Mellon University builds on an artificial intelligence and machine learning technology to predict the drug like molecules made by the microbes in our library. We have an ongoing scientific advisory board contract with Dr. Julia Oh of Duke University and have historically worked with Jackson Laboratories (Dr. Oh's previous employer) through sponsored research agreements for mouse and other experiments. We expect to leverage these partnerships and potentially expand them or form other academic partnerships to bolster our engineering platforms and expand our research and development pipeline.

- ***Experienced management team and Board of Directors***. We are led by Francisco D. Salva, our chief executive officer, and Travis Whitfill, our co-founder and chief operating officer, who have more than 35 years of combined experience in the management of biotechnology companies and healthcare investing. Mr. Salva was previously a co-founder of Acerta Pharma, which was sold to AstraZeneca for approximately $6.3 billion in a staged acquisition beginning in 2016. He also worked on the turnaround of Pharmacyclics, which subsequently sold to Abbvie for approximately $21 billion in 2015. Before that, Mr. Salva spent almost a decade in life sciences venture capital. Mr. Whitfill served as associate research scientist and currently serves as assistant professor adjunct at Yale University with appointments in the Departments of Pediatrics and Emergency Medicine. He spent nearly a decade in venture capital as a partner in a biotech-focused venture capital fund, Bios Partners. He has led numerous grant-funded projects, holds nearly a dozen patents and has co-authored over 60 publications. Our board of directors, or Board, is comprised of renowned group of senior executives, scientists and investors in the biotechnology industry.

Our Microbial and Microbial Drug Delivery Platform

Commensal microorganisms reside on either the surface of the body or in the mucosa without harming human health. They act on the host's immune system to induce protective responses that prevent colonization and invasion by infectious pathogens, and thereby play a crucial role in maintaining human health across a number of organ systems, particularly in the skin. Diverse communities of microorganisms populate the skin, and a square centimeter can contain up to a billion microorganisms. These diverse communities of bacteria, fungi, mites and viruses can provide protection against disease and form dynamic, yet distinct niches on the skin. Together, they make up the skin microbiome.

Many genetically driven human diseases are systemically or partially related to the dysfunction of specific proteins that are missing or functionally inert due to a mutation. Since approximately 1982, the biopharmaceutical industry has been genetically engineering recombinant proteins in bacterial microorganisms for purposes providing therapies that mimic or support the body's normally functioning proteins and peptides. For decades, the vast majority of genetic engineering has been limited to primary *E. coli* and a handful of other bacterial species, many of which can become pathogenic, inducing infection. In contrast, we have chosen to focus on *S. epidermidis* because of its beneficial effects as a commensal, naturally occurring microbe on the skin. Our goal is to leverage our platform and internal microbial library of over 60 bacterial species to engineer and deliver commensal skin bacteria directly to the target through the stratum corneum of the skin. At these deeper levels in the skin, engineered microbes can produce the missing or inert proteins and thereby resolve the underlying disease cause.

S. epidermidis and Our Proprietary Microbial Library

S. epidermidis is a strong therapeutic candidate species due to a number of well-described properties in the skin. *S. epidermidis* is a gram-positive bacterium that is ubiquitous in the human skin and mucosal flora. As one of the earliest colonizers of the skin, *S. epidermidis* plays an important role in cutaneous immunity and maintaining microbial community homeostasis. *S. epidermidis* is known to have a beneficial relationship with its host as a skin commensal. The species has shown inhibition of the pathogenic strain, *Staphylococcus aureus, or S. aureus,* as well as the strain *Propionibacterium acnes*, or *P. acnes*. *S. epidermidis* induces keratinocytes to produce antimicrobial peptides and produces non-inflammatory T cell accumulation of both CD4+ and CD8+ T cells via immune cell signaling. The T cell responses induce re-epithelization of the skin after injury, accelerating repair and wound closure. For these reasons, we believe *S. epidermidis* offers several advantages as a vector for topical delivery of therapeutic proteins.

In their 2019 study, Stacy and Belkaid, world-leading experts in the skin microbiome, described *S. epidermidis* as "a 'poster child' of the skin microbiota to illustrate the remarkable diversity of functions a microbe can exert on skin physiology and health." We believe that *S. epidermidis* has enormous strain diversity that can be exploited for therapeutic purposes. In the 2020 Oh Study, Julia Oh's lab reported that 1,482 unique strains of *S. epidermidis* were present on only five individuals. These strains had not only significant genetic diversity but also large phenotypic diversity. We believe this large inter-strain variation among *S. epidermidis* can be exploited. To that end, we collected samples from healthy volunteers to develop and characterize our own strain library of *S. epidermidis* that includes over 900 unique *S. epidermidis* strains with potential for therapeutic use. We have used this microbial library to screen against selected properties, including antimicrobial peptide secretion, *S. aureus* killing, antibiotic sensitivity, and other therapeutically relevant characteristics. We have also collected other species in our library that includes roughly 60 different skin commensal species that can also be screened for therapeutic purposes.

Figure 1. Representative Species in Azitra Microbial Library

Acinetobacter baumannii	*Finegoldia magna*	*Morganella morganii*	*Staphylococcus epidermidis*
Bacillus stearothermophilus	*Gardnerella vaginalis*	*Mucor circinelloides*	*Staphylococcus haemolyticus*
Bacillus subtilis	*Haemophilus influenzae*	*Neisseria gonorrhoeae*	*Staphylococcus hominis*
Candida albicans	*Haemophilus parainfluenzae*	*Proteus mirabilis*	*Staphylococcus lugdunensis*
Citrobacter freundii	*Haloarcula marismortui*	*Pseudomonas aeruginosa*	*Streptococcus mitis/oralis*
Corynebacteria	*Helicobacter pylori*	*Saccharomyces cerevisiae*	*Streptococcus pneumoniae*
Deinococcus radiodurans	*Klebsiella oxytoca*	*Salmonella oslo*	*Streptococcus pyogenes*
Enterobacter aerogenes	*Klebsiella pneumoniae*	*Salmonella* Senftenberg	*Streptomyces ambofaciens*
Enterobacter cloacae	*Kluyveromyces lactis*	*Salmonella typhimurium*	*Thermaerobacter marianensis*
Enterococcus faecalis	*Kocuria rhizophila*	*Serratia marcescens*	*Thermus thermophilus*
Enterococcus faecium	*Micrococcus luteus*	*Shigella sonnei*	*Vibrio cholerae*
Escherichia coli	*Moraxella catarrhalis*	*Staphylococcus aureus*	*Yersinia enterocolitica*

Predictive Analysis of Our Microbial Library

The biopharmaceutical industry has seen success in identifying and isolating thousands of bacterial species. Yet only a relatively few such species, believed to be less than 20, have been engineered to produce proteins or peptides with therapeutic potential. We have partnered with Chemia Biosciences, Inc., a research and development group from Carnegie Mellon University. Through our collaboration with Chemia Biosciences, we are able to use their proprietary genomic and peptidomic

artificial intelligence and machine learning system, NRPMiner, to develop and confirm natural product predictions of the proteins, peptides and small molecules that are generated by our proprietary bacterial library. These predictions are confirmed via tandem mass spectroscopy or nuclear magnetic resonance. The information is then fed back into the machine learning algorithm to refine the predictions. It can also be compared to existing 2D and 3D protein databases to look for structural homology of our products to existing protein and peptide drugs. We believe our collaboration with the Carnegie Mellon based team provides us with a scalable and modification tolerant way to accelerate therapeutic discoveries within our microbial library.

The Delivery of our Microbially Produced Drugs

The delivery of genetically engineered proteins to the subcutaneous target sites is hindered by the natural barrier and the defenses of the stratum corneum. This is the skin's outermost layer, which acts as a barrier that prevents unwanted materials from entering the body. To address this challenge, we have developed a proprietary process capable of facilitating protein delivery in a manner that bypasses the normally impenetrable stratum corneum. The strategy utilizes the ability of particular microbes to infiltrate into the deeper layers of the skin. There, the genetically modified microbes act as miniature factories to produce a therapeutic protein or molecule where it is needed.

Our protein delivery capability for treating skin conditions is based on engineering *S. epidermidis* and other microbes to secrete proteins for drug delivery into the skin. We believe any number of proteins can be engineered and encoded by our bacteria to be produced and delivered to the skin to treat a variety of skin conditions. We have also added key proprietary features in its platform to facilitate protein delivery. A key feature of this system is that it bypasses the normally impenetrable skin barrier, a problem of topical protein delivery. The skin barrier, composed of the stratum corneum, is sealed by enucleated keratinocytes and formed by numerous structural, physical, and biochemical properties. Other transdermal delivery challenges arise due to susceptibility of protein to enzymatic digestion by proteases and solubility and diffusion impediments due the hydrophobic surface and the layers of linked corneocytes comprising the stratum corneum. We address this issue by leveraging the natural homing of *S. epidermidis* to layers below the stratum corneum. In preclinical studies, we have shown that *S. epidermidis* homes to layers below the stratum corneum and delivers proteins into the deeper epidermis.

To expand upon our recombinant protein construction capabilities, we have acquired an exclusive license to proprietary technology that disguises our genetically engineered DNA sequences to enable the production of proteins in previously intractable bacterial species. The technology from the Fred Hutchinson Cancer Center, or Fred Hutch, expands the universe of bacterial species that can be genetically modified. It is based upon a restriction modification system-silent SyMPL toolset. The SyMPL technology platform makes human-made DNA invisible to the bacteria's defenses. In theory, the method can be applied to any type of bacteria. Our current product candidates do not incorporate the SyMPL technology platform, but we expect that some or all of our future product candidates will do so.

Virtually all strains of naturally occurring bacteria have defense mechanisms called restriction modification systems. The four types of restriction modification systems recognize and defend against insertion of foreign DNA used to code recombinant proteins. Functional genetic engineering of S. *epidermidis* (as well as *S. aureus*) has previously been limited due to the presence of Type I and IV restriction systems in virtually all strains of these bacterial species. These restriction systems recognize methylated cytosine bases in DNA from standard clone expansion systems (such as *E. coli)* and hinder incorporation of foreign DNA in the microbe. *S. epidermidis* was once believed to be an "untransformable" strain due to its genetic intractability. However, we have been able to overcome *S. epidermidis'* defenses.

Current genetic engineering processes add specific modifications to disguise human made DNA to trick the bacterium into thinking the intruder is a part of its own DNA. This approach often takes considerable time and resources to try to match the right disguise to each particular recognition motif. In contrast, Fred Hutch's SyMPL technology platform is a systematic "stealth-by-engineering" approach to overcome restriction modification defense systems. These restriction modification defense systems protect microbes from foreign DNA and hinder the vast majority of genetic engineering approaches. The SyMPL technology platform is based on the ability to build minicircle DNA plasmids which lack any of the target recognition motifs for the microbe's defense systems to identify. The technology uses the genome and methylome from a target bacteria's genomic sequence to identify the restriction modification target motifs. They are then eliminated from the nucleotide sequence of the genetic tool *in silico*. The resulting sequence is used to build the restriction modification, SyMPL tools. These are propagated and then used for genetic transformations. Not only does the "stealth by engineering" approach enable transformations in genetically intractable bacterial strains, but it has also been shown to drastically increase transformational efficiency. Proof of principle experiments have shown improvements of over 10,000x in yields of genetically engineered colonies.

In January 2022, Fred Hutch granted us an exclusive worldwide, royalty bearing license to the patent rights, and a non-exclusive worldwide, royalty bearing license to the related know-how, for the SyMPL technology platform in all fields of use. For more information related to the intellectual property acquired pursuant to the Fred Hutch license agreement, see the section titled "*Licenses and Intellectual Property Rights - Exclusive License Agreement with Fred Hutchinson Cancer Center*."

Our Product Candidates

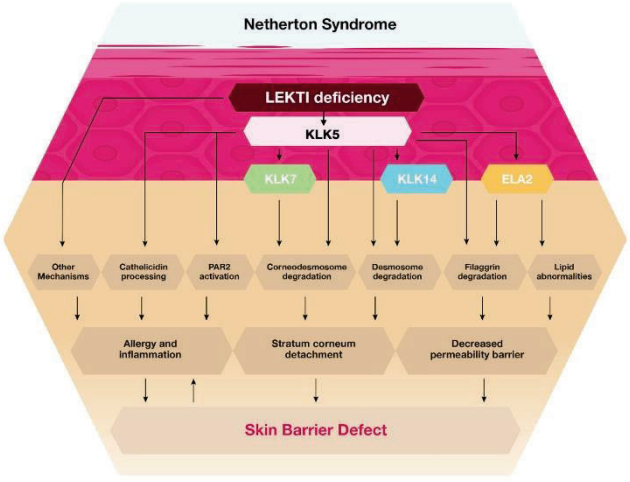
ATR-12 for the treatment of Netherton syndrome

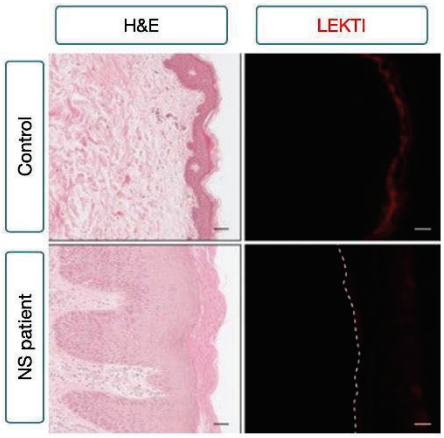
ATR-12 is our proprietary and patent-pending drug candidate that contains a novel strain of *S. epidermidis* which has been genetically modified to express and secrete an active fragment of the full-length protein called the lympho-epithelial Kazal-type related inhibitor, or LEKTI. It has also been engineered to be auxotrophic, meaning that it requires the D-alanine nutrient in its formulation to survive and propagate. This provides an additional level of safety against unintentional and environmental exposure to the strain. ATR-12 is a topical application intended to address the underlying cause of Netherton syndrome, by replacing deficient LEKTI with an active segment of human recombinant LEKTI, or rhLEKTI-D6, to counter the dysregulated skin serine protease activity observed in Netherton syndrome patients. The uncontrolled serine protease activity leads to a profound skin barrier defect and the release of pro-inflammatory and pro-allergic mediators by keratinocytes and immune cells. To date, there is no known therapy for the cure or effective treatment of Netherton syndrome. We believe ATR-12 has the potential to be the first therapy to effectively treat this disease of the skin. Based on the Barbati and Sun Studies, we believe that ATR-12 represents a potential $250 million global sales opportunity by mid-2030.

Netherton syndrome overview

Netherton syndrome is a rare, autosomal recessive disease estimated to affect approximately one in every 200,000, but its prevalence may be underestimated due to misdiagnosis. It is a chronic disease of the skin, characterized by severe inflammation, pruritus, scaling, red, and dehydrated skin. Infants born with Netherton syndrome may suffer from a failure to thrive, and it has been reported that approximately one in ten infants with Netherton syndrome die in their first year of life. Those that survive face a lifetime of skin disease challenges including red, scaly skin, hair defects and an ongoing higher than normal risk for infection and allergy.

Netherton syndrome is caused by mutations in the *SPINK5* gene, which codes for the serine protease inhibitor Lympho-epithelial Kazal-type related inhibitor, or LEKTI. The function of LEKTI is to inhibit enzymes in the epidermis, such as kallikreins 5, 7 and 14, or KLK5, KLK7 and KLK14, which facilitate the shedding of skin cells in a process known as desquamation. When LEKTI is absent or has reduced activity, excess shedding results and the skin is sensitive, open, and appears red and scaly. This is accompanied by the detachment of the stratum corneum, leading to severe barrier dysfunction, dehydration and potential exposure to environmental agents, such as chemicals. Histopathology and immunofluorescence staining of skin from a Netherton syndrome patient compared to healthy volunteer reveal an absence of LEKTI and abnormalities in the skin such hyperkeratosis, epidermal thickening, and reduction of the basophilic keratohyalin granules.





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- LEKTI fragments inhibit KLK5, KLK7 and KLK14 and controls desquamation
- In NS patients, overactive KLKs lead to disease
- Concurrent inflammation with high IL-36γ levels

- Netherton syndrome patients have undetectable levels of LEKTI in skin

Figure 2: Netherton syndrome pathophysiology and LETKI deficiency

Netherton syndrome can range in severity from mild, such as red patchy areas of the skin, to life threatening. The degree of severity of the disease correlates directly with the extent of loss of function of LEKTI on the skin. Netherton syndrome appears shortly after birth and is most severe in the first year of an infant's life. Survival beyond the first year is common in most cases, but the implications of the disease are a lifelong challenge.

To date, there is no known cure for Netherton syndrome and treatment options are limited. Dermatologic interventions to treat the severe skin manifestations of Netherton syndrome include moisturizers, topical corticosteroids, and calcineurin inhibitors, all of which are limited in that they do not provide sustained remediation. Given the severity of disease during neonatal stages, fluid/electrolyte and diet support are needed in addition to treating infections that often arise in these patients. While immunoglobulin therapy to address immunodeficiencies associated with Netherton syndrome has shown limited success, a sustained remediation of skin barrier defects, induced by dysregulation of LEKTI, is currently unavailable.

Our solution – ATR-12 for the treatment of Netherton syndrome

ATR-12 is a topical ointment containing an *S. epidermidis* strain, SE351, that has been genetically modified to express LEKTI from the chromosome. The SE351 strain has also been engineered to be auxotrophic for D-alanine, which means it cannot survive without the exogenous D-alanine nutrient provided in the formulation. ATR-12 is intended to address the underlying cause of Netherton syndrome by replacing deficient/dysfunctional LEKTI with an active, recombinant, human fragment of the full-length protein, rhLEKTI-D6. The treatment consists of applying ATR-12 to affected areas. rhLEKTI-D6 produced by SE351 will counter the dysregulated skin serine protease activity observed in Netherton syndrome patients, to restore skin barrier function and reduce inflammation. We believe that among the important advantages of this approach is the potential to deliver rhLEKTI-D6 over time into the lower layers of the stratum corneum and epidermis, the primary sites of dysregulation in patients with Netherton syndrome.

The *S. epidermidis* strain selected to deliver rhLEKTI-D6 to the skin, SE351, was selected from our proprietary strain collection. This strain is characterized by low virulence and is a non-biofilm forming host strain. To further enhance the safety of ATR-12, we have engineered the microbe for D-alanine to be auxotrophic. The key advantage to engineering auxotrophy is the ability to control growth and halt potential infection. Full length human LETKI, a 15-domain protein (145 kDa), is too large for reliable bacterial expression and secretion. Given evidence that fragments of the full-length protein are sufficient to counter the dysregulated skin serine protease activity observed in Netherton syndrome patients, we selected D6 for recombinant expression in *S. epidermidis*.

In May 2020, we received Rare Pediatric Disease Designation from the FDA for ATR-12. As a result, if we are able to obtain approval for ATR-12 from the FDA in pediatrics, we will be eligible to receive a Priority Review Voucher, which can be used by us to obtain FDA review of a New Drug Application or Biologics License Application for this or another drug candidate in an expedited period of six months. These vouchers are often transferable, and some have been sold for over $100 million. However, due to recent policy changes, the FDA, at this point, can not reward any prior review vouchers for rare pediatric disease product applications approved later than September 30, 2026.

Preclinical data for ATR-12

As of the date of this report, we have conducted several *in vivo* and *ex vivo* experiments that collectively support the potential efficacy of ATR-12 as a disease modifying therapy for patients with Netherton syndrome. The genetically engineered strain of S. epidermidis used in the formulated ATR-12 drug product is called SE351. In 2021, we conducted *in vitro* studies to assess the ability of exogenously applied SE351 to colonize sterile reconstructed human epidermis. SE351 successfully colonized the reconstructed human epidermis and, furthermore, no *S. epidermidis* colonization occurred without D-alanine present, confirming that D-alanine must be supplied for SE351 growth on skin. These data suggest that SE351 is capable of colonizing human skin, and that colonization can be controlled with D-alanine supplementation.

Additionally, *in vitro* studies using tape stripped skin from healthy volunteers spiked with KLK5 to mimic Netherton syndrome showed that diluted SE351 culture supernatant dose-dependently inhibited trypsin-like activity (KLK5 activity). Trypsin-like activity in the Netherton syndrome surrogates returned to normal healthy levels when a solution containing ≥0.5% of the SE351 culture supernatant was added.

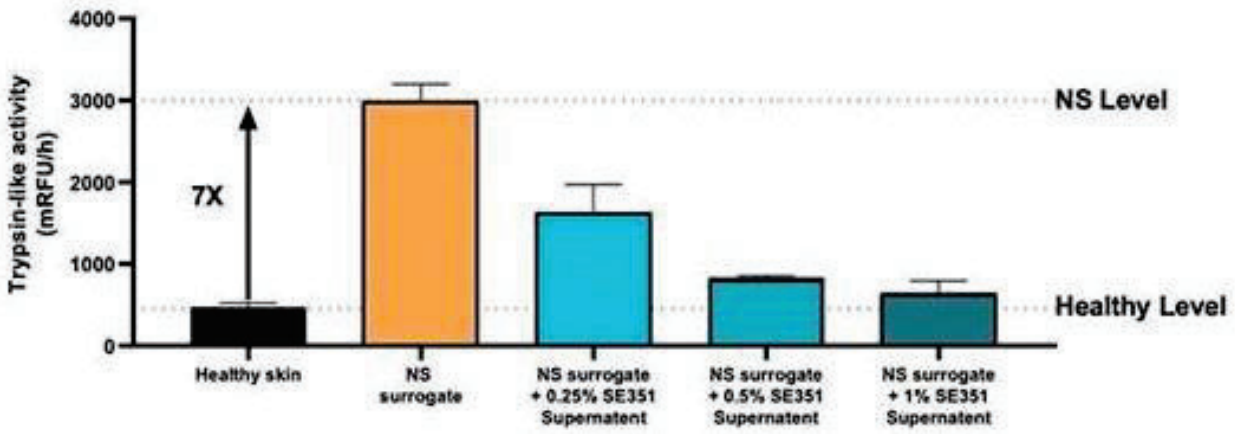


Figure 3: *In Vitro* Netherton Syndrome Model Using Human Skin Tape Strip Extracts Supplemented with Disease Level KLK5 Activity

In addition, results from an *ex vivo* pig skin model demonstrate that a single topical dose of ATR-12 at 3 dose levels led to secretion of active rhLEKTI-D6. Finally, data from an *ex vivo* healthy human skin model demonstrate that a single topical dose of ATR-12 administered at the maximum intended dose of 10^9 CFU/g delivers enough active rhLEKTI-D6 into the lower layers of the stratum corneum to effectively inhibit the protease, kallikrein 5, or KLK5, at levels typically observed in patients with Netherton syndrome.

In particular, data from an *ex vivo* healthy human skin model demonstrate that a single topical dose of ATR-12 administered at the maximum intended dose of 10^9 Colony Forming Units per gram, or CFU/g delivers enough active rhLEKTI-D6 into the lower layers of the stratum corneum to effectively inhibit KLK5 at levels typically observed in patients with Netherton syndrome. Amounts of LEKTI activity in layers extracted were from tape strip samples from *ex vivo* human skin treated with placebo and ATR-12. The collection proceeded right after skin application (T = 0 hours, white bars) or after 8 hours incubation at 30°C (T = 8 hours, black bars). Total LEKTI activity levels were obtained by adding the pmol amounts through layers 1 to 30 of placebo (grey bars) or ATR-12 (black bars) samples. Data are the average ± a standard deviation (SD) of 3 independent samples (N = 3). Statistical analysis was carried out using two-way ANOVA, and ** represents $p < 0.01$.

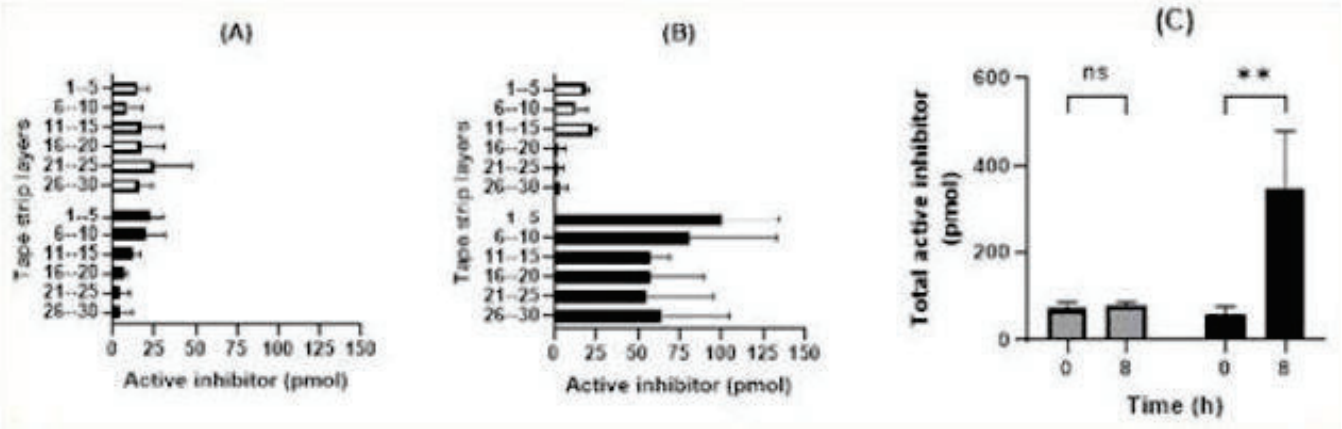


Figure 4: LETKI activity in Placebo and ATR-12-Treated Skin Samples Following 0- and 8-hour Incubation

In addition, a single therapeutic dose of ATR-12 over 24-hour incubation yielded ~2-fold higher LEKTI activity compared to 8-hour incubation. This indicates continuous production of functional rhLEKTI-D6 by ATR-12 over time.

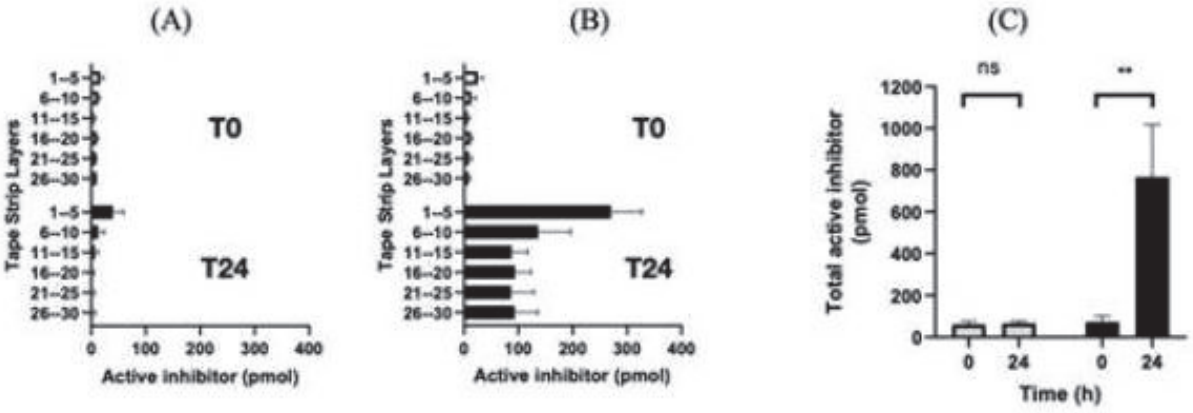


Figure 5: LETKI activity in Placebo and ATR-12-Treated Skin Samples Following 24-hour Incubation

In vitro stoichiometry work performed by Azitra indicates that KLK5 requires 2 molar equivalents on the rhLEKTI-D6 protein for inhibition (as measured by IC_{50}). Historical studies have indicated that Netherton syndrome patients to show up to ~6 fold the amount of KLK5 that the amounts found in normal skin. This equates to 60 pmol of KLK5 per given area. The studies shown above indicate that SE351 delivered 350 pmol of rhLEKTI-D6 at 8 hours and it delivered 700 pmol of rhLEKTI-D6 at 24 hours. This represents a 5- to 11-fold amount above the predicted amount required for activity.

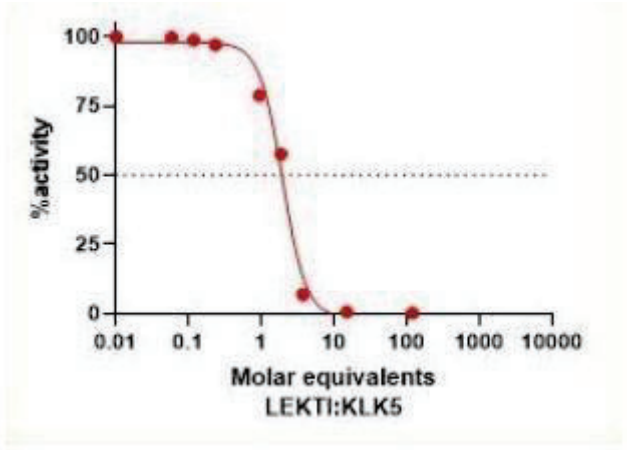


Figure 6: *In vitro* stoichiometry of LEKTI-D6 to inhibit KLK5

In 2022, we obtained pre-IND correspondence with the FDA for purposes of discussing our proposed regulatory pathway for ATR-12 and obtaining guidance from the FDA on the preclinical plan leading to the filing and acceptance of an IND application for ATR-12. In December 2022, we filed an IND for a first-in-human trial of ATR-12 in Netherton syndrome patients. Our IND proposes a Phase 1b multi-center, randomized, double-blind, single dose level, placebo-controlled clinical study of ATR-12 in patients with Netherton syndrome. The primary endpoint is safety, and secondary endpoints include signals of efficacy and pharmacokinetics. Exploratory endpoints include immune and inflammatory mechanism biomarkers. On January 27, 2023, we received notification from the FDA that the "study may proceed" with respect to the proposed Phase 1b clinical trial. We dosed the first patient in August 2024 and expect initial safety results in the first half of 2025.

ATR-04 for the Treatment of EGFRi-Associated Rash

ATR-04 is our proprietary and patent-pending drug candidate that contains a novel strain of *S. epidermidis*, SE484, which has been genetically modified to be auxotrophic tor D-alanine and inhibits both *S.aureus* and IL-36γ. ATR-04 is a topical application intended to address the papulopustular rash experienced by cancer patients undergoing epidermal growth factor receptor inhibitor, or EGFRi, targeted therapy. We believe this product candidate represents a potential $1 billion global sales opportunity by 2030.

EGFRi-Associated Rash Overview

Targeted cancer therapies have produced significant treatment advances for patients diagnosed with a variety of tumor types, but they are also associated with unique dermatologic toxicities that may hamper treatment efforts and cause significant physical and psychological discomfort for patients. Prevention and management of these toxicities may allow patients to tolerate treatments better, remain on therapy longer and thereby potentially receive maximum clinical benefit from the drug. One such class of targeted cancer therapy includes EGFR inhibitors. EGFR is a protein on the surface of cells that helps them grow and divide. It is also a key factor in certain malignancies, and its activity enhances tumor growth, invasion, and metastasis. While systemic exposure to EGFRi agents suppresses EGFR at the target cancer site, it also suppresses EGFR throughout the body. In the skin, EGFR regulates multiple keratinocyte functions including proliferation, adhesion and migration, survival, and differentiation. Consequently, inhibition of EGFR in the skin results in adverse skin reactions, which make it difficult for patients to stay on these effective therapies.

Dermatologic toxicities are amongst the most prevalent side effects seen with EGFRi-targeted therapies. The papulopustular rash is the earliest and most common dermatologic adverse event of EGFRi treatment, often occurring in 50-80% of patients, depending on the drug, the cancer being treated, and the treatment regimen. The appearance of the papulopustular rash is a dose-dependent skin drug reaction, which usually develops in the first one to two weeks and peaks at three to four weeks on therapy. The intensity of the rash may start to decrease after two weeks but can persists over the entire course of EGFRi treatment. The rash is characterized clinically as tender erythematous papules, which after a few days evolve into pustules and then into crusts on the face, scalp, chest, and upper back. The rash is often accompanied by severe xerosis and at times serious cutaneous bacterial infection, primarily *S. aureus*. While most skin rash episodes are considered mild to moderate, some are severe. In many cases, the rash leads to severe quality of life issues and can even lead to the interruption or cessation of the EGFRi treatment.

The current standard of care for rash treatment in patients undergoing EGFRi treatment varies depending on the rash severity. Typically, skin moisturizers, topical steroids and doxycycline are administered prophylactically from the start of EGFRi therapy and are continued throughout the entire treatment period. If the rash continues to advance, oral steroids and/or antibiotics are administered. However, there are known systemic adverse events associated with these adjunctive therapies, and we believe that physicians and patients try to limit their use. In addition, research indicates that oral antibiotics lead to a disruption in the gut microbiome, which in turn leads to a decrease in the effectiveness of targeted therapies, including EGFRi. Given the high incidence rate of rash that continues with these patients, as well as the concerns related to potential impacts of antibiotics on these therapies, we believe there is a clear unmet medical need for additional safe and effective adjunctive therapies for addressing papulopustular skin rash.

Based on studies conducted by Satoh and Lichtenberger, the cytokine, Interleukin-36 gamma, or IL-36γ, and *S. aureus* are linked to and play a significant role in the rashes experienced by patients treated with EGFRis. IL-36γ, is elevated in the skin of patients undergoing EGFRi therapy. In 2020, Satoh used gene expression profiling to identify IL-36γ as a candidate driver of EGFRi/MEKi skin toxicity. It is induced by EGFR inhibition and *Cutibacterium acnes* that synergistically induce IL-36γ in the skin and subsequently IL-8 and NF-κB, which leads to cutaneous neutrophilia. IL-36γ could be a key therapeutic target in treating EGFRi-induced rashes. In 2013, Lichtenberger noted high rates (70%) of bacterial infection in patients (n=107) on EGFRi and proposed a mechanism of EGFR ablation leading to *S. aureus*-induced infection in mice. The study noted a majority of the patients were positive with *S. aureus* (54%). Mechanistically, the authors noted that EGFRi therapy impairs host defense: impaired expression of antimicrobial peptides, especially against *S. aureus*; and lowered expression of tight junctions. Also, the study revealed EGFR ablation leads to skin barrier defects as well as impaired cutaneous immune response and cytokine expression.

Our solution – ATR-04 for the treatment of EGFRi-associated rash

ATR-04 is our formulated, drug product candidate for the treatment of EGFRi associated rash. It includes a strain of *S. epidermidis* strain that was selected from our microbial strain library, based on desired properties of IL-36γ reduction and inhibition of *S. aureus* and its biofilms. The current lead strain is called SE484. We then genetically engineered SE484 to be auxotrophic tor D-alanine and to create our drug product candidate, ATR-04.

SE484 was chosen from our microbial library based on key characteristics such as inhibition of IL-36γ as well as its effect against *S. aureus*. Together, we expect these mechanisms of action to lead to significant reductions in rash severity among patients undergoing EGFRi therapy.

We believe that ATR-04 has the potential to address current limitations to treatment of EGFRi-associated rash:

- **Reduced antibiotic use.** From our surveys of clinicians and key opinion leaders, practitioners are reluctant to prescribe systemic antibiotics to patients undergoing EGFRi therapy. These patients can often be prescribed antibiotics for more than 12 months and suffer from antibiotic-related adverse events. We believe ATR-04 would reduce the need for antibiotics in these patients and lead to fewer adverse events due to EGFRi and antibiotic use.

- **Better EGFRi compliance.** Up to 20% of patients undergoing EGFRi therapy discontinue due to adverse events, primarily due to rashes. We believe we can reduce discontinuation rate in patients undergoing EGFRi therapy and thus increase compliance.

- **Higher quality of life.** Many patients on EGFRi therapy report a poor quality of life due to adverse events and papulopustular rashes. Current treatment options fail to adequately reduce these adverse events. We believe ATR-04 therapy in patients undergoing EGFRi therapy will have reduced rash severity and thus a higher quality of life.

Preclinical data of ATR-04

EGFRi-associated rash is a condition that is characterized by redness, itchiness, and irritation of the skin, and is induced by certain cancer treatments. It was shown, by gene expression profiling (Satoh et al 2020), that skin biopsy samples from patients suffering from EGFRi-associated rash had elevated levels of cytokines IL-36γ and IL-8 compared to skin from healthy donors. These are proinflammatory cytokines that are signaling molecules of the immune system that increase the intensity of an immune response and can cause tissue damage. In addition to elevated cytokine levels, EGFRi-treated patients have impaired skin barrier function. Infection with pathogenic strains of *S. aureus* exacerbates the EGFRi-induced cutaneous disease.

Our work was focused on identifying an *S. epidermidis* strain that reduces IL-36γ levels and thus reduces the rash associated with EGFRi. We believed that many species of bacteria that live on human skin probably survive there because they have evolved ways to reduce the human immune system's response to their presence, and we might be able to identify a resident human skin commensal bacteria that survives thereby specifically reducing IL-36γ activity.

To identify such a *S. epidermidis* strain, we developed an *in vitro* assay to measure the levels of IL-36γ and IL-8 that are produced by human skin cells that are grown in culture. The cell line we used is called HaCaT and is derived from human keratinocytes, which are a cell type in the epidermis. In order to simulate the inflammatory phenotype of EGFRi-related disease of the skin, HaCaT cells were stimulated with an immunostimulant, polyinosinic:polycytidylic acid, or poly I:C, which causes them to secrete elevated levels of IL-36γ and IL-8. This assay was used to identify and evaluate the ability of different *S. epidermidis* strains to lower IL-36γ and IL-8 levels.

We screened over 100 strains based on safety (e.g., lack of antibiotic resistance) and biological activity (IL-36γ inhibition and activity against *S. aureus*) and designated SE484 as our lead candidate strain. After engineering this strain to be auxotrophic for D-alanine, so that it will grow only if provided with D-alanine, we also eliminated an anti-biotic resistance gene. Then, we nominated this candidate for use as the active microbe in the ATR-04 drug product formulation.

To test the ability of SE484 to reduce IL-36γ on a skin-like model, erlotinib was used to induce IL-36γ secretion on reconstructed human epidermis, or RHE. Simultaneous application of SE484 with erlotinib reduced IL-36γ to a level comparable RHE that had not been treated with erlotinib, showing that SE484 acts on a skin-like model to reduce this pro-inflammatory cytokine. Figure 7 shows the results of two experiments to measure IL-36γ reduction by SE484. In Figure 7A, a cell-free supernatant (CFS) from a culture of SE484 was applied to RHE, while in Figure 7B live cells of SE484 (either $1x10^8$ CFU or $1x10^9$ CFU) were applied to RHE to measure the ability of SE484 to reduce IL-36γ. In both cases, cell-free supernatant or SE484 cells, erlotinib-induced IL-36γ levels were reduced.

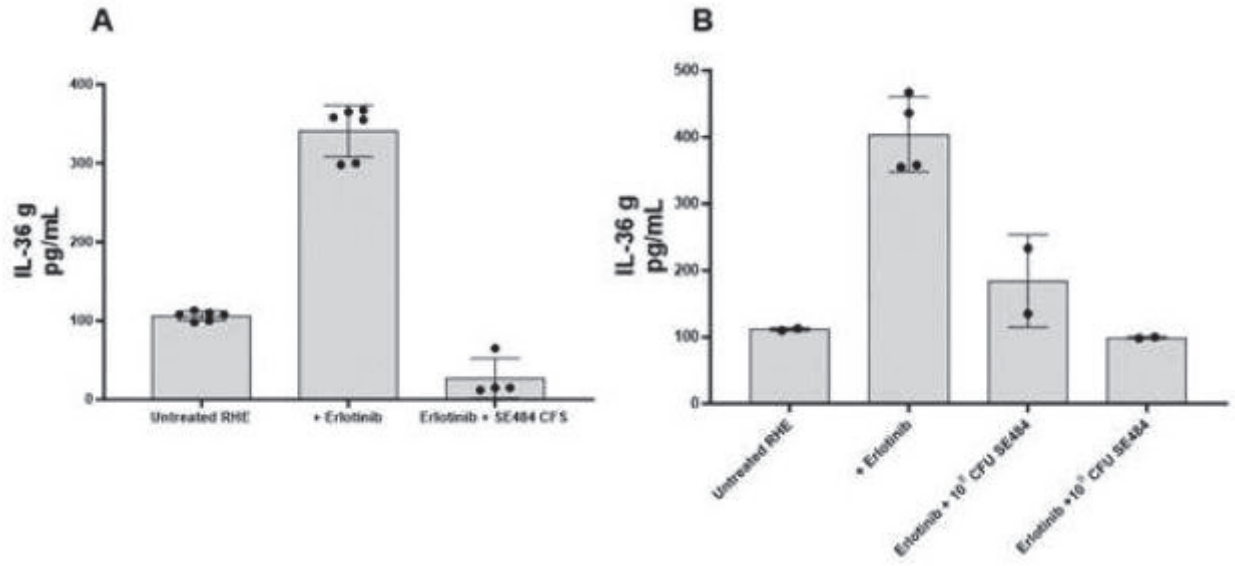


Figure 7. The anti-IL-36g activity of SE484 on RHE. Reconstructed human epidermis, or RHE, was treated for 72 hours with 1 mM erlotinib alone or with cell-free supernatant (CFS) from SE484 culture (A), or with approximately 10^8 or 10^9 CFU of SE484 (B). RHE feeding media was then assayed by ELISA for IL-36γ levels.

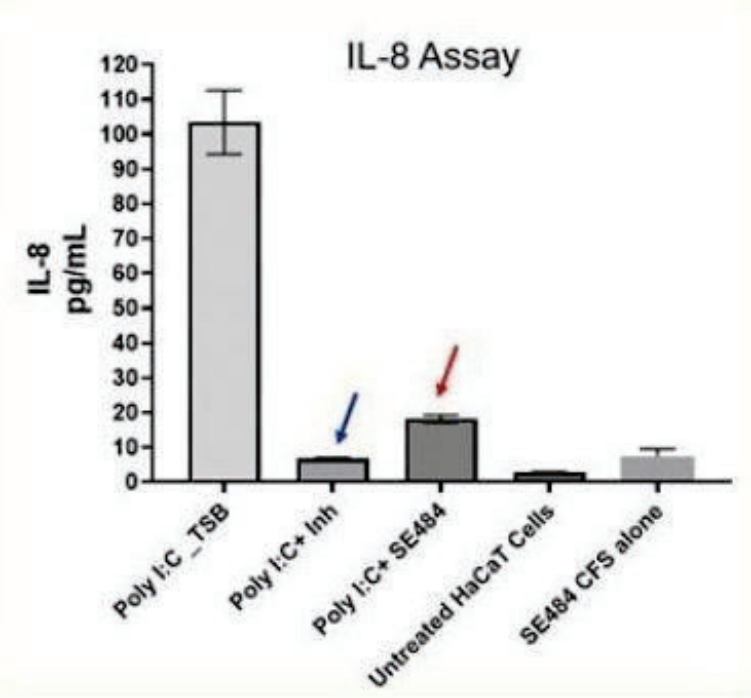


Figure 8. IL-8 induction by Poly I:C is Reduced by CS of SE484. The presence of culture medium from SE484 prevents the stimulation and release of IL-8 by poly I:C (red arrow). An inhibitor of poly I:C is used as control (blue arrow). Data are representative of two independent experiments. CFS = cell free supernatant.

Figure 8 shows the inhibitory effect of SE484 culture supernatant on the induction of IL-8 by poly I:C. Similar to IL-36γ, when poly I:C is added to HaCaT cells, IL-8 is also secreted, several fold above background (as seen in untreated HaCaT and SE484-treated HaCaT). However, in the presence of SE484, lower levels of IL-8 were detected, thus further demonstrating the efficacy of SE484 to inhibiting the proinflammatory pathway involved in EGFRi-related rash.

Our results show that culture media of *S. epidermidis strain* SE484, which was isolated from a healthy human volunteer, can reduce the level of IL-36γ and IL-8 produced by HaCaT cells (Figure 7 and Figure 8, respectively) and thus help in the treatment of EGFRi-associated rash. In addition to its anti-IL-36γ property, SE484 also has broad activity against different methicillin-resistant *S. aureus*, or MRSA, strain types as well as methicillin sensitive *S. aureus*, or MSSA. The ability of SE484 to reduce IL-36γ/IL-8 levels as well as its activity against *S. aureus* and the engineered D-alanine auxotrophy enabled us to nominate strain SE484 for use as the active microbe in the ATR-04 drug product formulation to form the basis of a treatment and reduce the severity of EGFRi rash.

We have also shown that SE484 leads to *in vitro* inhibition of known virulent strains USA300, which is resistant to methicillin, and MSSA, which is sensitive to methicillin. The following data show that ATR-04 reduces the ability of the pathogenic *S. aureus* bacterial species to grow and instigate infections that are seen in patients with EGFRi rash.

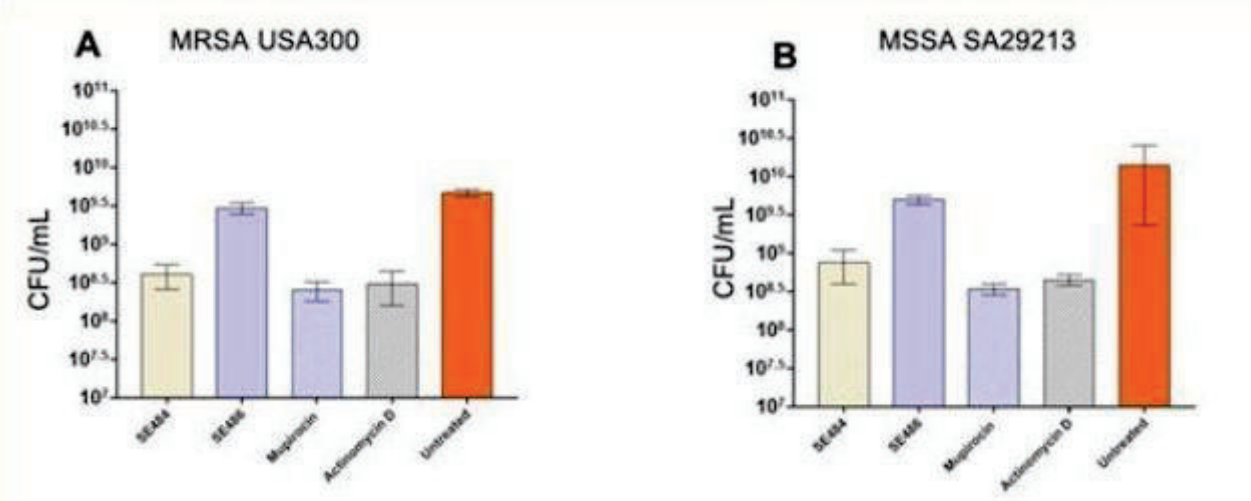


Figure 9. Epidermin-expressing SE484 kills *S. aureus* with similar activity as mupirocin on in vitro agar plates.

We are proposing an initial study of SE484 in the ATR-04 formulation in patients. It is contemplated to be a Phase 1/2 multi-center, randomized, double-blind, single-dose, placebo-controlled trial in patients with colorectal or head and neck cancer who are initiating EGFRi therapies. The primary endpoint is safety, and secondary endpoints will include efficacy and Quality of Life, or QoL. We received IND clearance for ATR-04 in August 2024 and we plan to dose the first pateint in the first half of 2025.

ATR-01 for the treatment of ichthyosis vulgaris

ATR-01 is our drug product candidate intended to treat ichthyosis vulgaris. The program is currently investigating a proprietary and patent-pending novel engineering segment of human filaggrin protein. ATR-01 is being developed as a topical application intended to address ichthyosis vulgaris, a chronic scaly skin disease with an estimated incidence and prevalence of 1 in 250, which gives a total patient population of 1.3 million in the United States. Ichthyosis vulgaris is caused by loss-of-function mutations in the gene encoding filaggrin Using synthetic biology tools for protein engineering, we attached a cell penetrating peptide to filaggrin, which helps facilitate deeper skin delivery for filaggrin. This is designed to overcome the impenetrability of the skin barrier, which would otherwise limit topical protein delivery.

Ichthyosis vulgaris overview

Ichthyosis vulgaris, or IV, is a chronic, xerotic, scaly skin disease with an estimated incidence and prevalence of 1 in 250, which gives a total patient population of 1.3 million in the United States. Clinical features of IV usually appear at around 2 months of age and include generalized xerosis and fine, white to gray scales that are prominent on the abdomen, chest, and extensor surfaces of the extremities. Although rare, some IV patients also experience hypohidrosis and heat intolerance. The pathogenesis of IV has long been identified as a decrease in the size or number, or even a complete absence of, epidermal keratohyaline granules. In addition, patients with IV are at increased risk for atopic dermatitis, asthma and allergies.

Ichthyosis vulgaris is an autosomal semidominant disease caused by loss-of-function mutations in the gene encoding filaggrin. Filaggrin is an essential structural protein that is derived from profilaggrin, which breaks down into individual filaggrin units in the stratum corneum. These reinforce the skin barrier by binding to keratins and other intermediate filament proteins in the keratinocyte cytoskeleton. Many studies have identified loss-of-function mutations in *FLG* in IV patients, and these mutations are associated with disorganized keratin filaments, skin barrier defects and microfractures in the stratum corneum leading to enhanced percutaneous allergen sensitization. Moreover, filaggrin and its breakdown products have significant additional functions in the skin including moisturizing the skin (via hygroscopic amino acids or "natural moisturizing factors"), effecting production of antimicrobial molecules (particularly against *S. aureus*) and maintaining both a beneficial lipid profile and pH in the skin.

There are few effective therapies for the treatment of IV. Current treatment options for IV include primarily topical water evaporation suppressants (e.g., sodium chloride, urea, lactic acid, salicylic acid), and, to a lesser extent, moisturizers (e.g., glycerol, propylene glycol,). Topical retinoids may also be prescribed in an effort to slow the body's production of skin cells. However, long-term retinoid use is not ideal. Of particular concern is the teratogenic effect of all retinoids, which limits their use in women of child-bearing potential. Chronic toxicities from long term therapy with retinoids may result in skeletal abnormalities. Furthermore, the chronic use of retinoids in children may inhibit their growth. Notably, many patients with IV experience a significantly reduced quality of life, due to self-consciousness and social embarrassment, and see a negative impact on domestic life, educational/professional lives and even leisure/sports activities.

Our solution – ATR-01 for the treatment of ichthyosis vulgaris

It is now known that IV is caused by loss-of-function mutations in the gene encoding filaggrin, leading to disorganized keratin filaments, skin barrier defects and microfractures in the stratum corneum, and resulting in enhanced percutaneous allergen sensitization as well as bacterial and viral skin infection. We are developing ATR-01 as a novel treatment modality for IV that directly addresses the disease pathophysiology. ATR-01 consists of FLG9-10 functional unit of the human FLG protein with an attached cell penetrating peptide. The goal is to supplement the skin with stable delivery of hFLG via topical application and deeper skin penetration with a cell penetrating peptide.

Preclinical data for ATR-01

Human FLG units (domains 9-10) were evaluated on human skin explants (from plastic surgery) *ex vivo*. The skin barrier of the explants was compromised by repeated tape-stripping such that transepidermal water loss, or TEWL values were significantly increased compared to normal skin. As shown in the example below, daily topical application of a human filaggrin unit with a cell penetrating peptide for five days resulted in a dose-dependent (not shown) rapid improvement in TEWL, suggesting improved skin barrier. Thus, topical delivery of a recombinant hFLG unit coupled with a cell penetrating peptide can improve/accelerate the repair of damaged human skin barrier.

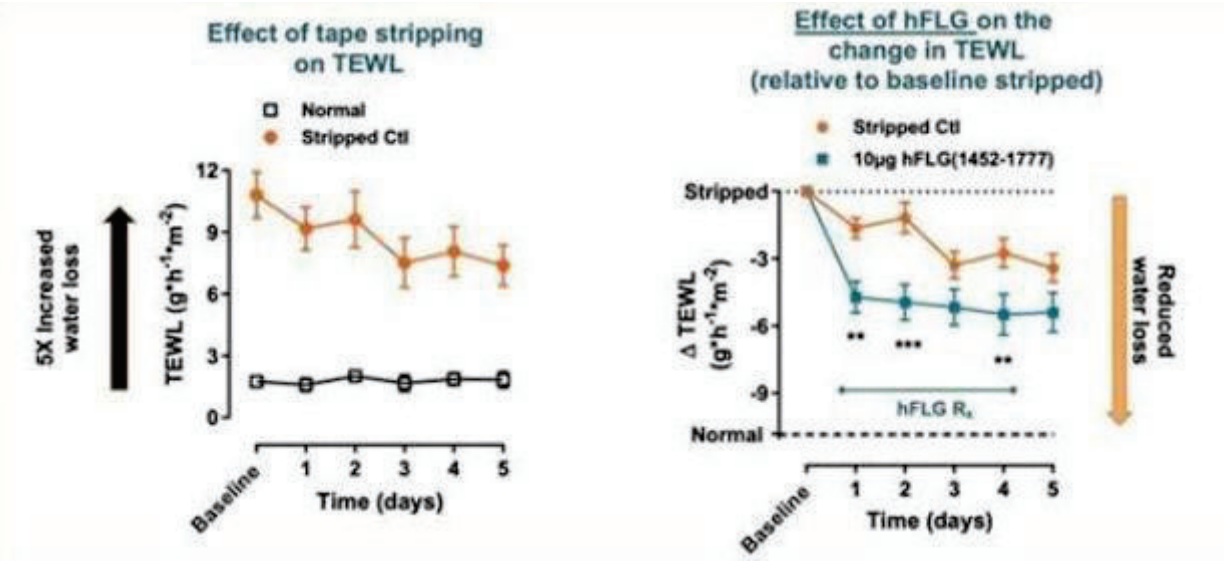
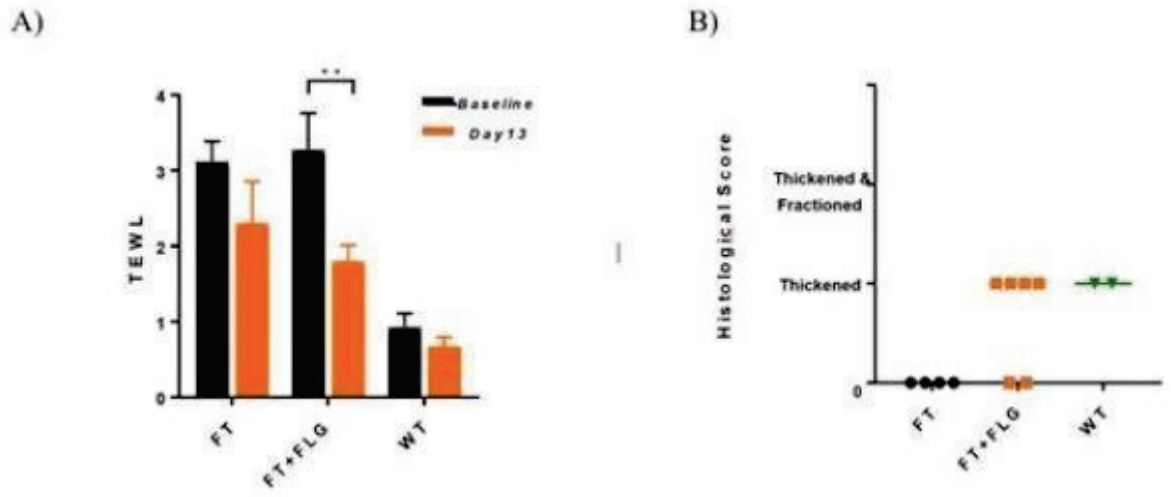


Figure 10: Topical filaggrin application on tape stripped *ex vivo* human skin following human filaggrin application.

Lastly, we have shown that topical filaggrin can improve skin barrier defects in filaggrin-deficient mouse models. Recombinant mouse filaggrin, or mFlg, was applied to the tail of flaky tail, or FT, mice (a mouse model that has a knockout in the *filaggrin* gene) once daily for 2 weeks (50 µg total protein/tail sections or 15.2 µg total protein/cm^2). Daily treatment with mFlg significantly improved transepidermal water loss in FT mice when treated (FT+FLG group) compared to vehicle ("baseline" group). The third group on the X-axis is a normal, control, wild type group (WT) that does not have the *filaggrin* gene knocked out. Treatment of damaged mouse skin with recombinant mFlg combined to a cell penetrating peptide improved damaged mouse skin barrier (Figure A below). Additionally, histological analysis of the epidermis of the mouse tail sections showed tendency for improved stratum corneum thickness with mFlg treatment (Figure B below). In this graph, the Y-axis represents thickening of the stratum corneum, which starts to fractionate or scale after growing past a normal thickness. Treatment with mFlg improved the thickness in four of six of the samples.



Other Potential Product Candidates

Beyond our three lead product candidates, our goal is to develop a broad portfolio of product candidates focused on expanding the application of our platforms for precision dermatology. We have a proprietary platform for discovering and developing therapeutic products for precision dermatology. Our platform is built around a microbial library comprised of approximately 1,500 unique bacterial strains to allow screening for unique therapeutic characteristics and utilizes microbial genetic technology that analyzes, predicts and engineers the proteins, peptides and molecules made by skin microbes. Our ability to genetically engineer intractable microbial species is uniquely leveraged by our exclusive license to the SyMPL technology.

Bayer Joint Development Agreement

In December 2019, we entered into a Joint Development Agreement, or JDA, with Bayer pursuant to which we agreed to the joint development of certain strains selected from our proprietary microbial library. We and Bayer have agreed to cooperate in the identification and *in vitro* and *ex vivo* characterization of microbial strains for topical formulations. Bayer paid us a one-time $150,000 payment upon execution of the JDA and has agreed to reimburse us for our development costs. In October 2021, Bayer expanded the option agreement and paid us $375,000 for additional characterization work. We have granted Bayer an option to acquire an exclusive royalty bearing license for up to six strains subject to development activities under the JDA, including an exclusive royalty bearing license to any related patent rights. After screening through hundreds of strains, we and Bayer have selected two particular strains to move forward with *in vitro* and *ex vivo* characterization, which we intend to develop as potential over-the-counter cosmetic products. Upon the conclusion of the characterization studies and our delivery of the data to Bayer, the JDA will end, but Bayer has the option to license the strains and related patents. As of the date of this report, we have not negotiated a commercial license agreement with Bayer and we will not do so until such time, if ever, as Bayer exercises its option to acquire an exclusive royalty bearing license.

Sales and Marketing

Given our stage of development, we have not yet established a commercial organization or distribution capabilities. We plan to build focused capabilities in the United States to commercialize our development programs focused on live biotherapeutic products and recombinant proteins for the treatment of skin diseases, where we believe the patient populations and medical specialists for the indications we are targeting are sufficiently concentrated to allow us to effectively promote our products, if approved for commercial sale, with a targeted sales team. In other markets for which commercialization may be less capital efficient for us, we may selectively pursue strategic collaborations with third parties in order to maximize the commercial potential of our product candidates.

Manufacturing

We do not own or operate manufacturing facilities for the production of our current product candidates. We currently rely on third-party contract manufacturers for all of our required raw materials, manufacturing devices and active pharmaceutical ingredients and for our preclinical research and clinical trials. Although we are able to manufacture finished product in our Groton Connecticut facility for our clinical trials, we will rely on third parties for the manufacture of our finished product for commercial sale. We do not have long-term agreements with any of these third parties. We also do not have any current contractual relationship for the manufacture of Phase 3 clinical trials or commercial supplies. We intend to enter into agreements with third-party contract manufacturers and one or more backup manufacturers for future production. We are analyzing the feasibility of building manufacturing capabilities for future development and commercial quantities of any products that we develop. Such products will need to be manufactured in facilities, and by processes, that comply with the requirements of the FDA and the regulatory agencies of other jurisdictions in which we are seeking approval.

Competition

The biopharmaceutical industry is characterized by rapidly advancing technologies, intense competition and a strong emphasis on proprietary drugs. While we believe that our knowledge, experience and scientific resources provide us with competitive advantages, we face potential competition from many different sources, including other biopharmaceutical companies, academic institutions and governmental agencies as well as public and private research institutions. Any drug candidates that we successfully develop and commercialize will compete with existing treatments and new treatments that may become available in the future.

Netherton syndrome

With respect to Netherton syndrome, no drug has been approved by the FDA, specifically for Netherton syndrome, to date. Standard of care includes cleansing of the skin with a gentle/soft non-detergent liquid cleansing oil, preferably with an acidic pH (5). Because Netherton syndrome patient skin is most often dry, scaly and peeling, emollients and moisturizers are also often used. Keratolytics such as salicylic acid, urea or alpha-hydroxy acids are often irritative and not well tolerated by Netherton syndrome patients. The skin of Netherton syndrome patients is prone to frequent bacterial infections. Limited infections are treated with topical antibiotics for a short period of up to 2 weeks. Oral antibiotics may also be used to treat the pathogenic *Staphylococcus aureus* and *Streptococcus* strains that can drive more extreme infections. Bleach baths are also recommended two to three times a week for their antimicrobial effects. Topical corticosteroids are often used to treat the inflammatory and hyperproliferation associated with non-infected Netherton syndrome lesions, but due to their adverse effects, must be limited. These adverse events include aminoaciduria, Cushing syndrome, skin atrophy, adrenal insufficiency, growth retardation, hypertension and weakness. Overuse of topical steroids can even aggravate the defective skin barrier by inducing loss of the stratum corneum. Systemic retinoids have shown varying degrees of efficacy in Netherton syndrome, but also carry bone toxicity and teratogenicity as adverse effects. Topical calcineurin inhibitors have been used to reduce erythema (redness) but patients have shown a tachyphylaxis and reduced efficacy with prolonged treatment. These immunomodulators also carry risks of serious adverse effects including increased risk of infections, swelling, burning sensations and tingling. Phototherapy (narrowband UVB (NB-UVB) and psoralen-UVA (PUVA)) has also been investigated in Netherton syndrome patients but has been limited due to its potential to cause erythema and increases in the risk of skin cancer.

We are also aware that Sixera Pharma initiated a clinical trial in Europe with SXR-1096, a topical small molecule KLK inhibitor in December 2021 for Netherton syndrome. In addition, Quoin Pharmaceuticals initiated two clinical trials with QRX003, a topical small molecule broad-spectrum serine protease inhibitor, in December 2022 and March 2023. Boehringer Ingelheim is also recruiting for a Phase 2/3 clinical trial for Netherton syndrome with spesolimab, an IL-36 inhibitor. Krystal Biotech, MatriSys, and BridgeBio have reported they are developing Netherton syndrome programs that are at a preclinical stage.

Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize drugs that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than ATR-12 or any other drug that we may develop. Our competitors also may obtain FDA or other regulatory approval for their drugs more rapidly than we may obtain approval for our drug, which could result in our competitors establishing a strong market position before we are able to enter the market. Many of the companies against which we are competing, or against which we may compete in the future, have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved drugs than we do. Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and subject registration for clinical trials, as well as in acquiring technologies complementary to, or that may be necessary for, our programs.

EGFRi-Associated Rash

To date, no drug has been specifically approved by the FDA for the treatment of EGFRi-associated rash. The majority of patients (estimated to be up to 90%) treated continuously with anti-EGFR therapies suffer from dermatological adverse events, especially papulopustular rash, pruritus (itching), xerosis (dryness), and paronychia (nail infections). Papulopustular or acneiform rash is the most common adverse event of EGFRis on the skin. This rash negatively impacts compliance with EGFRi treatment in many patients. Dose modification or discontinuation treatment occurs in severe cases. Because evidence-based controlled trials are still very sparse, treatment of EGFRi skin toxicity primarily relies on physician experience, and recommendations from expert consensus conferences. As a result, there are geographical variations and even inconsistencies in the clinical treatment of EGFRi skin rash. Topical corticosteroids are avoided in Europe with respect to acneiform rash but are often used in the United States. Furthermore, topical treatment is frequently customized to the individual patient and may change on a case-by-case basis. No topical treatment scheme is universally applicable for all patients.

We are aware of the following Phase 2 programs developing investigational drug candidates for EGFRi associated rash; Hoth Therapeutics is developing HT-001, or topical aprepitant, a neurokinin 1 inhibitor in the US; Lutris Pharma is developing LUT014, a topical B-Raf inhibitor, in the US and Israel. Daewoong Pharmaceutical Co. Ltd. is developing DWP708 in Korea.

Intellectual Property

Overview

We actively seek to protect our proprietary technology, inventions, improvements to inventions and other intellectual property that is commercially important to the development of our business by a variety of means, such as seeking, maintaining and defending patent rights, whether developed internally or licensed from third parties. We also may rely on trade secrets and know-how relating to our proprietary technology platform, on continuing technological innovation and on future in-licensing opportunities to develop, strengthen and maintain the strength of our position in the field of gene therapy that may be important for the development of our business. Additional regulatory protection may also be afforded through data exclusivity, market exclusivity and patent-term extensions where available.

As of the date of this report, we own or exclusively license three issued U.S. patents, 12 pending U.S. patent applications, three pending PCT application and 57 other foreign patents and patent applications that are important to the development of our business.

Our policy is to file patent applications to protect proprietary technology, inventions and improvements to inventions and other intellectual property that may be commercially important to the development of our business. We also intend to seek additional patent protection or rely upon know-how or trade secret rights to protect other technologies that may be used to manufacture and develop our live biotherapeutic products. As described below, we are a party to exclusive license agreements that grant us rights to use specific technologies in our live biotherapeutic products and in the manufacturing and development of our products.

Our Patent Portfolio

Our patent portfolio has broad coverage for therapeutic bacteria pharmaceutical compositions containing these therapeutic bacteria for treating abnormal skin conditions and methods of making and using these recombinant bacteria. In our broadest filing, we have secured a US patent that protects pharmaceutical compositions for treating abnormal skin conditions using a bacterial strain expressing a therapeutically effective amount of a recombinant polypeptide. This patent expires in May 2035. Specifically, this issued patent covers a pharmaceutical composition containing one or more of the following bacterial strains: *Bifidobacterium, Brevibacterium, Propionibacterium, Lactococcus, Streptococcus, Staphylococcus, Lactobacillus, Enterococcus, Pediococcus, Leuconostoc, or Oenococcu*s, wherein the bacterial strain has been engineered to produce a therapeutical polypeptide for treating the abnormal skin conditions. We believe that this patent gives us broad protection for using recombinant bacteria to treat skin diseases and disorders. through its expiration in May 2035.

Patent applications directed to our most advanced programs are summarized below.

ATR-12

Our ATR-12 product candidate is subject to three issued US patents, seven pending US patent applications, and 40 pending foreign patents and patent applications. These patents and patent applications represent ten families of claims covering, among other aspects, the pharmaceutical composition of *S. epidermidis* expressing a recombinant therapeutic polypeptide, the auxotrophic strain of *S. epidermidis*, and the recombinant *S. epidermidis* strain expressing a therapeutic LEKTI protein, and formulations of ATR-12. One of the issued US patents covers a recombinant bacterial strain containing a therapeutic polypeptide for treating abnormal skin conditions and expires in 2035. The second issued US patent covers an auxotrophic *S. epidermidis* that will expire in 2039. If additional patents were to grant from the pending patent applications, they would expire between 2035 and 2044.

ATR-04

Our ATR-04 product candidate is subject to one issued US patent, two pending US patent applications, and 20 pending foreign applications. These patents and patent applications represent two families of claims directed to auxotrophic strains of bacteria and their therapeutic use for treating disease. We have one issued US patent that covers ATR-04. If additional patents were to grant, they would also expire in 2039.

Patent Term and Term Extension

Individual patents have terms for varying periods depending on the date of filing of the patent application or the date of patent issuance and the legal term of patents in the countries in which they are obtained. Generally, utility patents issued for applications filed in the United States are granted a term of 20 years from the earliest effective filing date of a non-provisional patent application. In addition, in certain instances, the term of a U.S. patent can be extended to recapture a portion of the United States Patent and Trademark Office, or the USPTO, delay in issuing the patent as well as a portion of the term effectively lost as a result of the FDA regulatory review period. However, as to the FDA component, the restoration period cannot be longer than five years and the restoration period cannot extend the patent term beyond 14 years from FDA approval. In addition, only one patent applicable to an approved drug is eligible for the extension, and only those claims covering the approved drug, a method for using it, or a method of manufacturing may be extended. The duration of foreign patents varies in accordance with provisions of applicable local law, but typically is also 20 years from the earliest effective filing date. All taxes, annuities or maintenance fees for a patent, as required by the USPTO and various foreign jurisdictions, must be timely paid in order for the patent to remain in force during this period of time.

The actual protection afforded by a patent may vary on a product-by-product basis, from country to country, and can depend upon many factors, including the type of patent, the scope of its coverage, the availability of regulatory-related extensions and the availability of legal remedies in a particular country and the validity and enforceability of the patent.

Our patents and patent applications may be subject to procedural or legal challenges by others. We may be unable to obtain, maintain and protect the intellectual property rights necessary to conduct our business, and we may be subject to claims that we infringe or otherwise violate the intellectual property rights of others, which could materially harm our business. For more information, see the section titled "*Risk Factors—Risks Related to Our Intellectual Property*."

Trade Secrets and Know-How

We may also rely on trade secrets, know-how, continuing technological innovation and confidential information to develop and maintain our proprietary position and protect aspects of our business that are not amenable to, or that we do not consider appropriate for, patent protection, including our proprietary processes for manufacturing our live biotherapeutic products. We seek to protect our proprietary technology and processes, in part, by confidentiality agreements and invention assignment agreements with our employees, consultants, scientific advisors, contractors and others who may have access to proprietary information, under which they are bound to assign to us inventions made during the term of their employment or term of service. These agreements may be breached, and we may not have adequate remedies for any breach. In addition, our trade secrets may otherwise become known or be independently discovered by competitors. To the extent that our contractors, commercial partners, collaborators, employees, and consultants 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 more information, see the section titled "*Risk Factors—Risks Related to Our Intellectual Property*."

We also seek to preserve the integrity and confidentiality of our data and trade secrets by maintaining physical security of our premises and physical and electronic security of our information technology systems.

Exclusive License Agreement with Fred Hutchison Cancer Center

In January 2022, we entered into an Exclusive License Agreement with the Fred Hutchinson Cancer Center, or Fred Hutch. Pursuant to our agreement with Fred Hutch, we obtained an exclusive worldwide license under certain patents related to SyMPL technologies developed and owned by Fred Hutch to develop, make, manufacture, have manufactured, distribute, have distributed, use, research, improve, import, offer to sell and sell and otherwise commercialize products that are covered by such patents. Such exclusive license is subject to certain rights retained by Fred Hutch and the U.S. government. The patent rights licensed to us by Fred Hutch consist of two families of patent applications directed to methods of bypassing restriction modification systems in order to more easily introduce xenogeneic DNA into engineered microbes. These patents applications and any patents that issue from these applications will allow us to produce more modified microbes for the treatment of disease. Our current product candidates do not incorporate the SyMPL technology platform, but we expect that some or all of our future product candidates will do so. If issued, these two families will expire in 2037 and 2040, respectively.

In consideration of the license granted to us under the Fred Hutch license agreement, we paid Fred Hutch a nominal upfront payment. In addition, we are required to pay Fred Hutch certain development and commercial milestone payments and running single digit royalty on net sales of the licensed products. The Fred Hutch agreement also requires us to reimburse Fred Hutch for the cost of the prosecution and maintenance of the licensed patents.

Pursuant to the Fred Hutch license agreement, we are required to use commercially reasonable efforts to bring a licensed product to market through a vigorous and diligent program for exploitation of the licensed patent rights. The term of the Fred Hutch license agreement will continue until the later of (i) the expiration of the licensed patents or (ii) ten years from the first sale of a licensed product. We may terminate the Fred Hutch license agreement at will at any time upon prior written notice to Fred Hutch. Fred Hutch has the right to terminate the Fred Hutch license agreement if we materially breach the agreement and fail to cure such breach within a specified cure period or if we become bankrupt or insolvent. For more information related to the intellectual property acquired pursuant to the Fred Hutch license agreement, see the section titled "*Business-Licenses and Intellectual Property Rights*."

We also hold registered trademarks for our corporate name and design in the U.S. and in seven foreign countries.

Government Regulations

Pharmaceutical companies are subject to extensive regulation by foreign, federal, state and local agencies, such as the U.S. FDA, and various similar agencies in most countries worldwide. The research, development, testing, manufacture, distribution, packaging, labeling, storage, recordkeeping, marketing and sale of pharmaceutical products are subject to government regulation in the U.S. and various foreign countries. Additionally, in the U.S., we must follow rules and regulations established by the FDA requiring the presentation of data indicating that our product candidates are safe and effective and are manufactured in accordance with current Good Manufacturing Practices, or cGMP, regulations. If we do not comply with applicable requirements, we may be fined, the government may refuse to approve our marketing applications or allow us to manufacture or market our product candidates, and we may be criminally prosecuted. We, our manufacturers and clinical research organizations may also be subject to regulations under other foreign, federal, state and local laws, including, but not limited to, the U.S. Occupational Safety and Health Act, the Resource Conservation and Recovery Act, the Clean Air Act and

import, export and customs regulations as well as the laws and regulations of other countries. The U.S. government has increased its enforcement activity regarding illegal marketing practices domestically and internationally. As a result, pharmaceutical companies must ensure their compliance with the Foreign Corrupt Practices Act and federal healthcare fraud and abuse laws, including the False Claims Act.

These regulatory requirements impact our operations and differ from one country to another, so that securing the applicable regulatory approvals of one country does not imply the approval of another country. The approval procedures involve high costs and are manpower intensive, usually extend over many years and require highly skilled and professional resources.

FDA Market Approval Process

In the U.S., our product candidates are regulated by the FDA as biologics under the Federal Food, Drug, and Cosmetic Act, or FDCA, the Public Health Service Act, or PHSA, and regulations promulgated by the FDA. The failure to comply with the applicable requirements at any time during the product development process, including preclinical testing, clinical testing, the approval process or post-approval process, may subject an applicant to delays in the conduct of clinical trials, regulatory review and approval, and/or administrative or judicial sanctions. These sanctions may include, but are not limited to, the FDA's refusal to allow an applicant to proceed with clinical testing, refusal to approve pending applications, license suspension or revocation, withdrawal of an approval, warning letters, adverse publicity, customer notification, product recalls, product seizures, refusal to grant export or import approval, total or partial suspension of production or distribution, consent decrees, injunctions, fines, and civil or criminal investigations and penalties brought by the FDA or the U.S. Department of Justice, or other governmental entities.

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

- completion of preclinical laboratory tests and animal studies performed in accordance with the FDA's current Good Laboratory Practices regulation;
- submission to the FDA of an IND, which must become effective before clinical trials may begin and must be updated annually or when significant changes are made;
- approval by an independent Institutional Review Board, or IRB, or ethics committee at each treatment site before the trial is commenced;
- approval of an Institutional Biologics Committee or similar committee at each treatment site, where applicable, before the trial is commenced;
- performance of adequate and well controlled human clinical trials to establish the safety, purity and potency of the proposed biologic product candidate for its proposed indication for use;
- submission of data supporting safety and efficacy as well as detailed information on the manufacture and composition of the product in clinical development and proposed labeling;
- preparation of and submission to the FDA of a BLA after completion of all pivotal clinical trials;
- satisfactory completion of an FDA Advisory Committee review, if applicable;
- a determination by the FDA within 60 days of its receipt of a BLA to file the application for review;
- satisfactory completion of an FDA pre-approval inspection of the manufacturing facility or facilities at which the proposed product is produced to assess compliance with cGMP standards and to assure that the facilities, methods and controls are adequate to preserve the biological product's continued safety, purity and potency, and of selected clinical investigation sites to assess compliance with Good Clinical Practices, or GCP;
- satisfactory completion of any FDA audits of the non-clinical and clinical trial sites to assure compliance with CGP requirements and the integrity of clinical data in support of the BLA;
- payment of user fees and securing FDA approval of the BLA for the proposed indication for use;

- FDA review and approval of the BLA to permit commercial marketing of the product for particular indications for use in the United States; and

- compliance with any post-approval requirements, including REMS and any post-approval studies required by the FDA.

Preclinical Studies and Investigational New Drug Application

Preclinical tests include laboratory evaluations of product chemistry, formulation and stability, as well as animal studies to evaluate the potential for efficacy and toxicity in animals. The conduct of the preclinical tests and formulation of the compounds for testing must comply with federal regulations and requirements. The results of the preclinical tests, together with manufacturing information and analytical data, are submitted to the FDA as part of an IND application. Some preclinical tests may continue even after submission of the IND application. The IND automatically becomes effective 30 days after receipt by the FDA, unless before that time the FDA raises concerns or questions about the product or conduct of the proposed clinical trial, including concerns that human research volunteers will be exposed to unreasonable health risks. In that case, the IND sponsor and the FDA must resolve any outstanding FDA concerns before the clinical trial can begin.

As a result, submission of the IND may result in the FDA not allowing the clinical trials to commence or allowing the clinical trial to commence on the terms originally specified by the sponsor in the IND. If the FDA raises concerns or questions either during this initial 30-day period, or at any time during the IND process, it may choose to impose a partial or complete clinical hold. This order issued by the FDA would delay either a proposed clinical trial or cause delay in initiation of a phase of an ongoing clinical trial, until all outstanding concerns have been adequately addressed and the FDA has notified the company that investigations may proceed. This could cause significant delays or difficulties in completing planned clinical trials in a timely manner.

Clinical Trials

Clinical trials involve the administration of the investigational product candidate to healthy volunteers or patients with the disease to be treated under the supervision of a qualified principal investigator in accordance with good clinical practice, or GCP, requirements. Clinical studies are conducted under protocols detailing, among other things, the objectives of the study, what types of patients may enter the study, schedules of tests and procedures, drugs, dosages, and length of study, as well as the parameters to be used in monitoring safety, and the efficacy criteria to be evaluated. A protocol for each clinical study and any subsequent protocol amendments must be submitted to the FDA as part of the IND process.

A sponsor who wishes to conduct a clinical trial outside the U.S. may, but need not, obtain FDA authorization to conduct the clinical trial under an IND. If a clinical trial outside the U.S. is not conducted under an IND, the sponsor may submit data from the clinical trial to the FDA in support of a BLA so long as the clinical trial is conducted consistent with the spirit of GCP and in compliance with an international guideline for the ethical conduct of clinical research known as the Declaration of Helsinki and/or the laws and regulations of the country or countries in which the clinical trial is performed, whichever provides the greater protection to the participants in the clinical trial.

An IRB, either centrally or individually, must also review each clinical trial at each institution at which the clinical trial will be conducted. The IRB will consider, among other things, clinical trial design, patient informed consent, ethical factors, the safety of human subjects, the possible liability of the institution, and, where appropriate, the protection of privacy of the human subjects. An IRB must operate in compliance with the FDA regulations. The FDA, IRB, or the clinical trial sponsor, or the principal investigator may suspend or discontinue a clinical trial at any time for various reasons, including a finding that the clinical trial is not being conducted in accordance with FDA requirements or the subjects or patients are being exposed to an unacceptable health risk. Clinical testing also must satisfy extensive GCP rules and the requirements for informed consent. Additionally, some clinical studies are overseen by an independent group of qualified experts organized by the clinical study sponsor, known as a data safety monitoring board or committee. This group recommends whether or not a trial may move forward at designated check points based on access to certain data from the study. The clinical study sponsor may also suspend or terminate a clinical trial based on evolving business objectives and/or competitive climate.

Clinical trials are usually conducted in three sequential phases, but the phases may overlap or be combined. Annual progress detailing the results of the clinical trial phases must be submitted to the FDA.

- *Phase 1* clinical trials are normally conducted in small groups of healthy volunteers to assess safety and tolerability of various dosing regimens and pharmacokinetics. For some products for orphan, severe or life-threatening diseases, especially if the product may be too toxic to administer to healthy humans, the initial clinical trials may be conducted in individuals having a specific disease for which use the tested product is indicated. These trials in patients are often referred to as Phase 1b trials. If they include a design to establish a particular dose, they are commonly referred to as Phase 1b/2a clinical trials. Nevertheless, additional Phase 2 (sometimes called Phase 2b) clinical trials are often necessary to refine the final dose chosen to take into a pivotal Phase 3 clinical trial.

- *Phase 2* clinical trials are generally conducted in a limited patient population to identify possible adverse effects and safety risks, evaluate the efficacy of the product candidate for specific targeted indications and determine does tolerance and optimal dosage. Multiple Phase 2 clinical trials may be conducted by the sponsor to obtain information prior to beginning larger and more costly Phase 3 clinical trials.

- *Phase 3* clinical trials proceed if the Phase 2 clinical trials demonstrate that a dose range of the product candidate is potentially effective and has an acceptable safety profile. Phase 3 clinical trials are undertaken to further evaluate, in a larger number of patients, dosage, provide substantial evidence of clinical efficacy and further test for safety in an expanded and diverse patient population at multiple, geographically dispersed clinical trial sites. A well-controlled, statistically robust Phase 3 trial may be designed to deliver the data that regulatory authorities will use to decide whether or not to approve, and, if approved, how to appropriately label a drug: such Phase 3 studies are referred to as "pivotal."

The FDA may order the temporary or permanent discontinuation of a clinical study at any time or impose other sanctions if it believes that the clinical study is not being conducted in accordance with FDA requirements or that the participants are being exposed to an unacceptable health risk. In some cases, the FDA may approve a BLA for a product candidate but require the sponsor to conduct additional clinical trials to further assess the drug's safety and effectiveness after BLA approval. Such post-approval trials are typically referred to as Phase 4 clinical trials. These studies are used to gain additional experience data from the treatment of patients in the intended therapeutic indication and to document a clinical benefit in the case of drugs or biologics approved under accelerated approval regulations. If the FDA approves a product while a company has ongoing clinical trials that were not necessary for approval, a company may be able to use the data from these clinical trials to meet all or part of any Phase 4 clinical trial requirement or to request a change in the product labeling. Failure to exhibit due diligence with regard to conducting Phase 4 clinical trials could result in withdrawal of approval for products.

Compliance with cGMP Requirements

As a product candidate moves through the clinical testing phases, manufacturing processes are further defined, refined, controlled and validated. The level of control and validation required by the FDA increases as clinical studies progress. The FDA typically will not approve a BLA application unless it determines that the manufacturing processes and facilities are in full compliance with cGMP requirements and able to assure consistent production of the product within required specifications. The PHSA emphasizes the importance of manufacturing control for products like biologics whose attributes cannot be precisely defined.

We and the third-party manufacturers on which we rely for the manufacture of our product candidates and their respective components (including the active pharmaceutical ingredient, or API) are subject to requirements that drugs be manufactured, packaged and labeled in conformity with cGMPs. To comply with cGMP requirements, manufacturers must continue to spend time, money and effort to meet requirements relating to personnel, facilities, equipment, production and process, labeling and packaging, quality control, recordkeeping and other requirements.

Manufacturers and others involved in the manufacture and distribution of products must also register their establishments with the FDA and certain state regulatory bodies. Both U.S. and non-U.S. manufacturing establishments must register and provide additional information to the FDA upon their initial participation in the manufacturing process. Any product manufactured by or imported from a facility that has not registered, whether U.S. or non-U.S., is deemed misbranded under the FDCA. Establishments may be subject to periodic unannounced inspections by government authorities to ensure compliance with cGMPs and other laws. Inspections must follow a "risk-based schedule" that may result in certain establishments being inspected more frequently. Manufacturers may also have to provide, on request, electronic or physical records regarding their establishments. Delaying, denying, limiting, or refusing inspection by the FDA may lead to a product being deemed to be adulterated.

BLA Submission and Review

Assuming completion of all required testing in accordance with all applicable regulatory requirements, detailed information on the product candidate is submitted to the FDA in the form of a BLA, requesting approval to market the product for one or more indications, together with payment of a user fee, unless waived. A BLA includes all relevant data available from pertinent nonclinical and clinical studies, including negative or ambiguous results as well as positive findings, together with detailed information on the chemistry, manufacture, controls and proposed labeling, among other things. To support marketing approval, the data submitted must be sufficient in quality and quantity to establish the safety and efficacy of the product candidate for its intended use to the satisfaction of the FDA. The FDA also conducts a pre-approval inspection of the manufacturer and laboratory prior to approval of the BLA.

If a BLA submission is accepted for filing, the FDA begins an in-depth review of the BLA. Under the Prescription Drug User Fee Act, or PDUFA, the FDA's goal is to complete its initial review and respond to the applicant within ten months of submission, unless the application relates to an unmet medical need, or is for a serious or life-threatening indication, in which case the goal may be within six months of BLA submission. However, PDUFA goal dates are not legal mandates, and the FDA response often occurs several months beyond the original PDUFA goal date. Further, the review process and the target response date under PDUFA may be extended if the FDA requests or the BLA sponsor otherwise provides additional information or clarification regarding information already provided in the BLA. The BLA review process can, accordingly, be very lengthy. During its review of a BLA, the FDA may refer the application to an advisory committee for review, evaluation and recommendation as to whether the application should be approved. The FDA is not bound by the recommendation of an advisory committee, but it typically follows such recommendations. Data from clinical studies are not always conclusive and the FDA and/or any advisory committee it appoints may interpret data differently than the applicant.

After the FDA evaluates the BLA and inspects manufacturing facilities where the drug product and/or its API will be produced and tested, it will either approve commercial marketing of the drug product with prescribing information for specific indications or issue a complete response letter indicating that the application is not ready for approval and stating the conditions that must be met in order to secure approval of the BLA. If the complete response letter requires additional data and the applicant subsequently submits that data, the FDA nevertheless may ultimately decide that the BLA does not satisfy its criteria for approval. The FDA could also approve the BLA with a Risk Evaluation and Mitigation Strategies, or REMS, plan to mitigate risks, which could include medication guides, physician communication plans, or elements to assure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. The FDA also may condition approval on, among other things, changes to proposed labeling, development of adequate controls and specifications, or a commitment to conduct post-marketing testing. Such post-marketing testing may include Phase 4 clinical trials and surveillance to further assess and monitor the product's safety and efficacy after approval. Regulatory approval of products for serious or life-threatening indications may require that participants in clinical studies be followed for long periods to determine the overall survival benefit of the drug.

If the FDA approves one of our product candidates, we will be required to comply with a number of post-approval regulatory requirements. We would be required to report, among other things, certain adverse reactions and production problems to the FDA, provide updated safety and efficacy information and comply with requirements concerning advertising and promotional labeling for any of our product candidates. Also, quality control and manufacturing procedures must continue to conform to cGMPs after approval, and the FDA periodically inspects manufacturing facilities to assess compliance with cGMPs, which imposes extensive procedural, substantive and record keeping requirements. If we seek to make certain changes to an approved product, such as certain manufacturing changes, we may need FDA review and approval before the change can be implemented.

While physicians may use products for indications that have not been approved by the FDA, we may not label or promote the product for an indication that has not been approved. Securing FDA approval for new indications is similar to the process for approval of the original indication and requires, among other things, submitting data from adequate and well-controlled studies that demonstrate the product's safety and efficacy in the new indication. Even if such studies are conducted, the FDA may not approve any change in a timely fashion, or at all.

The FDA may also require post-marketing testing, or Phase 4 testing, as well as risk minimization action plans and surveillance to monitor the effects of an approved product or place conditions or an approval that could otherwise restrict the distribution or use of the product.

Fast Track, Breakthrough Therapy and Priority Review Designations

The FDA is authorized to designate certain products for expedited review if they are intended to address an unmet medical need in the treatment of a serious or life-threatening disease or condition, or in the event of an emergency. These programs are Fast Track designation, breakthrough therapy designation and priority review designation.

Specifically, the FDA may designate a product for Fast Track review if it is intended, whether alone or in combination with one or more other products, for the treatment of a serious or life-threatening disease or condition, and it demonstrates the potential to address unmet medical needs for such a disease or condition. For Fast Track products, sponsors may have greater interactions with the FDA and the FDA may initiate review of sections of a Fast Track product's application before the application is complete. This rolling review may be available if the FDA determines, after preliminary evaluation of clinical data submitted by the sponsor, that a Fast Track product may be effective. The sponsor must also provide, and the FDA must approve, a schedule for the submission of the remaining information and the sponsor must pay applicable user fees. However, the FDA's time period goal for reviewing a Fast Track application does not begin until the last section of the application is submitted. In addition, the Fast Track designation may be withdrawn by the FDA if the FDA believes that the designation is no longer supported by data emerging in the clinical trial process.

Additionally, in 2012, Congress enacted the Food and Drug Administration Safety and Innovation Act, or FDASIA. This law established a new regulatory scheme allowing for expedited review of products designated as "breakthrough therapies." A product may be designated as a breakthrough therapy if it is intended, either alone or in combination with one or more other products, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the product may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. The FDA may take certain actions with respect to breakthrough therapies, including holding meetings with the sponsor throughout the development process; providing timely advice to the product sponsor regarding development and approval; involving more senior staff in the review process; assigning a cross-disciplinary project lead for the review team; and taking other steps to design the clinical trials in an efficient manner.

Moreover, the FDA may designate a product for priority review if it is a product that treats a serious condition and, if approved, would provide a significant improvement in safety or effectiveness. The FDA determines, on a case-by-case basis, whether the proposed product represents a significant improvement when compared with other available therapies. Significant improvement may be illustrated by evidence of increased effectiveness in the treatment of a condition, elimination or substantial reduction of a treatment-limiting product reaction, documented enhancement of patient compliance that may lead to improvement in serious outcomes, and evidence of safety and effectiveness in a new subpopulation. A priority designation is intended to direct overall attention and resources to the evaluation of such applications, and to shorten the FDA's goal for taking action on a marketing application from ten months to six months.

Furthermore, the Secretary of Health and Human Services may authorize unapproved drugs and biologics to be marketed in the event an actual or potential emergency has been designated by the U.S. government. After an emergency has been designated, the FDA may issue an Emergency Use Authorization, or EUA, for the use of a specific product based on criteria established by the FDCA. An EUA is product specific and is subject to specific conditions and restrictions. Once the emergency underlying the EUA ends, then the EUA terminates.

Pediatric Rare Disease Designation and Priority Review Vouchers

Under the FDCA, as amended, the FDA incentivizes the development of drugs and biologics that meet the definition of a "rare pediatric disease," defined to mean a serious or life-threatening disease in which the serious of life-threatening manifestations primarily affect individuals aged from birth to 18 years and the disease affects fewer than 200,000 individuals in the United States or affects 200,000 or more in the United States and for which there is no reasonable expectation that the cost of developing and making in the United States a drug or biologic for such disease or condition will be received from sales in the United States of such drug or biologic. The sponsor of a product candidate for a rare pediatric disease may be eligible for a voucher that can be used to obtain a priority review for a subsequent human drug or biologic application after the date of approval of the rare pediatric disease drug product, referred to as a priority review voucher, or PRV. A sponsor may request rare pediatric disease designation from the FDA prior to the submission of its NDA or BLA. A rare pediatric disease designation does not guarantee that a sponsor will receive a PRV upon approval of its NDA or BLA. Moreover, a sponsor who chooses not to submit a rare pediatric disease designation request may nonetheless receive a PRV upon approval of their marketing application if they request such a voucher in their original. marketing application and meet all of the eligibility criteria. If a PRV is received, it may be sold or transferred an unlimited number of times. Congress did not extend the PRV program past its December 20, 2024 deadline for new applications. Previously granted rare pediatric disease designations for programs with the potential for PRVs may still receive PRVs upon approval through September 30, 2026.

Post-Approval Regulation

Once regulatory approval for marketing of a product or new indication for an existing product is obtained, the sponsor will be required to comply with post-approval regulatory requirements, including any post-approval requirements that the FDA may have imposed as a condition of approval. The sponsor will be required to report certain adverse reactions and production problems to the FDA, provide updated safety and efficacy information and comply with requirements concerning advertising and promotional labeling requirements. Manufacturers and certain of their subcontractors 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 ongoing regulatory requirements, including cGMP regulations, which impose certain procedural and documentation requirements upon drug manufacturers. Accordingly, the sponsor and its third-party manufacturers must continue to expend time, money and effort in the areas of production and quality control to maintain compliance with cGMP regulations and other regulatory requirements.

A product may also be subject to official lot release, meaning that 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, the manufacturer must submit samples of each lot, 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, to the FDA. The FDA may in addition perform certain confirmatory tests on lots of some products before releasing the lots for distribution. Finally, the FDA will conduct laboratory research related to the safety, purity, potency, and effectiveness of pharmaceutical products.

After an approval is granted, the FDA may withdraw the approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical trials to assess new safety risks; or imposition of distribution or other restrictions under a REMS program. Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of the product, complete withdrawal of the product from the market or product recalls;
- fines, warning letters or holds on post-approval clinical trials;
- refusal of the FDA to approve pending BLAs or supplements to approved BLAs, or suspension or revocation of product license approvals;
- product seizure or detention, or refusal to permit the import or export of products; or
- injunctions or the imposition of civil or criminal penalties.

The FDA strictly regulates marketing, labeling, advertising and promotion of products that are placed on the market. Drugs and biologics may be promoted only for the approved indications and in accordance with the provisions of the approved label. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant liability.

Orphan Drug Designation

Under the Orphan Drug Act, the FDA may grant orphan designation to a drug intended to treat a rare disease or condition affecting fewer than 200,000 individuals in the United States, or in other limited cases. Orphan drug designation (ODD) provides for seven years of market exclusivity, independent of patent protection, to the company with ODD that brings a particular product to market. In addition, companies developing orphan drugs are eligible for certain incentives, including tax credits for qualified clinical testing. In addition, a BLA for a product that has received orphan drug designation is not subject to a prescription drug user fee unless the application includes an indication other than the rare disease or condition for which the drug was designated.

To gain exclusivity, if a product that has orphan drug designation subsequently receives the first FDA approval for the disease or condition for which it has such designation, the product is entitled to the orphan drug exclusivity, which means that the FDA may not approve any other applications to market the same active moiety for the same indication for seven years, except in limited circumstances, such as another drug's showing of clinical superiority over the drug with orphan exclusivity. In addition, doctors may prescribe products for off-label uses and undermine our exclusivity. Orphan drug exclusivity could block the approval of one of our product candidates for seven years if a competitor obtains approval for the same active moiety for the same indication before we do, unless we are able to demonstrate that our product is clinically superior.

A sponsor may request orphan drug designation of a previously unapproved product or new orphan indication for an already marketed product. In addition, a sponsor of a product that is otherwise the same product as an already approved orphan drug may seek and obtain orphan drug designation for the subsequent product for the same rare disease or condition if it can present a plausible hypothesis that its product may be clinically superior to the first, approved product. More than one sponsor may receive orphan drug designation for the same product for the same rare disease or condition, but each sponsor seeking orphan drug designation must file a complete request for designation, and only the first sponsor that obtains approval for that drug for the orphan indication will obtain market exclusivity, effectively preventing the FDA from approving products under development by competitors for the same drug and same indication, unless the competitor is able to demonstrate that the product under development is clinically superior to the approved product or the approved product is not available in sufficient quantities. To permit the FDA to end another manufacturer's orphan exclusivity period, the FDA must determine that the manufacturer has demonstrated clinical superiority by showing the later drug is safer, more effective, or otherwise makes a major contribution to patient care.

The period of exclusivity begins on the date that the marketing application is approved by the FDA and applies only to the indication for which the product has been designated. The FDA may approve a second application for the same product for a different use or a subsequent application for a different drug for the same indication. Orphan drug designation neither shortens the development time or regulatory review time of a drug nor gives the drug any advantage in the regulatory review or approval process.

We may plan to pursue orphan drug designation and exclusivity for some of our product candidates in the United States, European Union, and other geographies of interest for specific products. We cannot guarantee that we will obtain orphan drug designation for any products in any jurisdiction. Even if we are able to obtain orphan drug designation for a product, we cannot be sure that such product will be approved, that we will be able to obtain orphan drug exclusivity upon approval, if ever, or that we will be able to maintain any exclusivity that is granted.

Biosimilars and Exclusivity

The Patient Protection and Affordable Care Act, or ACA, which was signed into law on March 23, 2010, included a subtitle called the Biologics Price Competition and Innovation Act of 2009, or BPCIA. The BPCIA established a regulatory scheme authorizing the FDA to approve biosimilars and interchangeable biosimilars. The FDA has issued several draft guidance documents outlining an approach to review and approval of biosimilars. Complexities associated with the larger, and often more complex, structures of biological products, as well as the processes by which such products are manufactured, pose significant hurdles to implementation, which are still being worked out by the FDA.

Under the BPCIA, a manufacturer may submit an application for licensure of a biologic product that is "biosimilar to" or "interchangeable with" a previously approved biological product or "reference product." In order for the FDA to approve a biosimilar product, it must find that there are no clinically meaningful differences between the reference product and proposed biosimilar product in terms of safety, purity, and potency. For the FDA to approve a biosimilar product as interchangeable with a reference product, the agency must find that the biosimilar product can be expected to produce the same clinical results as the reference product, and (for products administered multiple times) that 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.

Under the BPCIA, an application for a biosimilar product may not be submitted to the FDA until 4 years following the date of approval of the reference product. The FDA may not approve a biosimilar product until 12 years from the date on which the reference product was approved. Even if a product is considered to be a reference product eligible for exclusivity, another company could market a competing version of that product if the FDA approves a full BLA for such product containing the sponsor's own preclinical data and data from adequate and well-controlled clinical trials to demonstrate the safety, purity and potency of their product. The BPCIA also created certain exclusivity periods for biosimilars approved as interchangeable products.

Regulation Outside the United States

In order to market any product outside of the United States, a company must also comply with numerous and varying regulatory requirements of other countries and jurisdictions regarding quality, safety and efficacy that govern, among other things, clinical trials, marketing authorization, commercial sales and distribution of drug products. Whether or not it obtains FDA approval for a product, the company would 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. The approval process ultimately varies between countries and jurisdictions and can involve additional product testing and additional administrative review periods. The time required to obtain approval in other countries and jurisdictions might differ from and be longer than that required to obtain FDA approval. Regulatory approval in one country or jurisdiction does not ensure regulatory approval in another, but a failure or delay in obtaining regulatory approval in one country or jurisdiction may negatively impact the regulatory process in others.

Regulation and Marketing Authorization in the European Union

The European Medicines Agency, or EMA, is the scientific agency of the European Union, or EU, that coordinates the evaluation and monitoring of new and approved medicinal products such as drugs and biologics. It is responsible for the scientific evaluation of applications for EU marketing authorizations, as well as the development of technical guidance and the provision of scientific advice to sponsors.

The process regarding approval of medicinal products in the EU follows roughly the same lines as in the United States and likewise generally involves satisfactorily completing each of the following:

- preclinical laboratory tests, animal studies and formulation studies all performed in accordance with the applicable EU Good Laboratory Practice regulations;
- submission to the relevant regulatory agencies in EU member states, or national authorities, of a clinical trial application, or CTA, for each clinical trial, which must be approved before human clinical trials may begin;
- performance of adequate and well-controlled clinical trials to establish the safety and efficacy of the product for each proposed indication;
- submission to the relevant national authorities of a Marketing Authorisation Application, or MAA, which includes the data supporting safety and efficacy as well as detailed information on the manufacture and composition of the product in clinical development and proposed labeling;
- satisfactory completion of an inspection by the relevant national authorities of the manufacturing facility or facilities, including those of third parties, at which the product is produced to assess compliance with cGMP;
- potential audits of the non-clinical and clinical trial sites that generated the data in support of the MAA; and
- review and approval by the relevant national authority of the MAA before any commercial marketing, sale or shipment of the product.

Preclinical Studies

Preclinical tests include laboratory evaluations of product chemistry, formulation and stability, as well as studies to evaluate the potential efficacy and toxicity in animals. The conduct of the preclinical tests and formulation of the compounds for testing must comply with the relevant EU regulations and requirements. The results of the preclinical tests, together with relevant manufacturing information and analytical data, are submitted as part of the CTA when seeking approval to start a clinical trial, and with the MAA when seeking marketing authorization.

Clinical Trial Approval

Requirements for the conduct of clinical trials in the EU including cGCP, are implemented in the currently Clinical Trials Directive 2001/20/EC and the GCP Directive 2005/28/EC. Pursuant to Directive 2001/20/EC and Directive 2005/28/EC, as amended, a system for the approval of clinical trials in the EU has been implemented through national legislation of the EU member states. Under this system, approval must be obtained from the competent national authority in which a trial is planned

to be conducted, or in multiple member states if the clinical trial is to be conducted in a number of member states. To this end, a CTA is submitted, which must be supported by an investigational medicinal product dossier, or IMPD, and further supporting information prescribed by Directive 2001/20/EC and Directive 2005/28/EC and other applicable guidance documents. Furthermore, a clinical trial may only be started after a competent ethics committee has issued a favorable opinion on the clinical trial application in that country.

On January 31, 2022, the Clinical Trials Regulation (EU) No. 536/2014 replaced the current Clinical Trials Directive 2001/20/EC. To ensure that the rules for clinical trials are identical throughout the EU, the Clinical Trials Regulation (EU) No. 536/2014 was passed as a regulation which is directly applicable in all EU member states. The Clinical Trials Directive 2001/20/EC will, however, still apply three years from the date of entry into application of the Clinical Trials Regulation to (i) clinical trials applications submitted before the entry into application and (ii) clinical trials applications submitted within one year after the entry into application if the sponsor opts for the old system.

Regulation (EU) No 536/2014 aims to simplify and streamline the approval of clinical trial in the EU. The main characteristics of the regulation include:

- A streamlined application procedure via a single entry point, known as the Clinical Trials Information System;
- A single set of documents to be prepared and submitted for the application as well as simplified reporting procedures which will spare sponsors from submitting broadly identical information separately to various and different national authorities;
- A harmonized procedure for the assessment of applications for clinical trials, which is divided in two parts;
- Strictly defined deadlines for the assessment of clinical trial application; and
- The involvement of the ethics committees in the assessment procedure in accordance with the national law of the member state concerned but within the overall timelines defined by the Regulation (EU) No 536/2014.

Marketing Authorization

Authorization to market a product in the member states of the EU proceeds under one of four procedures: a centralized procedure, a mutual recognition procedure, a decentralized procedure or a national procedure.

Centralized Procedure

The centralized procedure enables applicants to obtain a marketing authorization that is valid in all EU member states based on a single application. Certain medicinal products, including products developed by means of biotechnological processes must undergo the centralized authorization procedure for marketing authorization, which, if granted by the European Commission, based on the opinion of the EMA, is automatically valid in all EU member states. Sponsors may elect to file an MAA through the centralized procedures for other classes of products.

The centralized procedure is mandatory for certain types of products such as, medicines derived from biotechnology processes such as genetic engineering, advanced-therapy medicines such as gene-therapy or tissue engineered medicine, orphan medicines, and medicinal products containing a new active substance indicated for the treatment of HIV, AIDS, cancer, diabetes, neurodegenerative disorders, autoimmune and other immune dysfunctions, and viral diseases.

The centralized authorization procedure is optional for other medicinal products if they contain a new active substance, if the applicant shows that the medicinal product concerned constitutes a significant therapeutic, scientific or technical innovation, or that the granting of authorization is in the public interest of the EU.

Administration Procedure

Under the centralized procedure, the EMA's Committee for Human Medicinal Products, or CHMP serves as the scientific committee that renders opinions about the safety, efficacy and quality of medicinal products for human use on behalf of the EMA. The CHMP is composed of experts nominated by each member state's national authority for medicinal products, with one of them appointed to act as Rapporteur for the co-ordination of the evaluation with the possible assistance of a further member of the Committee acting as a Co-Rapporteur. After approval, the Rapporteur(s) continue to monitor the product throughout its life cycle. The CHMP has 210 active days to adopt an opinion as to whether a marketing authorization should be granted. The process usually takes longer in case additional information is requested, which triggers clock-stops in the procedural timelines. The process is complex and involves extensive consultation with the regulatory authorities of member states and a number of experts. When an application is submitted for a marketing authorization in respect of a drug which is of

major interest from the point of view of public health and in particular from the viewpoint of therapeutic innovation, the applicant may, pursuant to Article 14(9) Regulation (EC) No 726/2004, request an accelerated assessment procedure. If the CHMP accepts such request, the time-limit of 210 days will be reduced to 150 days, but it is possible that the CHMP can revert to the standard time-limit for the centralized procedure if it considers that it is no longer appropriate to conduct an accelerated assessment. Once the procedure is completed, a European Public Assessment Report, or EPAR, is produced. If the opinion is negative, information is given as to the grounds on which this conclusion was reached. After the adoption of the CHMP opinion, a decision on the MAA must be adopted by the European Commission, after consulting the EU member states, which in total can take more than 60 days. After a drug has been authorized and launched, it is a condition of maintaining the marketing authorization that all aspects relating to its quality, safety and efficacy must be kept under review.

Conditional Approval

In specific circumstances, EU legislation (Article 14(7) Regulation (EC) No. 726/2004 and Regulation (EC) No. 507/2006 on Conditional Marketing Authorizations for Medicinal Products for Human Use) enables applicants to obtain a conditional marketing authorization prior to obtaining the comprehensive clinical data required for an application for a full marketing authorization. Such conditional approvals may be granted for products (including medicines designated as orphan medicinal products), if (1) the risk-benefit balance of the product is positive, (2) it is likely that the applicant will be in a position to provide the required comprehensive clinical trial data, (3) the product fulfills unmet medical needs, and (4) 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 are still required. A conditional marketing authorization may contain specific obligations to be fulfilled by the marketing authorization holder, including obligations with respect to the completion of ongoing or new studies, and with respect to the collection of pharmacovigilance data. Conditional marketing authorizations are valid for one year, and may be renewed annually, if the risk-benefit balance remains positive, and after an assessment of the need for additional or modified conditions and/or specific obligations. The timelines for the centralized procedure described above also apply with respect to the review by the CHMP of applications for a conditional marketing authorization.

Marketing Authorization Under Exceptional Circumstances

As per Article 14(8) Regulation (EC) No 726/2004, products for which the applicant can demonstrate that comprehensive data (in line with the requirements laid down in Annex I of Directive 2001/83/EC, as amended) cannot be provided (due to specific reasons foreseen in the legislation) might be eligible for marketing authorization under exceptional circumstances. This type of authorization is reviewed annually to reassess the risk-benefit balance. The fulfillment of any specific procedures/obligations imposed as part of the marketing authorization under exceptional circumstances is aimed at the provision of information on the safe and effective use of the product and will normally not lead to the completion of a full dossier/approval.

Pediatric Studies

Prior to obtaining a marketing authorization in the EU, applicants have to demonstrate compliance with all measures included in an EMA-approved Pediatric Investigation Plan, or PIP, covering all subsets of the pediatric population, unless the EMA has granted (1) a product-specific waiver, (2) a class waiver, or (3) 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, the so-called 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, or PDCO, may grant deferrals for some medicines, allowing a company to delay development of the medicine in 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 in children is not needed or is not appropriate, such as for diseases that only affect the elderly population.

Before a marketing authorization application can be filed, or an existing marketing authorization can be amended, the EMA determines that companies actually comply with the agreed studies and measures listed in each relevant PIP.

Period of Authorization and Renewals

A marketing authorization will be valid for five years in principle, and 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 a national authority. 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 nine months before the marketing authorization ceases to be valid. Once renewed, the marketing authorization will be valid for an unlimited period, unless the European Commission or the national authority decides on justified grounds relating to pharmacovigilance, to proceed with one additional five-year renewal. Any authorization that is not followed by the actual placing of the drug on the EU market (in case of centralized procedure) or on the market of the authorizing member state within three years after authorization will cease to be valid, the so-called "sunset clause."

Orphan Drug Designation and Exclusivity

The European Commission can grant orphan medicinal product designation to products for which the sponsor can establish that it is intended for the diagnosis, prevention, or treatment of (1) a life-threatening or chronically debilitating condition affecting not more than five in 10,000 people in the EU, or (2) a life threatening, seriously debilitating or serious and chronic condition in the EU and that without incentives it is unlikely that sales of the drug in the EU would generate a sufficient return to justify the necessary investment. In addition, the sponsor must establish that there is no other satisfactory method approved in the EU of diagnosing, preventing or treating the condition, or if such a method exists, the proposed orphan drug will be of significant benefit to patients.

Orphan drug designation provides a number of benefits, including fee reductions, regulatory assistance, and the possibility to apply for a centralized EU marketing authorization (see "—Government Regulation and Product Approval—Regulation Outside the United States—Centralized Authorization Procedure"), as well as 10 years of market exclusivity following a marketing authorization. During this market exclusivity period, neither the EMA, nor the European Commission nor the Member States can accept an application or grant a marketing authorization for 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. The market exclusivity period for the authorized therapeutic indication may be reduced to six years if, at the end of the fifth year, it is established that the orphan drug designation criteria are no longer met, including where it is shown that the product is sufficiently profitable not to justify maintenance of market exclusivity. In addition, a competing similar medicinal product may be authorized prior to the expiration of the market exclusivity period, including if it is shown to be safer, more effective or otherwise clinically superior to the already approved orphan drug or if the holder of the marketing authorization for the already approved orphan drug is unable to supply sufficient quantities of the product.

If the MAA of a medicinal product designated as an orphan drug includes the results of all studies conducted in compliance with an agreed PIP, and a corresponding statement is subsequently included in the marketing authorization granted, the ten-year period of market exclusivity will be extended to twelve years.

Regulatory Data Protection

EU legislation also provides for a system of regulatory data and market exclusivity. Upon receiving marketing authorization, new chemical entities approved on the basis of complete independent data package benefit from eight years of data exclusivity and an additional two years of market exclusivity. Data exclusivity prevents regulatory authorities in the EU from referencing the innovator's data to assess a generic or biosimilar (abbreviated) application. During the additional two-year period of market exclusivity, a generic or biosimilar marketing authorization can be submitted, and the innovator's data may be referenced, but no generic or biosimilar medicinal product can be marketed until the expiration of the market exclusivity. The overall ten-year period will be extended to a maximum of eleven years if, during the first eight years of those 10 years, the marketing authorization holder, or MAH, 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 a compound is considered to be a new chemical entity and the innovator is able to gain the period of data exclusivity, another company nevertheless could also market another version of the drug if such company obtained marketing authorization based on an MAA with a complete independent data package of pharmaceutical test, preclinical tests and clinical trials. However, products designated as orphan medicinal products enjoy, upon receiving marketing authorization, a period of 10 years of orphan market exclusivity (see also "Item 4.B—Government Regulation and Product Approval—Regulation and Marketing Authorization in the European Union—Orphan Drug Designation and Exclusivity"). Depending upon the timing and duration of the EU marketing authorization process, products may be eligible for up to five years' supplementary protection certificates, or SPCs. Such SPCs extend the rights under the basic patent for the drug.

Regulatory Requirements After a Marketing Authorization Has Been Obtained

If we obtain authorization for a medicinal product in the EU, we will be required to comply with a range of requirements applicable to the manufacturing, marketing, promotion and sale of medicinal products:

Pharmacovigilance

We will, for example, have to comply with the EU's stringent pharmacovigilance or safety reporting rules, pursuant to which post-authorization studies and additional monitoring obligations can be imposed.

Other requirements relate to, for example, the manufacturing of products and APIs in accordance with good manufacturing practice standards. EU regulators may conduct inspections to verify our compliance with applicable requirements, and we will have to continue to expend time, money and effort to remain compliant. Non-compliance with EU requirements regarding safety monitoring or pharmacovigilance, and with requirements related to the development of products for the pediatric population, can also result in significant financial penalties in the EU. Similarly, failure to comply with the EU's requirements regarding the protection of individual personal data can also lead to significant penalties and sanctions. Individual EU member states may also impose various sanctions and penalties in case we do not comply with locally applicable requirements.

Manufacturing

The manufacturing of authorized drugs, for which a separate manufacturer's license is mandatory, must be conducted in compliance with the EMA's cGMP requirements and comparable requirements of other national authorities, which mandate the methods, facilities and controls used in manufacturing, processing and packing of drugs to assure their safety and identity. The EMA enforces its cGMP requirements through mandatory registration of facilities and inspections of those facilities. The EMA may have a coordinating role for these inspections while the responsibility for carrying them out rests with the member states competent authority under whose responsibility the manufacturer falls. Failure to comply with these requirements could interrupt supply and result in delays, unanticipated costs and lost revenues, and could subject the applicant to potential legal or regulatory action, including but not limited to warning letters, suspension of manufacturing, seizure of product, injunctive action or possible civil and criminal penalties.

Marketing and Promotion

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 EU. The applicable regulations aim to ensure that information provided by holders of marketing authorizations regarding their products is truthful, balanced and accurately reflects the safety and efficacy claims authorized by the EMA or by the national authority of the authorizing member state. Failure to comply with these requirements can result in adverse publicity, warning letters, corrective advertising and potential civil and criminal penalties.

Other U.S. Healthcare Laws and Compliance Requirements

For products distributed in the United States, we will also be subject to additional healthcare regulation and enforcement by the federal government and the states in which we conduct our business. Applicable federal and state healthcare laws and regulations include the following:

- The federal healthcare anti-kickback statute prohibits, among other things, persons from knowingly and willfully soliciting, offering, 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 under federal healthcare programs such as Medicare, Medicaid, or other governmental programs. A person or entity does not need to have actual knowledge of the federal anti-kickback statute or specific intent to violate it to have committed a violation; in addition, items or services resulting from a violation of the federal anti-kickback statute may constitute a false or fraudulent claim for purposes of the False Claims Act;

- The Ethics in Patient Referrals Act, commonly referred to as the Stark Law, and its corresponding regulations, prohibit physicians from referring patients for designated health services (including outpatient drugs) reimbursed under the Medicare or Medicaid programs to entities with which the physicians or their immediate family members have a financial relationship or an ownership interest, subject to narrow regulatory exceptions, and prohibits those entities from submitting claims to Medicare or Medicaid for payment of items or services provided to a referred beneficiary;

- The federal False Claims Act imposes criminal and civil penalties, including civil whistleblower or qui tam actions, against individuals or entities for knowingly presenting, or causing to be presented, to the federal government claims for payment that are false or fraudulent or making a false statement to avoid, decrease, or conceal an obligation to pay money to the federal government;

- Health Insurance Portability and Accountability Act of 1996, imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program and also imposes obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information. This statute also 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 healthcare benefits, items, or services;

- The federal false statements statute 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 Physician Payments Sunshine Act, created under the ACA, and its implementing regulations, which requires specified manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program, with specific exceptions, to report annually to the Centers for Medicare & Medicaid Services, or CMS, information related to payments or other "transfers of value" made to physicians. All such reported information is publicly available; and

- Analogous state laws and regulations, such as state anti-kickback and false claims laws, may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers, and 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.

Because of the breadth of these laws and the narrowness of the statutory exceptions and safe harbors available, it is possible that some of our future business activities could be subject to challenge under one or more of such laws. Efforts to ensure that our business arrangements with third parties will comply with applicable laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other health care laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, exclusion from government funded healthcare programs, such as Medicare and Medicaid, and the curtailment or restructuring of our operations. If any of the physicians or other providers or entities with whom we expect to do business are found to be not in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded health care programs.

Reimbursement

Sales of our product candidates in the United States may depend, in part, on the extent to which the costs of the product candidates may be covered by third-party payers, such as government health programs, commercial insurance and managed health care organizations. These third-party payers are increasingly challenging the prices charged for medical products and services. Additionally, the containment of health care costs has become a priority of federal and state governments, and the prices of drugs have been a focus in this effort. The United States government, state legislatures and foreign governments have shown significant interest in implementing cost-containment programs, including price controls, restrictions on reimbursement and requirements for substitution of generic 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 our net revenue and results. If these third-party payers do not consider our product candidates to be cost-effective compared to other available therapies, they may not cover our product candidates after approval as a benefit under their plans or, if they do, the level of payment may not be sufficient to allow us to sell our product candidates on a profitable basis.

In order to secure coverage and reimbursement for any product that might be approved for sale, we 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, EMA or other comparable regulatory approvals. Our product candidates may not be considered medically necessary or cost-effective. A payer's decision to provide coverage for a drug product does not imply that an adequate reimbursement rate will be approved. Third-party reimbursement may not be sufficient to enable us to maintain price levels high enough to realize an appropriate return on our investment in product development.

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. The conduct of such studies could be expensive and result in delays in our commercializing efforts. The EU provides options for its 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. EU member states may approve a specific price for a drug product or may instead adopt a system of direct or indirect controls on the profitability of the company placing the drug product on the market. Other member states allow companies to fix their own prices for drug products but monitor and control company profits. The downward pressure on health care costs in general, particularly prescription drugs, has become very intense. As a result, increasingly high barriers are being erected to the entry of new products. In addition, in some countries, cross-border imports from low-priced markets exert competitive pressure that may reduce pricing within a country. There can be no assurance that any country that has price controls or reimbursement limitations for drug products will allow favorable reimbursement and pricing arrangements for any of our products.

The marketability of any products for which we receive regulatory approval for commercial sale may suffer if the government and third-party payors fail to provide adequate coverage and reimbursement. In addition, emphasis on managed care in the United States has increased and we expect will continue to increase the pressure on drug pricing. Coverage policies, third-party reimbursement rates and drug pricing regulation may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which we receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

Healthcare Reform

In the United States, there have been and continue to be a number of significant legislative initiatives to contain healthcare costs. The Affordable Care Act, or ACA, was enacted in the United States in March 2010 and contains provisions that may reduce the profitability of drug products, including, for example, increased rebates for drugs subject to the Medicaid Drug Rebate Program, extension of Medicaid rebates to Medicaid managed care plans, mandatory discounts for certain Medicare Part D beneficiaries and annual fees based on pharmaceutical companies' share of sales to federal health care programs.

In addition, other legislative changes have been proposed and adopted since the ACA was enacted. These changes included aggregate reductions to Medicare payments to providers of 2% per fiscal year, effective April 1, 2013 and, due to subsequent legislative amendments to the statute, will stay in effect through 2027, unless additional Congressional action is taken; however, pursuant to the CARES Act, and subsequent legislation, these reductions are suspended from May 1, 2020 through March 31, 2022 due to the COVID-19 pandemic. In January 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, among other things, reduced Medicare payments to several providers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These new laws may result in additional reductions in Medicare and other healthcare funding, which could have a material adverse effect on customers for our drugs, if approved, and, accordingly, our financial operations.

Moreover, recently there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their commercial products. 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 cost of drugs under Medicare, and reform government program reimbursement methodologies for drugs. The FDA released a final rule on September 24, 2020, effective November 30, 2020, providing guidance for states to build and submit importation plans for drugs from Canada. Further, on November 20, 2020, the U.S. Department of Health and Human Services, or HHS, finalized a regulation removing safe harbor protection for price reductions from pharmaceutical manufacturers to plan sponsors under Part D, either directly or through pharmacy benefit managers, unless the price reduction is required by law. The rule also creates a new safe harbor for price reductions reflected at the point-of-sale, as well as a safe harbor for certain fixed fee arrangements between pharmacy benefit managers and manufacturers. At the state level, legislatures have increasingly passed legislation and implemented 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.

Most recently, on August 16, 2022, the Inflation Reduction Act of 2022, or the IRA, was signed into law. Among other things, the IRA directs the Department of Health and Human Services, or the HHS to negotiate the price of certain high-expenditure, single-source drugs and biologics covered under Medicare. The negotiated prices, which will first become effective in 2026, will be capped at a statutory ceiling price representing a significant discount from average prices to wholesalers and direct purchasers. The law will also, beginning in 2023, penalize drug manufacturers that increase prices of Medicare Part B and Part D drugs at a rate greater than the rate of inflation. Further, the IRA eliminates the "donut hole" under the Medicare Part D program beginning in 2025 by significantly lowering the beneficiary maximum out-of-pocket cost and creating a new manufacturer discount program. The IRA permits the Secretary of the HHS, to implement many of these provisions through guidance, as opposed to regulation, for the initial years. HHS has and will continue to issue and update guidance as these programs are implemented, although the IRA may be subject to legal challenges. It is currently unclear how the IRA will be implemented but is likely to have a significant impact on the pharmaceutical industry In addition, in response to the Biden administration's October 2022 executive order, on February 14, 2023, HHS released a report outlining three new models for testing by the Center for Medicare and Medicaid Innovation which will be evaluated on their ability to lower the cost of drugs, promote accessibility, and improve quality of care. It is unclear whether the models will be utilized in any health reform measures in the future.

Although a number of these, and other proposed measures may require authorization through additional legislation to become effective, Congress has indicated that it will continue to seek new legislative measures to control drug costs.

CMS issued a final rule, effective on July 9, 2019, that requires direct-to-consumer advertisements of prescription drugs and biological products, for which payment is available through or under Medicare or Medicaid, to include in the advertisement the Wholesale Acquisition Cost, or list price, of that drug or biological product if it is equal to or greater than $35 for a monthly supply or usual course of treatment. Prescription drugs and biological products that are in violation of these requirements will be included on a public list.

Any adopted health reform measure could reduce the ultimate demand for our products, if approved, or put pressure on our product pricing. Individual states in the United States have also become increasingly active in passing legislation and implementing regulations designed to control pharmaceutical 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 healthcare 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 healthcare programs. We expect that additional state and federal healthcare reform measures will be adopted in the future.

We expect that additional state and federal healthcare reform measures, as well as legal changes by foreign governments, will be adopted in the future, any of which could limit the amounts that governments will pay for healthcare products and services, which could result in reduced demand for our product candidates or additional pricing pressures.

Employees

As of the date of this report, we have 12 employees and full-time consultants, including our executive officers, providing management and financial services, and general administrative responsibilities. We believe that we maintain a satisfactory working relationship with our employees, and we have not experienced any significant labor disputes or any difficulty in recruiting staff for our operations. None of our employees are represented by a labor union.

Human Capital Resources

Our human capital resources objectives include, as applicable, identifying, recruiting, retaining, incentivizing and integrating our existing and new employees, advisors and consultants. The principal purposes of our equity and cash incentive plans are to attract, retain and reward personnel through the granting of stock-based and cash-based compensation awards, in order to increase stockholder value and the success of our company by motivating such individuals to perform to the best of their abilities and achieve our objectives.

Available Information

Our website is located at www.azitrainc.com. The information on or accessible through our website is not part of this annual report on Form 10-K. A copy of this annual report on Form 10-K is located at the SEC's Public Reference Room at 100 F Street, NE, Washington, D.C. 20549. Information on the operation of the Public Reference Room can be obtained by calling the SEC at 1-800-SEC-0330. The SEC also maintains an internet site that contains reports and other information regarding our filings at www.sec.gov.

Item 1A. Risk Factors

Investing in our common stock involves a high degree of risk. Before purchasing our common stock, you should read and consider carefully the following risk factors as well as all other information contained in this report, including our financial statements and the related notes. Each of these risk factors, either alone or taken together, could adversely affect our business, operating results and financial condition, as well as adversely affect the value of an investment in our common stock. There may be additional risks that we do not presently know of or that we currently believe are immaterial, which could also impair our business and financial position. If any of the events described below were to occur, our financial condition, our ability to access capital resources, our results of operations and/or our future growth prospects could be materially and adversely affected and the market price of our common stock could decline. As a result, you could lose some or all of any investment you may make in our common stock.

Risks Relating to Our Business

We are an early-stage clinical biopharmaceutical company with limited operating history.

We are an early-stage clinical biopharmaceutical company incorporated on January 2, 2014, and have limited operating history. We have not commenced revenue-producing operations apart from limited grant and service revenue. To date, our operations have consisted of the development of our proprietary microbial library, the identification, characterization, genetic engineering and testing of certain bacterial species to provide therapeutic effect and the development of our initial product candidates. Our limited operating history makes it difficult for potential investors to evaluate our technology or prospective operations. As an early-stage clinical biopharmaceutical company, we are subject to all the risks inherent in the organization, financing, expenditures, complications and delays involved with a new business. Accordingly, you should consider our prospects in light of the costs, uncertainties, delays and difficulties frequently encountered by companies in the early stages of development, especially early-stage clinical-stage biopharmaceutical companies such as ours. Potential investors should carefully consider the risks and uncertainties that a company with a limited operating history will face. In particular, potential investors should consider that we may be unable to:

- successfully implement or execute our business plan, or that our business plan is sound;
- successfully complete preclinical and clinical trials and obtain regulatory approval for the marketing of our product candidates;
- successfully demonstrate a favorable differentiation between our precision dermatological product candidates and the current products on the market;
- successfully contract for the manufacture of our clinical drug products and establish a commercial drug supply;
- secure market exclusivity or adequate intellectual property protection for our product candidates;
- attract and retain an experienced management and advisory team; and
- raise sufficient funds in the capital markets to effectuate our business plan, including product and clinical development, regulatory approval and commercialization for our product candidates.

Investors should evaluate an investment in us in light of the uncertainties encountered by developing companies in a competitive environment. There can be no assurance that our efforts will be successful or that we will ultimately be able to attain profitability. If we cannot successfully execute any one of the foregoing, our business may not succeed and your investment will be adversely affected. You must be prepared to lose all of your investment.

We have a history of significant operating losses and anticipate continued operating losses for the foreseeable future.

For the fiscal years ended December 31, 2024 and 2023, we incurred a net loss of $9.0 million and $11.3, respectively. As of December 31, 2024, we had an accumulated deficit of $57.6 million. We expect to continue to incur substantial expenses without any meaningful revenues unless and until we are able to obtain regulatory approval and successfully commercialize at least one of our product candidates. We also believe that, at a minimum, it will take us four to six years from the date of this report for us to obtain regulatory approval of our first drug candidates, assuming we are able to get regulatory approval at all. Even if we are able to commercialize our product candidates, there can be no assurance that we will generate significant revenues or ever achieve profitability.

We expect to have significant research, regulatory and development expenses as we advance our product candidates towards commercialization. As a result, we expect to incur substantial losses for the foreseeable future, and these losses will be increasing. We are uncertain when or if we will be able to achieve or sustain profitability. If we achieve profitability in the future, we may not be able to sustain profitability in subsequent periods. Failure to become and remain profitable may impair our ability to sustain operations and adversely affect our business and our ability to raise capital. If we are unable to generate positive cash flow within a reasonable period of time, we will be unable to further pursue our business plan or continue operations, in which case you may lose your entire investment.

The report of our independent registered public accounting firm for the year ended December 31, 2024 states that due to our accumulated deficit, recurring and negative cash flow from operations there is substantial doubt about our ability to continue as a going concern.

We expect we will need additional financing to execute our business plan and fund operations, which additional financing may not be available on reasonable terms or at all.

As of December 31, 2024, we had total assets of $7.4 million and working capital of $3.9 million. In January, 2025, we completed a public offering of 4,857,780 shares of our common stock, at an offering price of $0.30 per share, in which we received net proceeds of approximately $1.3 million, after deducting underwriter discounts and offering expenses, and February 2025 we completed a registered direct offering of 2,495,518 shares of our common stock, at an offering price of $0.2785 per share, in which we received net proceeds of approximately $695 thousand, after deducting placement agent commissions and offering expenses. After giving effect to both offerings, we believe that our cash on hand as of the date of this report will not be sufficient to cover our proposed plan of operations beyond six months from the date of this report. We intend to seek additional funds through various financing sources, including the sale of our equity, licensing fees for our technology and joint ventures with industry partners. In addition, we will consider alternatives to our current business plan that may enable us to achieve revenue producing operations and meaningful commercial success with a smaller amount of capital. However, there can be no guarantees that such funds will be available on commercially reasonable terms, if at all. If such financing is not available on satisfactory terms, we may be unable required to scale back our proposed plan of operations and we may be unable to continue operations, in which case you may lose your entire investment.

The clinical and commercial utility of our microbial library and genetic engineering platform is uncertain and may never be realized.

We have built a proprietary platform that includes a microbial library comprised of approximately 1,500 unique bacterial strains that can be screened for unique therapeutic characteristics. The platform is augmented by artificial intelligence, machine learning and genetic engineering technologies. To date, our focus is on the development of genetically engineered strains of *S. epidermidis,* which we consider to be an optimal therapeutic candidate species for engineering of dermatologic therapies. However, we believe that the genetic engineering of *S. epidermidis* is a novel and unproven mode of therapy. We recently initiated our Phase 1b clinical trial for ATR-12 and dosed our first patient in August 2024 and expect to dose the first patient in the Phase 1/2 trial of ATR-04 in the first half of 2025. However, success in early clinical trials does not ensure that large-scale clinical trials will be successful, nor does it predict final results. Even after the completion of our proposed Phase 1b clinical trials, our initial product candidates will have only been tested in a small number of patients. Results from these clinical trials may not necessarily be indicative of the safety and tolerability or efficacy of our product candidates or our as we expand into larger clinical trials. Until such time, if ever, as we are able to provide the FDA with substantial clinical evidence to support a claim of safety, efficacy, purity and potency sufficient to enable the FDA to approve our proprietary product candidates for any indication, our proprietary microbial library and genetic engineering platform will remain unproven.

Our product candidates are in early-stage clinical trials or early stages of preclinical development, and therefore they will require extensive additional preclinical and clinical testing. Success in preclinical studies or early-stage clinical trials may not be indicative of results in future clinical trials and we cannot assure you that any ongoing, planned or future clinical trials will lead to results sufficient for the necessary regulatory approvals.

Because our product candidates are in early stages clinical trials or of preclinical development, they will require extensive preclinical and clinical testing. We dosed the first patient in our Phase 1b clinical trial for ATR-12 in August 2024,and we expect to dose the first patient in our Phase 1/2 clinical trial for ATR-04 in the first half of 2025. However, we have not conducted meaningful preclinical studies for any of our other product candidates. Success in preclinical testing and early-stage clinical trials does not ensure that later clinical trials will generate the same results or otherwise provide adequate data to demonstrate the efficacy and safety of a product candidate. Preclinical studies and Phase 1b clinical trials are primarily designed to test safety, to study pharmacokinetics and pharmacodynamics and to understand the side effects of product candidates at

various doses and schedules. Phase 1b clinical trials also test how well a certain disease responds to a new treatment. Success in preclinical studies and earlier clinical trials does not ensure that later efficacy trials will be successful, nor does it predict final results. Our product candidates may fail to show the desired safety and efficacy in clinical development despite positive results in preclinical studies or even if they successfully advance through earlier clinical trials.

In addition, the design of a clinical trial can determine whether its results will support approval of a product, and flaws in the design of a clinical trial may not become apparent until the clinical trial is well advanced. As an organization, we have limited experience designing clinical trials and may be unable to design and execute a clinical trial to support regulatory approval. Many companies in the pharmaceutical and biotechnology industries have suffered significant setbacks, including failure in late-stage clinical trials even after achieving promising results in preclinical testing and earlier clinical trials. Data obtained from preclinical and clinical activities are subject to varying interpretations, which may delay, limit or prevent regulatory approval.

Further, we cannot predict with any certainty if or when we might submit a Biologics License Application, or BLA, for regulatory approval for any of our product candidates or whether any such BLA will be accepted for review by the FDA, or whether any BLA will be approved upon review. Even if our clinical trials are completed as planned, we cannot be certain that their results will support our proposed indications. Success in preclinical testing and early clinical trials does not ensure that later clinical trials will be successful, and we cannot be sure that the results of later clinical trials will replicate the results of prior clinical trials and preclinical testing. The clinical trial process may fail to demonstrate that our product candidates are safe and effective for their proposed uses. This failure could cause us to abandon a product candidate and may delay development of other product candidates. Any delay in, or termination of, our clinical trials will delay and possibly preclude the filing of any BLAs with the FDA and, ultimately, our ability to commercialize our product candidates and generate product revenues.

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

As our development and commercialization plans and strategies develop, we will need to expand the size of our employee and consultant/contractor base. Future growth would impose significant added responsibilities on members of management, including the need to identify, recruit, maintain, motivate and integrate additional employees. In addition, our management may have to divert a disproportionate amount of its attention away from our day-to-day activities and devote a substantial amount of time to managing these growth activities. Our future financial performance and our ability to commercialize our product candidates and any other future product candidates and our ability to compete effectively will depend, in part, on our ability to effectively manage our future growth.

If we are not successful in attracting and retaining highly qualified personnel, we may not be able to successfully implement our business strategy. In addition, the loss of the services of our senior management would adversely impact our business prospects.

Our management team has expertise in many different aspects of drug development and commercialization. However, our ability to compete in the highly competitive pharmaceuticals industry depends in large part upon our ability to attract and retain highly qualified managerial, scientific and medical personnel. We will need to hire additional personnel as we further develop our product candidates. Competition for skilled personnel in our market is intense and competition for experienced scientists may limit our ability to hire and retain highly qualified personnel on acceptable terms. Despite our efforts to retain valuable employees, members of our management, scientific and medical teams may terminate their employment with us on short notice. The loss of the services of any of our executive officers or other key employees, or our inability to hire targeted executives, could potentially harm our business, operating results or financial condition. In particular, we believe that the loss of the services of our chief executive officer would have a material adverse effect on our business.

Other biopharmaceutical companies with which we compete for qualified personnel have greater financial and other resources, different risk profiles, and a longer history in the industry than we do. They also may provide more diverse opportunities and better chances for career advancement. Some of these characteristics may be more appealing to high-quality candidates than what we have to offer. If we are unable to continue to attract and retain high-quality personnel, the rate and success at which we can develop and commercialize product candidates would be limited.

We currently have no sales and marketing organization. If we are unable to establish satisfactory sales and marketing capabilities or secure a third-party sales and marketing relationship, we may not be able to successfully commercialize any of our product candidates.

At present, we have no sales or marketing personnel. Upon and subject to initial receipt of the requisite regulatory approvals for one or more of our drug products, we plan to build focused capabilities in the United States to commercialize our development programs focused on live biotherapeutic products and recombinant proteins for the treatment of skin diseases, where we believe the patient populations and medical specialists for the indications we are targeting are sufficiently concentrated to allow us to effectively promote our products with a targeted sales team. In other markets for which commercialization may be less capital efficient for us, we may selectively pursue strategic collaborations with third parties in order to maximize the commercial potential of our product candidates. In some cases, we may pursue the licensing of our microbial library or patent rights or enter into a joint development arrangement. If we are not successful in recruiting sales and marketing personnel and building a sales and marketing infrastructure or entering into appropriate collaboration arrangements with third parties, we will have difficulty successfully commercializing our product candidates, which would adversely affect our business, operating results and financial condition.

Even if we enter into third-party marketing and distribution arrangements, we may have limited or no control over the sales, marketing and distribution activities of these third parties. Our future revenues may depend heavily on the success of the efforts of these third parties. In terms of establishing a sales and marketing infrastructure, we will have to compete with established and well-funded pharmaceutical and biotechnology companies to recruit, hire, train and retain sales and marketing personnel. Factors that may inhibit our efforts to build an internal sales organization or enter into collaboration arrangements with third parties include:

- our inability to recruit and retain adequate numbers of effective sales and marketing personnel;
- the inability of sales personnel to obtain access to or persuade adequate numbers of physicians to prescribe any of our product candidates;
- the lack of complementary products to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines; and
- unforeseen costs and expenses associated with creating an internal sales and marketing organization.

We will be completely dependent for the foreseeable future on third parties to manufacture our product candidates for commercial sale, and the commercialization of our product candidates could be halted, delayed or made less profitable if those third parties fail to obtain manufacturing approval from the FDA or comparable foreign regulatory authorities, fail to provide us with sufficient quantities of our product candidates or fail to do so at acceptable quality levels or prices.

We do not own or operate manufacturing facilities for the commercial production of our current product candidates. We currently rely on third-party contract manufacturers for all of our required raw materials, manufacturing devices, and active pharmaceutical ingredients for our preclinical research and clinical trials. Although we are able to manufacture finished product in our Groton, Connecticut facility for our clinical trials, we will rely on third parties for the manufacture of our finished product for commercial sale. We do not have long-term agreements with any of these third parties. We also do not have any current contractual relationship for commercial supplies. We intend to enter into agreements with third-party contract manufacturers and one or more backup manufacturers for future production. We are analyzing the feasibility of building manufacturing capabilities for future development and commercial quantities of any products that we develop. Such products will need to be manufactured in facilities, and by processes, that comply with the requirements of the FDA and the regulatory agencies of other jurisdictions in which we are seeking approval. In the meantime, we will be obligated to rely on contract manufacturers for our preclinical research and clinical trials and commercial production, if and when any of our product candidates are approved for commercialization.

The facilities used by us or any contract manufacturer to manufacture our raw materials, manufacturing devices, active pharmaceutical ingredients and finished products must be approved by the FDA or comparable foreign regulatory authorities. Such approvals are subject to inspections that will be conducted after we submit a BLA to the FDA or their equivalents to other relevant regulatory authorities. Until such time, if ever, as we establish our own manufacturing facilities, we will not control the manufacturing process of our product candidates and will be completely dependent on our contract manufacturing partners for compliance with Current Good Manufacturing Practices, or cGMPs, for manufacture of our raw materials, manufacturing devices, active pharmaceutical ingredients and finished products. These cGMP regulations cover all aspects of the manufacturing, testing, quality control, storage, distribution and record keeping relating to our product candidates. If our contract manufacturers do not successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA or others, we will not be able to secure or maintain regulatory approval for product made at their

manufacturing facilities. If the FDA or a comparable foreign regulatory authority does not approve these facilities for the manufacture of our product candidates or if it withdraws any such approval in the future, we may need to find alternative manufacturing facilities, which could significantly delay our clinical trials and impact our ability to develop, manufacture, obtain regulatory approval for or market our product candidates, if approved. Likewise, we could be negatively impacted if any of our contract manufacturers elect to discontinue their business relationship with us.

Our contract manufacturers will be subject to ongoing periodic unannounced inspections by the FDA and corresponding state and foreign agencies for compliance with cGMPs and similar regulatory requirements. We will not have control over our contract manufacturers' compliance with these regulations and standards. Failure by any of our contract manufacturers to comply with applicable regulations could result in sanctions being imposed on us, including fines, injunctions, civil penalties, failure to grant approval to market any of our product candidates, delays, suspensions or withdrawals of approvals, inability to supply product, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect our business. In addition, we will not have control over the ability of our contract manufacturers to maintain adequate quality control, quality assurance and qualified personnel. Failure by our contract manufacturers to comply with or maintain any of these standards could adversely affect our ability to develop, manufacture, obtain regulatory approval for or market any of our product candidates, if approved.

If, for any reason, these third parties are unable or unwilling to perform we may not be able to locate alternative manufacturers or formulators or enter into favorable agreements with them and we cannot be certain that any such third parties will have the manufacturing capacity to meet future requirements. If these manufacturers or any alternate manufacturer of finished drug product experiences any significant difficulties in its respective manufacturing processes for our required raw materials, manufacturing devices, active pharmaceutical ingredients or finished product or should cease doing business with us for any reason, we could experience significant delays in our clinical trials and significant interruptions in the supply of any of our product candidates or may not be able to create a supply of our product candidates at all.

Any manufacturing problem or the loss of a contract manufacturer could be disruptive to our operations and result in development and clinical trial delays and lost sales. Additionally, we will rely on third parties to supply the raw materials needed to manufacture our product candidates. Any such reliance on suppliers may involve several risks, including a potential inability to obtain critical materials and reduced control over production costs, delivery schedules, reliability and quality. Any unanticipated disruption to the operation of one of our contract manufacturers caused by problems with suppliers could delay our shipment of any of our product candidates, increase our cost of goods sold and result in delays in clinical trials or lost sales.

Our business model includes the potential out-licensing of strains from our proprietary microbial library or our product candidates to other biopharmaceutical companies, however technology licensing in the biopharmaceutical industry is a lengthy process and subject to several risks and factors outside of our control, and we cannot forecast our ability to successfully out-license our technology or the length of time it takes to establish a new licensing relationship.

Our business model includes the potential out-licensing or joint development of strains from our proprietary microbial library or our product candidates to other biopharmaceutical companies. Any such arrangement would typically begin with preliminary feasibility testing and evaluation by our potential partner or licensee. Assuming the feasibility testing is successful, our ability to convert the successful test into a commercial license or joint development agreement is dependent on a number of risks and factors, many of which are outside our control, including:

- the rate of adoption and incorporation of new technologies, by members of the pharmaceutical industry generally;
- our potential licensee's internal evaluation of the economic benefits of marketing a dermatological product that may be competitive with other products currently in development or commercial sale by our potential partner or licensee regardless of the perceived benefits or advantages of our technology or product;
- our potential partner's/licensee's internal budgetary and product development issues, including their ability to commit the capital and human resources towards the development and commercialization of our technology or product; and
- our potential partner's/licensee's willingness to accept our requirements for upfront fees and ongoing royalties.

In addition, we believe that in many cases our potential partners or licensee may engage with us in the early-stage feasibility testing as part of their evaluation of multiple drug and drug delivery options and prior to making any decision or commitment to the development of a new drug product. Consequently, even if our platform is successful in early feasibility studies, our potential partner/licensee may decide, for reasons unrelated to the performance of our technology, not to enter into a license agreement with us. Therefore, we are unable to predict the degree to which our proposed licensing model will be successful.

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

We will face a potential risk of product liability as a result of the clinical testing of our product candidates and will face an even greater risk of such liability if we commercialize any of our product candidates. For example, we may be sued if any product we develop, including any of our product candidates, or any materials that we use in our product candidates allegedly causes injury or is found to be otherwise unsuitable during product testing, manufacturing, marketing or sale. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product, negligence, strict liability and a breach of warranties. In the U.S., claims could also be asserted against us under state consumer protection acts. If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit commercialization of our product candidates. Even successful defense of these claims would require us to employ significant financial and management resources. Regardless of the merits or eventual outcome, liability claims may result in:

- decreased demand for any of our product candidates or any future products that we may develop;
- injury to our reputation;
- failure to obtain regulatory approval for our product candidates;
- withdrawal of participants in our clinical trials;
- costs associated with our defense of the related litigation;
- a diversion of our management's time and our resources;
- substantial monetary awards to trial participants or patients;
- product recalls, withdrawals or labeling, marketing or promotional restrictions;
- the inability to commercialize some or all of our product candidates; and
- a decline in the value of our stock.

As of the date of this report, we carry product liability insurance that we consider adequate for our current level of clinical testing and development. However, we will need additional product liability coverage at the time we commence commercial sale of our initial product. Our inability to obtain and retain sufficient product liability insurance at an acceptable cost to protect against potential product liability claims could prevent or inhibit the commercialization of products we develop. Although we will endeavor to obtain and maintain such insurance in coverage amounts we deem adequate, any claim that may be brought against us could result in a court judgment or settlement in an amount that is not covered, in whole or in part, by our insurance or that is in excess of the limits of our insurance coverage. Our insurance policies would also have various exclusions, and we may be subject to a product liability claim for which we have no coverage. As a result, we may have to pay any amounts awarded by a court or negotiated in a settlement that exceed our coverage limitations or that are not covered by our insurance, and we may not have, or be able to obtain, sufficient capital to pay such amounts.

Our internal computer systems, or those of our collaborators or other contractors or consultants, may fail or suffer security breaches, which could result in a material disruption of our product development programs.

Our internal computer systems and those of our current and any future collaborators and other contractors or consultants are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. While we have not experienced any such material system failure, accident or security breach to date, if such an event were to occur and cause interruptions in our operations, 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 proprietary information or other similar disruptions. For example, the loss of clinical trial data 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 or proprietary information, we could incur liability, our competitive position could be harmed and the further development and commercialization of our product candidates could be delayed.

We could be subject to risks caused by misappropriation, misuse, leakage, falsification or intentional or accidental release or loss of information maintained in the information systems and networks of our company and our vendors, including personal information of our employees and study subjects, and company and vendor confidential data. In addition, outside parties may attempt to penetrate our systems or those of our vendors or fraudulently induce our personnel or the personnel of our vendors to disclose sensitive information in order to gain access to our data and/or systems. We may experience threats to our data and systems, including malicious codes and viruses, phishing and other cyberattack. The number and complexity of these threats continue to increase over time. If a material breach of, or accidental or intentional loss of data from, our information technology systems or those of our vendors occurs, the market perception of the effectiveness of our security measures could

be harmed and our reputation and credibility could be damaged. We could be required to expend significant amounts of money and other resources to repair or replace information systems or networks. In addition, we could be subject to regulatory actions and/or claims made by individuals and groups in private litigation involving privacy issues related to data collection and use practices and other data privacy laws and regulations, including claims for misuse or inappropriate disclosure of data, as well as unfair or deceptive practices.

Although we develop and maintain systems and controls designed to prevent these events from occurring, and we have a process to identify and mitigate threats, the development and maintenance of these systems, controls and processes is costly and requires ongoing monitoring and updating as technologies change and efforts to overcome security measures become increasingly sophisticated. Moreover, despite our efforts, the possibility of these events occurring cannot be eliminated entirely. As we outsource more of our information systems to vendors, engage in more electronic transactions with payors and patients, and rely more on cloud-based information systems, the related security risks will increase and we will need to expend additional resources to protect our technology and information systems. In addition, there can be no assurance that our internal information technology systems or those of our third-party contractors, or our consultants' efforts to implement adequate security and control measures, will be sufficient to protect us against breakdowns, service disruption, data deterioration or loss in the event of a system malfunction, or prevent data from being stolen or corrupted in the event of a cyberattack, security breach, industrial espionage attacks or insider threat attacks which could result in financial, legal, business or reputational harm.

We face significant competition from other biotechnology and pharmaceutical companies targeting medical dermatological indications, and our operating results will suffer if we fail to compete effectively.

The dermatological therapies market is highly competitive and led by significant technologic developments. We anticipate that, if we are successful in obtaining regulatory approval of our candidates, we will face significant competition from other approved therapies or drugs that will become available in our industry. Even if another branded, generic, or OTC product is less effective, it may be quickly adopted by physicians and patients than our product based upon cost or convenience.

Risks Related to Product Regulation

Our success is entirely dependent on our ability to obtain the marketing approval for our product candidates by the FDA and the regulatory authorities in foreign jurisdictions in which we intend to market our product candidates, of which there can be no assurance.

We are not permitted to market our product candidates as prescription pharmaceutical products in the United States until we receive approval of a BLA from the FDA, or in any foreign countries until we receive the requisite approval from such countries. In the United States, the FDA generally requires the completion of clinical trials of each biologic to establish its safety and efficacy and extensive pharmaceutical development to ensure its quality before a BLA is approved. Of the large number of biologics in development, only a small percentage result in the submission of a BLA to the FDA and even fewer are eventually approved for commercialization. As of the date of this report, we have not submitted a BLA to the FDA or comparable applications to other regulatory authorities for any of our product candidates.

Our success depends on our receipt of the regulatory approvals described above, and the issuance of such regulatory approvals is uncertain and subject to a number of risks, including the following:

- such authorities may disagree with the number, design, size, conduct or implementation of our clinical trials or any of our collaborators' clinical trials;
- such authorities may disagree with our interpretation of data from preclinical studies or clinical trials or the use of results from studies that served as precursors to our current or future product candidates;
- the results of toxicology studies may not support the filing of an Investigational New Drug Application, or IND, or a BLA for our product candidates;
- the FDA or comparable foreign regulatory authorities or Institutional Review Boards, or IRBs, may disagree with the design or implementation of our clinical trials;
- we may not be able to provide acceptable evidence of our product candidates' safety and efficacy;
- the results of our clinical trials may not be satisfactory or may not meet the level of statistical or clinical significance required by the FDA, European Medicines Agency, or EMA, or other regulatory agencies for us to receive marketing approval for any of our product candidates;
- the dosing of our product candidates in a particular clinical trial may not be at an optimal level;
- patients in our clinical trials may suffer adverse effects for reasons that may or may not be related to our product candidates;

- the data collected from clinical trials may not be sufficient to support the submission of a BLA or other submission or to obtain regulatory approval in the United States or elsewhere;
- the FDA may require development of a Risk Evaluation and Mitigation Strategy, or REMS, as a condition of approval;
- the FDA or comparable foreign regulatory authorities may fail to approve the manufacturing processes or facilities of third-party manufacturers with which we contract for clinical and commercial supplies; and
- the approval policies or regulations of the FDA or comparable foreign regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval of our product candidates.

The process of obtaining regulatory approvals is expensive, often takes many years, if approval is obtained at all, and can vary substantially based upon, among other things, the type, complexity and novelty of the product candidates involved, the jurisdiction in which regulatory approval is sought and the substantial discretion of the regulatory authorities. Changes in regulatory approval policies during the development period, changes in or the enactment of additional statutes or regulations, or changes in regulatory review for a submitted product application may cause delays in the approval or rejection of an application. Regulatory approval obtained in one jurisdiction does not necessarily mean that a product candidate will receive regulatory approval in all jurisdictions in which we may seek approval, but the failure to obtain approval in one jurisdiction may negatively impact our ability to seek approval in a different jurisdiction. Failure to obtain regulatory approval for our product candidates for the foregoing, or any other reasons, will prevent us from commercializing our product candidates, and our ability to generate revenue will be materially impaired.

In addition, the FDA, EMA or other regulatory agencies may also approve a product candidate for fewer or more limited indications than we request, may impose significant limitations related to use restrictions for certain age groups, warnings, precautions or contraindications or may grant approval contingent on the performance of costly post-marketing clinical trials or risk mitigation requirements. The FDA, EMA or other regulatory agencies may also not accept the labeling claims that we believe would be necessary or desirable for the successful commercialization of our product candidates.

In December 2022, the U.S. Congress enacted a new law, the Modernization of Cosmetics Regulation Act of 2022, or MOCRA. MOCRA will require a cosmetic manufacturer or importer to: ensure that it has on hand substantiation of the safety of its products and ingredients; meet increased registration, record-keeping and reporting requirements; include fragrance and allergen information on its labeling; and be prepared to meet FDA's to be promulgated good manufacturing practices requirements. These additional requirements may impact budgets and timelines.

Disruptions at the FDA and other government agencies caused by funding shortages or global health concerns could hinder their ability to hire, retain, or deploy key leadership and other personnel, or otherwise prevent new or modified products from being developed, approved, or commercialized in a timely manner or at all, which could negatively impact our business.

The ability of the FDA and other government agencies to review and approve new products can be affected by a variety of factors, including government budget and funding levels, statutory, regulatory, and policy changes, a government agency's ability to hire and retain key personnel and accept the payment of user fees, and other events that may otherwise affect the government agency's ability to perform routine functions. Average review times at the FDA and other government agencies have fluctuated in recent years as a result. In addition, government funding of other government agencies that fund research and development activities is subject to the political process, which is inherently fluid and unpredictable. Disruptions at the FDA and other agencies may also slow the time necessary for new drugs or modifications to approved drugs to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. For example, over the last several years, the U.S. government has shut down several times and certain regulatory agencies, such as the FDA, have had to furlough critical employees and stop critical activities. With the change in presidential administrations in 2025, there is substantial uncertainty as to how, if at all, the new administration will seek to modify or revise the requirements and policies of the FDA and other regulatory agencies with jurisdiction over our product candidates. The impending uncertainty could present new challenges or potential opportunities as we navigate the clinical development and approval process for our product candidates.

Our clinical trials may fail to demonstrate substantial evidence of the safety and efficacy of our product candidates or any future product candidates, which would prevent or delay or limit the scope of regulatory approval and commercialization.

Our business model depends entirely on the successful development, regulatory approval and commercialization of our product candidates, which may never occur. All of our product candidates are in the early stages of development and as of the date of this report we have not progressed any of our product candidates, other than ATR-12 and ATR-04, beyond performance characterization and animal testing We may not be successful in obtaining approval from the FDA or comparable foreign regulatory authorities to start clinical trials for any of our other product candidates. If we do not obtain such approvals as presently planned, the time in which we expect to commence clinical programs for any product candidate will be extended and such extension will increase our expenses, delay our potential receipt of any revenues and increase our need for additional capital. Moreover, there is no guarantee that we will receive approval to commence human clinical trials or, if we do receive approval, that our clinical trials will be successful or that we will continue clinical development in support of an approval from the FDA or comparable foreign regulatory authorities for any indication. We note that most product candidates never reach the clinical development stage and even those that do commence clinical development have only a small chance of successfully completing clinical development and gaining regulatory approval. Success in early phases of preclinical and clinical trials does not ensure that later clinical trials will be successful, and interim results of a clinical trial do not necessarily predict final results. A failure of one or more of our clinical trials can occur at any stage of testing. We may experience numerous unforeseen events during, or as a result of, the clinical trial process that could delay or prevent our ability to receive regulatory approval or commercialize our product candidates. Therefore, our business currently depends entirely on the successful development, regulatory approval and commercialization of our product candidates, which may never occur.

Results of preclinical studies of our product candidates may not be predictive of the results of future preclinical studies or clinical trials.

To obtain the requisite regulatory approvals to market and sell any of our product candidates, we must demonstrate through extensive preclinical studies and clinical trials that our product candidates are safe, pure, and potent in humans. Before an IND can be submitted to the FDA and become effective, which is a prerequisite for conducting clinical trials on human subjects in the United States, a product candidate must successfully progress through extensive preclinical studies, which include preclinical laboratory testing, animal studies, and formulation studies in accordance with Good Laboratory Practices. Success in preclinical studies does not ensure that later preclinical studies or clinical trials will be successful. A number of companies in the biotechnology and pharmaceutical industries have suffered significant setbacks in clinical trials, even after positive results in earlier preclinical studies. These setbacks have been caused by, among other things, preclinical findings made while clinical trials were underway and safety or efficacy observations made in clinical trials, including previously unreported adverse events. The design of a clinical trial can determine whether its results will support approval of a product, and flaws in the design of a clinical trial may not become apparent until the clinical trial is well advanced. Further, we or our investigators may have little control over whether subjects comply with important aspects of clinical trial protocols. In addition, preclinical and clinical data are often susceptible to varying interpretations and analyses. Notwithstanding any potential promising results in earlier studies, we cannot be certain that we will not face similar setbacks. In addition, the results of our preclinical animal studies may not be predictive of the results of outcomes in subsequent clinical trials on human subjects. Product candidates in clinical trials may fail to show the desired pharmacological properties or safety and efficacy traits despite having progressed through preclinical studies.

If we fail to receive positive results in preclinical studies or clinical trials of our product candidates, the development timeline and regulatory approval and commercialization prospects for our most advanced product candidates, and, correspondingly, our business and financial prospects would be negatively impacted.

Any termination or suspension of, or delays in the commencement or completion of, any necessary studies of any of our product candidates for any indications could result in increased costs to us, delay or limit our ability to generate revenue and adversely affect our commercial prospects.

The commencement and completion of clinical studies can be delayed for a number of reasons, including delays related to:

- the FDA or a comparable foreign regulatory authority failing to grant permission to proceed and placing the clinical study on hold;
- subjects for clinical testing failing to enroll or remain enrolled in our trials at the rate we expect;

- a facility manufacturing any of our product candidates being ordered by the FDA or other government or regulatory authorities to temporarily or permanently shut down due to violations of cGMP requirements or other applicable requirements, or cross-contaminations of product candidates in the manufacturing process;
- any changes to our manufacturing process that may be necessary or desired;
- subjects choosing an alternative treatment for the indications for which we are developing our product candidates, or participating in competing clinical studies;
- subjects experiencing severe or unexpected drug-related adverse effects;
- reports from clinical testing on similar technologies and products raising safety and/or efficacy concerns;
- third-party clinical investigators losing their license or permits necessary to perform our clinical trials, not performing our clinical trials on our anticipated schedule or employing methods consistent with the clinical trial protocol, cGMP requirements, or other third parties not performing data collection and analysis in a timely or accurate manner;
- inspections of clinical study sites by the FDA, comparable foreign regulatory authorities, or IRBs finding regulatory violations that require us to undertake corrective action, result in suspension or termination of one or more sites or the imposition of a clinical hold on the entire study, or that prohibit us from using some or all of the data in support of our marketing applications;
- third-party contractors becoming debarred or suspended or otherwise penalized by the FDA or other government or regulatory authorities for violations of regulatory requirements, in which case we may need to find a substitute contractor, and we may not be able to use some or any of the data produced by such contractors in support of our marketing applications;
- one or more IRBs refusing to approve, suspending or terminating the study at an investigational site, precluding enrollment of additional subjects, or withdrawing its approval of the trial; reaching agreement on acceptable terms with prospective contract research organizations, or CROs, and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
- deviations of the clinical sites from trial protocols or dropping out of a trial;
- adding new clinical trial sites;
- the inability of the CRO to execute any clinical trials for any reason; and
- government or regulatory delays or "clinical holds" requiring suspension or termination of a trial.

Product development costs for any of our product candidates will increase if we have delays in testing or approval or if we need to perform more or larger clinical studies than planned. Additionally, changes in regulatory requirements and policies may occur and we may need to amend study protocols to reflect these changes. Amendments may require us to resubmit our study protocols to the FDA, comparable foreign regulatory authorities, and IRBs for reexamination, which may impact the costs, timing or successful completion of that study. If we experience delays in completion of, or if we, the FDA or other regulatory authorities, the IRB, or other reviewing entities, or any of our clinical study sites suspend or terminate any of our clinical studies of any of our product candidates, its commercial prospects may be materially harmed and our ability to generate product revenues will be delayed. Any delays in completing our clinical trials will increase our costs, slow down our development and approval process and jeopardize our ability to commence product sales and generate revenues. Any of these occurrences may harm our business, financial condition and prospects significantly. In addition, many of the factors that cause, or lead to, termination or suspension of, or a delay in the commencement or completion of, clinical studies may also ultimately lead to the denial of regulatory approval of our product candidates. In addition, if one or more clinical studies are delayed, our competitors may be able to bring competing products to market before we do, and the commercial viability of any of our affected product candidates could be significantly reduced.

Even if we receive regulatory approval for any of our product candidates, we may not be able to successfully commercialize the product and the revenue that we generate from its sales, if any, may be limited.

If approved for marketing, the commercial success of our product candidates will depend upon each product's acceptance by the medical community, including physicians, patients and health care payors. The degree of market acceptance for any of our product candidates will depend on a number of factors, including:

- demonstration of clinical safety and efficacy;
- relative convenience, dosing burden and ease of administration;
- the prevalence and severity of any adverse effects;
- the willingness of physicians to prescribe our product candidates, and the target patient population to try new therapies;
- efficacy of our product candidates compared to competing products;

- the introduction of any new products that may in the future become available targeting indications for which our product candidates may be approved;
- new procedures or therapies that may reduce the incidences of any of the indications in which our product candidates may show utility;
- pricing and cost-effectiveness;
- the inclusion or omission of our product candidates in applicable therapeutic and vaccine guidelines;
- the effectiveness of our own or any future collaborators' sales and marketing strategies;
- limitations or warnings contained in approved labeling from regulatory authorities;
- our ability to obtain and maintain sufficient third-party coverage or reimbursement from government health care programs, including Medicare and Medicaid, private health insurers and other third-party payors or to receive the necessary pricing approvals from government bodies regulating the pricing and usage of therapeutics; and
- the willingness of patients to pay out-of-pocket in the absence of third-party coverage or reimbursement or government pricing approvals.

If any of our product candidates are approved, but do not achieve an adequate level of acceptance by physicians, health care payors, and patients, we may not generate sufficient revenue and we may not be able to achieve or sustain profitability. Our efforts to educate the medical community and third-party payors on the benefits of our product candidates may require significant resources and may never be successful.

In addition, even if we obtain regulatory approvals, the timing or scope of any approvals may prohibit or reduce our ability to commercialize our product candidates successfully. For example, if the approval process takes too long, we may miss market opportunities and give other companies the ability to develop competing products or establish market dominance. Any regulatory approval we ultimately obtain may be limited or subject to restrictions or post-approval commitments that render our product candidates not commercially viable. For example, regulatory authorities may approve any of our product candidates for fewer or more limited indications than we request, may not approve the price we intend to charge for any of our product candidates, may grant approval contingent on the performance of costly post-marketing clinical trials, or may approve any of our product candidates with a label that does not include the labeling claims necessary or desirable for the successful commercialization of that indication. Further, the FDA or comparable foreign regulatory authorities may place conditions on approvals or require risk management plans or a Risk Evaluation and Mitigation Strategy, or REMS, to assure the safe use of the drug. Moreover, product approvals may be withdrawn for non-compliance with regulatory standards or if problems occur following the initial marketing of the product. Any of the foregoing scenarios could materially harm the commercial success of our product candidates.

Even if we obtain marketing approval for any of our product candidates, we will be subject to ongoing obligations and continued regulatory review, which may result in significant additional expense. Additionally, our product candidates could be subject to labeling and other restrictions and withdrawal from the market and we may be subject to penalties if we fail to comply with regulatory requirements or if we experience unanticipated problems with our product candidates.

Even if we obtain regulatory approval for any of our product candidates for an indication, the FDA or foreign equivalent may still impose significant restrictions on their indicated uses or marketing or the conditions of approval, or impose ongoing requirements for potentially costly and time-consuming post-approval studies, including Phase 4 clinical trials, and post-market surveillance to monitor safety and efficacy. Our product candidates will also be subject to ongoing regulatory requirements governing the manufacturing, labeling, packaging, storage, distribution, safety surveillance, advertising, promotion, recordkeeping and reporting of adverse events and other post-market information. These requirements include registration with the FDA, as well as continued compliance with current Good Clinical Practices regulations, or cGCPs, for any clinical trials that we conduct post-approval. In addition, manufacturers of drug products and their facilities are subject to continual review and periodic inspections by the FDA and other regulatory authorities for compliance with current cGMPs, requirements relating to quality control, quality assurance and corresponding maintenance of records and documents.

The FDA has the authority to require a REMS as part of an BLA or after approval, which may impose further requirements or restrictions on the distribution or use of an approved drug, such as limiting prescribing to certain physicians or medical centers that have undergone specialized training, limiting treatment to patients who meet certain safe-use criteria or requiring patient testing, monitoring and/or enrollment in a registry.

With respect to sales and marketing activities related to our product candidates, advertising and promotional materials must comply with FDA rules in addition to other applicable federal, state and local laws in the United States and similar legal requirements in other countries. In the United States, the distribution of product samples to physicians must comply with the requirements of the U.S. Prescription Drug Marketing Act. Application holders must obtain FDA approval for product and manufacturing changes, depending on the nature of the change. We may also be subject, directly or indirectly through our customers and partners, to various fraud and abuse laws, including, without limitation, the U.S. Anti-Kickback Statute, U.S. False Claims Act, and similar state laws, which impact, among other things, our proposed sales, marketing, and scientific/educational grant programs. If we participate in the U.S. Medicaid Drug Rebate Program, the Federal Supply Schedule of the U.S. Department of Veterans Affairs, or other government drug programs, we will be subject to complex laws and regulations regarding reporting and payment obligations. All of these activities are also potentially subject to U.S. federal and state consumer protection and unfair competition laws. Similar requirements exist in many of these areas in other countries.

In addition, if any of our product candidates are approved for a particular indication, our product labeling, advertising and promotion would be subject to regulatory requirements and continuing regulatory review. The FDA strictly regulates the promotional claims that may be made about prescription products. In particular, a product may not be promoted for uses that are not approved by the FDA as reflected in the product's approved labeling. If we receive marketing approval for our product candidates, physicians may nevertheless legally prescribe our products to their patients in a manner that is inconsistent with the approved label. If we are found to have promoted such off-label uses, we may become subject to significant liability and government fines. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant sanctions. The 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 into consent decrees of permanent injunctions under which specified promotional conduct is changed or curtailed.

If we or a regulatory agency discover previously unknown problems with a product candidate, such as adverse events of unanticipated severity or frequency, problems with the facility where the product is manufactured, or we or our manufacturers fail to comply with applicable regulatory requirements, we may be subject to the following administrative or judicial sanctions:

- restrictions on the marketing or manufacturing of the product, withdrawal of the product from the market, or voluntary or mandatory product recalls;
- issuance of warning letters or untitled letters;
- clinical holds;
- injunctions or the imposition of civil or criminal penalties or monetary fines;
- suspension or withdrawal of regulatory approval;
- suspension of any ongoing clinical trials;
- refusal to approve pending applications or supplements to approved applications filed by us, or suspension or revocation of product license approvals;
- suspension or imposition of restrictions on operations, including costly new manufacturing requirements; or
- product seizure or detention or refusal to permit the import or export of product.

The occurrence of any event or penalty described above may inhibit our ability to commercialize our product candidates and generate revenue. Adverse regulatory action, whether pre- or post-approval, can also potentially lead to product liability claims and increase our product liability exposure.

We also cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the United States or abroad, and compliance with such regulation may be expensive and consume substantial financial and management resources. If we or any future marketing collaborators or contract manufacturers are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies or are not able to maintain regulatory compliance, it could delay or prevent the promotion, marketing or sale of our products, which would adversely affect our business and results of operations.

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.

Obtaining and maintaining regulatory approval of our product candidates in one jurisdiction 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 the FDA grants marketing approval of a product candidate, comparable regulatory authorities in foreign jurisdictions 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 the United States, including additional preclinical studies or clinical trials, as clinical studies conducted in one jurisdiction may not be accepted by regulatory authorities in other jurisdictions. In many jurisdictions outside the United States, 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.

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. If we fail to comply with the regulatory requirements in international markets and/ or to receive applicable marketing approvals, our target market will be reduced and our ability to realize the full market potential of our product candidates will be harmed.

Even though we may apply for orphan drug designation for a product candidate, we may not be able to obtain orphan drug marketing exclusivity.

We believe that in some cases our products candidates may qualify for the FDA's orphan drug status. There is no guarantee that the FDA will grant any future application for orphan drug designation for any of our product candidates, which would make us ineligible for the additional exclusivity and other benefits of orphan drug designation.

Under the Orphan Drug Act, the FDA may grant orphan drug designation to a drug intended to treat a rare disease or condition, which is generally a disease or condition that affects fewer than 200,000 individuals in the United States and for which there is no reasonable expectation that the cost of developing and making a drug available in the United States for this type of disease or condition will be recovered from sales of the product. Orphan drug designation must be requested before submitting an 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 product designation does not convey any advantage in or shorten the duration of regulatory review and approval process. In addition to the potential period of exclusivity, orphan designation makes a company eligible for grant funding of up to $650,000 per year for four years to defray costs of clinical trial expenses, tax credits for clinical research expenses and potential exemption from the FDA application user fee.

If a product that has orphan designation subsequently receives the first FDA approval for the disease or condition for which it has such designation, the product is entitled to orphan drug exclusivity, which means the FDA may not approve any other applications to market the same drug for the same indication for seven years, except in limited circumstances, such as (i) the drug's orphan designation is revoked; (ii) its marketing approval is withdrawn; (iii) the orphan exclusivity holder consents to the approval of another applicant's product; (iv) the orphan exclusivity holder is unable to assure the availability of a sufficient quantity of drug; or (v) a showing of clinical superiority to the product with orphan exclusivity by a competitor product. If a drug designated as an orphan product receives marketing approval for an indication broader than what is designated, it may not be entitled to orphan drug exclusivity. There can be no assurance that we will receive orphan drug designation for any of our product candidates in the indications for which we think they might qualify, if we elect to seek such applications.

For the purposes of the rare pediatric disease program, a "rare pediatric disease" is a serious or life-threatening disease in which the serious or life-threatening manifestations primarily affect individuals aged from birth to 18 years or a rare disease or conditions within the meaning of the Orphan Drug Act. Under the FDA's rare pediatric disease priority review voucher, or RPD-PRV, program, upon the approval of an NDA or BLA for the treatment of a rare pediatric disease, the sponsor of such application would be eligible for an RPD-PRV that can be used to obtain priority review for a subsequent NDA or BLA. The sponsor of the application may transfer (including by sale) the RPD-PRV to another sponsor. The voucher may be further transferred any number of times before the voucher is used, as long as the sponsor making the transfer has not yet submitted the application. Congress has extended the RPD-PRV program until December 20, 2024, with potential for vouchers to be granted until 2026. This program has been subject to criticism, including by the FDA. As such it is possible that even if we have obtained qualification for an RPD-PRV, the program may no longer be in effect at the time of approval. Also, although priority review vouchers may be sold or transferred to third parties, there is no guaranty that we will be able to realize any value if we obtained, and subsequently were able to sell a priority review voucher. The RPD-PRV program is currently scheduled to sunset as of September 30, 2026.

Current and future legislation may increase the difficulty and cost for us to obtain marketing approval of and commercialize our product candidates and affect the prices we may obtain.

In the United States and some foreign jurisdictions, there have been a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay marketing approval for our product candidates, restrict or regulate post-approval activities and affect our ability to profitably sell our product candidates. Legislative and regulatory proposals have been made to expand post-approval requirements and restrict sales and promotional activities for pharmaceutical products. We do not know whether additional legislative changes will be enacted, or whether the FDA regulations, guidance or interpretations will be changed, or what the impact of such changes on the marketing approvals of our product candidates, if any, may be. In addition, increased scrutiny by the U.S. Congress of the FDA's approval process may significantly delay or prevent marketing approval, as well as subject us to more stringent product labeling and post-marketing testing and other requirements.

In the United States, the Medicare Modernization Act, or MMA, changed the way Medicare covers and pays for pharmaceutical products. The legislation expanded Medicare coverage for drug purchases by the elderly and introduced a new reimbursement methodology based on average sales prices for drugs. In addition, this legislation authorized Medicare Part D prescription drug plans to use formularies where they can limit the number of drugs that will be covered in any therapeutic class. As a result of this legislation and the expansion of federal coverage of drug products, we expect that there will be additional pressure to contain and reduce costs. These cost reduction initiatives and other provisions of this legislation could decrease the coverage and price that we receive for our product candidates and could seriously harm our business. While the MMA applies only to drug benefits for Medicare beneficiaries, private payors often follow Medicare coverage policy and payment limitations in setting their own reimbursement rates, and any reduction in reimbursement that results from the MMA may result in a similar reduction in payments from private payors.

The Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act of 2010 or, collectively, the ACA, is a sweeping law intended to broaden access to health insurance, reduce or constrain the growth of healthcare spending, enhance remedies against fraud and abuse, add new transparency requirements for healthcare and health insurance industries, impose new taxes and fees on the health industry and impose additional health policy reforms. The ACA revised the definition of "average manufacturer price" for reporting purposes, which could increase the amount of Medicaid drug rebates to states. The law also imposed a significant annual fee on companies that manufacture or import branded prescription drug products. Further, on August 16, 2022, President Biden signed the Inflation Reduction Act of 2022, or IRA, into law which, among other things, extends enhanced subsidies for individuals purchasing health insurance coverage in ACA marketplaces through plan year 2025. The IRA also eliminates the "donut hole" under the Medicare Part D program beginning in 2025 by significantly lowering the beneficiary maximum out-of-pocket cost and creating a new manufacturer discount program. It is unclear how such challenges, and the healthcare reform measures of the Biden administration will impact the ACA and our business.

In addition, other legislative changes have been proposed and adopted in the United States since the ACA was enacted. In 2011, the U.S. Congress enacted the Budget Control Act of 2011, or the Budget Control Act, which included provisions intended to reduce the federal deficit. The Budget Control Act resulted in the imposition of 2% reductions in Medicare payments to providers beginning in 2013 and, due to subsequent legislative amendments to the statute, will remain in effect through 2027 absent additional congressional action. However, pursuant to the CARES Act, and subsequent legislation, these reductions are suspended from May 1, 2020 through March 31, 2022 due to the COVID-19 pandemic. In January 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, among other things, reduced Medicare payments to several providers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These new laws may result in additional reductions in Medicare and other healthcare funding, which could have a material adverse effect on customers for our drugs, if approved, and accordingly, our financial operations. If government spending is further reduced, anticipated budgetary shortfalls may also impact the ability of relevant agencies, such as the FDA, to continue to function at current levels, which may impact the ability of relevant agencies to timely review and approve research and development, manufacturing and marketing activities, which may delay our ability to develop, market and sell any product candidates we may develop. In addition, any significant spending reductions affecting Medicare, Medicaid or other publicly funded or subsidized health programs that may be implemented, or any significant taxes or fees that may be imposed on us, as part of any broader deficit reduction effort or legislative replacement to the Budget Control Act, could have an adverse impact on our anticipated product revenues.

Moreover, recently there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their commercial products. 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 cost of drugs under Medicare, and reform government program reimbursement methodologies for drugs. On September 24, 2020, the FDA released a final rule providing guidance for states to build and submit importation plans for drugs from Canada. Further, on November 20, 2020, the U.S. Department of Health and Human Services, or HHS, finalized a regulation removing safe harbor protection for price reductions from pharmaceutical manufacturers to plan sponsors under Part D, either directly or through pharmacy benefit managers, unless the price reduction is required by law. The rule also creates a new safe harbor for price reductions reflected at the point-of-sale, as well as a safe harbor for certain fixed fee arrangements between pharmacy benefit managers and manufacturers. On August 16, 2022, Congress enacted the Inflation Reduction Act of 2022 which contains several provisions relating to prescription drug costs, including requirements for federal government price negotiations, rebate requirements, and caps on out-of-pocket spending for Medicare Part D enrollees. At the state level, legislatures have increasingly passed legislation and implemented 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.

On November 20, 2020, the HHS Office of Inspector General finalized further modifications to the federal Anti-Kickback Statute. Under the final rules, the HHS Office of Inspector General added safe harbor protections under the Anti-Kickback Statute for certain coordinated care and value-based arrangements among clinicians, providers, and others, yet removed safe harbor protection for price reductions from pharmaceutical manufacturers to plan sponsors under Part D, either directly or through pharmacy benefit managers, unless the price reduction is required by law. The rule also creates a new safe harbor for price reductions reflected at the point-of-sale, as well as a safe harbor for certain fixed fee arrangements between pharmacy benefit managers and manufacturers. This rule (with exceptions) became effective January 19, 2021. We continue to evaluate what effect, if any, these rules will have on our business. CMS issued a final rule, effective on July 9, 2019, that requires direct-to-consumer advertisements of prescription drugs and biological products, for which payment is available through or under Medicare or Medicaid, to include in the advertisement the Wholesale Acquisition Cost, or list price, of that drug or biological product if it is equal to or greater than $35 for a monthly supply or usual course of treatment. Prescription drugs and biological products that are in violation of these requirements will be included on a public list. Any adopted health reform measure could reduce the ultimate demand for our products, if approved, or put pressure on our product pricing. Individual states in the United States have also become increasingly active in passing legislation and implementing regulations designed to control pharmaceutical 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 healthcare 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 healthcare programs. We expect that additional state and federal healthcare reform measures will be adopted in the future.

The delivery of healthcare in the European Union, or EU, including the establishment and operation of health services and the pricing and reimbursement of medicines, is almost exclusively a matter for national, rather than EU, 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 EU member states have resulted in restrictions on the pricing and reimbursement of medicines by relevant health service providers. Coupled with ever-increasing EU 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. Both in the United States and in the EU, legislative and regulatory proposals have been made to expand post-approval requirements and restrict sales and promotional activities for pharmaceutical products. We do not know whether additional legislative changes will be enacted, or whether the regulations, guidance or interpretations will be changed, or what the impact of such changes on the marketing approvals of our product candidates, if any, may be.

Third-party coverage and reimbursement and health care cost containment initiatives and treatment guidelines may constrain our future revenues.

Our ability to successfully market our product candidates will depend in part on the level of reimbursement that government health administration authorities, private health coverage insurers and other organizations provide for the cost of our product candidates and related treatments. Countries in which any of our product candidates are sold through reimbursement schemes under national health insurance programs frequently require that manufacturers and sellers of pharmaceutical products

obtain governmental approval of initial prices and any subsequent price increases. In certain countries, including the United States, government-funded and private medical care plans can exert significant indirect pressure on prices. We may not be able to sell our product candidates profitably if adequate prices are not approved or coverage and reimbursement is unavailable or limited in scope. Increasingly, third-party payors attempt to contain health care costs in ways that are likely to impact our development of products including:

- failing to approve or challenging the prices charged for health care products;
- introducing reimportation schemes from lower priced jurisdictions;
- limiting both coverage and the amount of reimbursement for new therapeutic products;
- denying or limiting coverage for products that are approved by the regulatory agencies but are considered to be experimental or investigational by third-party payors; and
- refusing to provide coverage when an approved product is used in a way that has not received regulatory marketing approval.

Our relationships with customers and payors are subject to applicable anti-kickback, fraud and abuse and other healthcare laws and regulations, which, if violated, could expose us to criminal sanctions, civil penalties, exclusion from government healthcare programs, contractual damages, reputational harm and diminished profits and future earnings.

Healthcare providers, physicians and others will play a primary role in the recommendation and prescription of any products for which we obtain marketing approval. Our future arrangements with third-party payors and customers may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations, primarily in the United States, that may constrain the business or financial arrangements and relationships through which we market, sell and distribute our products for which we obtain marketing approval. Restrictions under applicable healthcare laws and regulations, include the following:

- the federal Anti-Kickback Statute prohibits, among other things, the knowing and willful offer, payment, solicitation or receipt of any form of remuneration in return for, or to induce, (i) the referral of a person, (ii) the furnishing or arranging for the furnishing of items or services reimbursable under the Medicare, Medicaid or other governmental programs, or (iii) the purchase, lease or order or arranging or recommending purchasing, leasing or ordering of any item or service reimbursable under the Medicare, Medicaid or other governmental programs. A person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation. In addition, the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the False Claims Act;
- the federal False Claims Act imposes civil penalties, and provides for civil whistleblower or qui tam actions, against individuals or entities for knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false or fraudulent or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government;
- the Health Insurance Portability and Accountability Act, or HIPAA imposes criminal and civil liability for executing a scheme to defraud any health care benefit program or making false statements relating to health care matters. Similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;
- the federal false statements statute 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 Physician Payments Sunshine Act, created under the ACA, and its implementing regulations, which requires specified manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program, with specific exceptions, to report annually to CMS information related to payments or other "transfers of value" made to physicians. All such reported information is publicly available;
- analogous state and non-U.S. laws and regulations, such as certain state anti-kickback and false claims laws which may apply to items or services reimbursed by any third-party payor, including commercial insurers; state laws that require pharmaceutical companies to comply with the industry's voluntary compliance guidelines and the applicable 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
- regulation by CMS and enforcement by the HHS Office of Inspector General or the U.S. Department of Justice.

Because of the breadth of these laws and the narrowness of the statutory exceptions and safe harbors available, it is possible that some of our future business activities could be subject to challenge under one or more of such laws.

Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices may 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 governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, exclusion from U.S. government funded healthcare programs, such as Medicare and Medicaid, and the curtailment or restructuring of our operations. If any of the physicians or other providers or entities with whom we expect to do business with are found to be not in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs.

Risks Relating to Our Intellectual Property Rights

It is difficult and costly to protect our intellectual property rights, and we cannot ensure the protection of these rights.

Our commercial success will depend, in part, on our ability to prosecute and defend, if necessary, our patent rights against third-party challenges and successfully enforcing these patent rights against third party competitors. The patent positions of biotech companies can be highly uncertain and involve complex legal, scientific and factual questions for which important legal principles remain unresolved. Changes in either the patent laws or in interpretations of patent laws may diminish the value of our intellectual property. Accordingly, we cannot predict the breadth of claims that may be allowable or enforceable in any patent applications filed by us or our licensors of patent rights. The patents and patent applications held by or licensed to us relating to our microbial platform and related technologies may be challenged, invalidated or circumvented by third parties and might not protect us against competitors with similar products or technologies.

The degree of future protection afforded by the patent rights held by or licensed to us is uncertain, because legal means afford only limited protection and may not adequately protect our rights, permit us to gain or keep our competitive advantage, or provide us with any competitive advantage at all. We cannot be certain that any patent application owned by a third party will not have priority over patent applications filed by us or in which we hold license rights or that we will not be involved in interference, opposition or invalidity proceedings before United States or foreign patent offices.

Additionally, if we were to initiate legal proceedings against a third party to enforce a patent covering any of our product candidates, the defendant could counterclaim that such patent is invalid and/or unenforceable. In patent litigation in the United States, defendant counterclaims alleging invalidity and/or unenforceability are commonplace. Grounds for a validity challenge include alleged failures to meet any of several statutory requirements, including lack of novelty, obviousness or non-enablement. Grounds for unenforceability assertions include allegations that someone connected with prosecution of the patent withheld relevant information from the United States Patent and Trademark Office, or the USPTO, or made a misleading statement, during prosecution. Third parties may also raise similar claims before administrative bodies in the United States or abroad, even outside the context of litigation. Such mechanisms include re-examination, post grant review and equivalent proceedings in foreign jurisdictions, e.g., opposition proceedings. Such proceedings could result in revocation or amendment of patents held by or licensed to us in such a way that they no longer cover our product candidates or competitive products. The outcome following legal assertions of invalidity and unenforceability is unpredictable. With respect to validity, for example, we cannot be certain that there is no invalidating prior art, of which, we, any licensor of our patent rights or the patent examiner were unaware during prosecution. If a defendant were to prevail on a legal assertion of invalidity and/or unenforceability, we would lose at least part, and perhaps all, of the patent protection on any of our product candidates. Such a loss of patent protection would have a material adverse impact on our business.

We rely on know-how and trade secrets to protect technology, especially in cases where we believe patent protection is not appropriate or obtainable. However, know-how and trade secrets are difficult to protect. While we require employees, academic collaborators, consultants and other contractors to enter into confidentiality agreements, we may not be able to adequately protect our trade secrets or other proprietary or licensed information. Typically, research collaborators and scientific advisors have rights to publish data and information in which we may have rights. Enforcing a claim that a third party illegally obtained and is using any of our trade secrets is expensive and time consuming, and the outcome is unpredictable. In addition, courts are sometimes less willing to protect trade secrets than patents. Moreover, our competitors may independently develop equivalent knowledge, methods and know-how.

If we fail to obtain or maintain patent protection or trade secret protection for our product candidates or our technologies, third parties could use our proprietary information, which could impair our ability to compete in the market and adversely affect our ability to generate revenues and attain profitability.

Our product candidates may infringe the intellectual property rights of others, which could increase our costs and delay or prevent our development and commercialization efforts.

Our success depends in part on avoiding infringement of the proprietary technologies of others. The pharmaceutical industry has been characterized by frequent litigation regarding patent and other intellectual property rights. Identification of third-party patent rights that may be relevant to our proprietary technology is difficult because patent searching is imperfect due to differences in terminology among patents, incomplete databases and the difficulty in assessing the meaning of patent claims. Additionally, because patent applications are maintained in secrecy until the application is published, we may be unaware of third-party patents that may be infringed by commercialization of any of our product candidates or any future product candidate. There may be certain issued patents and patent applications claiming subject matter that we may be required to license in order to research, develop or commercialize any of our product candidates, and we do not know if such patents and patent applications would be available to license on commercially reasonable terms, or at all. Any claims of patent infringement asserted by third parties would be time-consuming and may:

- result in costly litigation;
- divert the time and attention of our technical personnel and management;
- prevent us from commercializing a product until the asserted patent expires or is held finally invalid or not infringed in a court of law;
- require us to cease or modify our use of the technology and/or develop non-infringing technology; or
- require us to enter into royalty or licensing agreements.

Third parties may hold proprietary rights that could prevent any of our product candidates from being marketed. Any patent-related legal action against us claiming damages and seeking to enjoin commercial activities relating to any of our product candidates or our processes could subject us to potential liability for damages and require us to obtain a license to continue to manufacture or market any of our product candidates or any future product candidates. We cannot predict whether we would prevail in any such actions or that any license required under any of these patents would be made available on commercially acceptable terms, if at all. In addition, we cannot be sure that we could redesign our product candidates or any future product candidates or processes to avoid infringement, if necessary. Accordingly, an adverse determination in a judicial or administrative proceeding, or the failure to obtain necessary licenses, could prevent us from developing and commercializing any of our product candidates or a future product candidate, which could harm our business, financial condition and operating results.

We expect that there are other companies, including major biopharmaceutical companies, working in the areas competitive to our proposed product candidates which either has resulted, or may result, in the filing of patent applications that may be deemed related to our activities. If we were to challenge the validity of these or any issued United States patent in court, we would need to overcome a statutory presumption of validity that attaches to every issued United States patent. This means that, in order to prevail, we would have to present clear and convincing evidence as to the invalidity of the patent's claims. If we were to challenge the validity of these or any issued United States patent in an administrative trial before the Patent Trial and Appeal Board in the USPTO, we would have to prove that the claims are unpatentable by a preponderance of the evidence. There is no assurance that a jury and/or court would find in our favor on questions of infringement, validity or enforceability. Even if we are successful, litigation could result in substantial costs and be a distraction to management.

We may be subject to claims that we have wrongfully hired an employee from a competitor or that we or our employees have wrongfully used or disclosed alleged confidential information or trade secrets of their former employers.

As is commonplace in our industry, we will employ individuals who were previously employed at other biopharmaceutical companies, including our competitors or potential competitors. Although no claims against us are currently pending, we may be subject in the future to claims that our employees or prospective employees are subject to a continuing obligation to their former employers (such as non-competition or non-solicitation obligations) or claims that our employees or we have inadvertently or otherwise used or disclosed trade secrets or other proprietary information of their former employers. Litigation may be necessary to defend against these claims. Even if we are successful in defending against these claims, litigation could result in substantial costs and be a distraction to management.

Risks Related to Owning Our Common Stock

The market price of our shares may be subject to fluctuation and volatility. You could lose all or part of your investment.

The market price of our common stock is subject to wide fluctuations in response to various factors, some of which are beyond our control. Since shares of our common stock were sold in our initial public offering, or IPO, in June 2023 at a price of $150.00 per share, the reported high and low sales prices of our common stock have ranged from $5.18 to $0.20 through February 24, 2025. The market price of our shares on the NYSE American may fluctuate as a result of a number of factors, some of which are beyond our control, including, but not limited to:

- actual or anticipated variations in our and our competitors' results of operations and financial condition;
- changes in earnings estimates or recommendations by securities analysts, if our shares are covered by analysts;
- market acceptance of our product candidates;
- development of technological innovations or new competitive products by others;
- announcements of technological innovations or new products by us;
- publication of the results of preclinical or clinical trials for our product candidates;
- failure by us to achieve a publicly announced milestone;
- delays between our expenditures to develop and market new or enhanced products and the generation of sales from those products;
- developments concerning intellectual property rights, including our involvement in litigation brought by or against us;
- regulatory developments and the decisions of regulatory authorities as to the approval or rejection of new or modified products;
- changes in the amounts that we spend to develop, acquire or license new products, technologies or businesses;
- changes in our expenditures to promote our product candidates;
- our sale or proposed sale, or the sale by our significant stockholders, of our shares or other securities in the future;
- changes in key personnel;
- success or failure of our research and development projects or those of our competitors;
- the trading volume of our shares; and
- general economic and market conditions and other factors, including factors unrelated to our operating performance.

These factors and any corresponding price fluctuations may materially and adversely affect the market price of our shares and result in substantial losses being incurred by our investors. In the past, following periods of market volatility, public company stockholders have often instituted securities class action litigation. If we were involved in securities litigation, it could impose a substantial cost upon us and divert the resources and attention of our management from our business.

Our failure to meet the continued listing requirements of the NYSE American could result in a delisting of our common stock.

If we fail to satisfy the continued listing requirements of the NYSE American, such as the corporate governance requirements or the minimum closing bid price requirement, the NYSE American may take steps to delist our common stock. Such a delisting would likely have a negative effect on the price of our common stock and would impair your ability to sell or purchase our common stock when you wish to do so. In the event of a delisting, we can provide no assurance that any action taken by us to restore compliance with listing requirements would allow our common stock to become listed again, stabilize the market price or improve the liquidity of our common stock, prevent our common stock from dropping below the NYSE American's minimum bid price requirement or prevent future non-compliance with the NYSE American's listing requirements.

Future capital raises may dilute your ownership and/or have other adverse effects on our operations.

If we raise additional capital by issuing equity securities, our existing stockholders' percentage ownership will be reduced and these stockholders may experience substantial dilution. If we raise additional funds by issuing debt securities, these debt securities would have rights senior to those of our common stock and the terms of the debt securities issued could impose significant restrictions on our operations, including liens on our assets. If we raise additional funds through collaborations and licensing arrangements, we may be required to relinquish some rights to our intellectual property or candidate products, or to grant licenses on terms that are not favorable to us.

Shares eligible for future sale may adversely affect the market for our common stock.

As of the date of this report, we have 12,483,836 shares of common stock issued and outstanding, all of which are eligible for sale by means of ordinary brokerage transactions in the open market pursuant to Rule 144, promulgated under the Securities Act, subject to certain limitations under Rule 144. Any substantial sale of our common stock pursuant to Rule 144 or pursuant to any resale report may have a material adverse effect on the market price of our common stock.

We are an "emerging growth company" under the JOBS Act and we cannot be certain if the reduced disclosure requirements applicable to emerging growth companies will make our common stock less attractive to investors.

We are an "emerging growth company," as defined in the JOBS Act and we may take advantage of certain exemptions from various reporting requirements that are applicable to other public companies that are not "emerging growth companies" including, but not limited to:

- not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act;
- reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements;
- exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments; and
- extended transition periods available for complying with new or revised accounting standards.

We have chosen to take advantage of all of the benefits available under the JOBS Act, including the exemptions discussed above. We cannot predict if investors will find our common stock less attractive because we may rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile.

We will remain an "emerging growth company" for up to five years, although we will lose that status sooner if our revenues exceed $1.235 billion, if we issue more than $1 billion in non-convertible debt in a three-year period, or if the market value of our common stock that is held by non-affiliates exceeds $700 million as of June 30 in any future year.

Our status as an "emerging growth company" under the JOBS Act may make it more difficult to raise capital as and when we need it.

Because of the exemptions from various reporting requirements provided to us as an "emerging growth company," we may be less attractive to investors and it may be difficult for us to raise additional capital as and when we need it. Investors may be unable to compare our business with other companies in our industry if they believe that our reporting is not as transparent as other companies in our industry. If we are unable to raise additional capital as and when we need it, our financial condition and results of operations may be materially and adversely affected.

We have not paid dividends on our common stock in the past and have no immediate plans to pay such dividends.

We plan to reinvest all of our earnings, to the extent we have earnings, to cover operating costs and otherwise become and remain competitive. We do not plan to pay any cash dividends with respect to our common stock in the foreseeable future. We cannot assure you that we would, at any time, generate sufficient surplus cash that would be available for distribution to the holders of our common stock as a dividend. Therefore, you should not expect to receive cash dividends on our common stock.

If equity research analysts do not publish research or reports about our business or if they issue unfavorable commentary or downgrade our shares, the price of our shares could decline.

The trading market for our shares will rely in part on the research and reports that equity research analysts publish about us and our business, if at all. We do not have control over these analysts and we do not have commitments from them to write research reports about us. The price of our shares could decline if no research reports are published about us or our business, or if one or more equity research analysts downgrades our shares or if those analysts issue other unfavorable commentary or cease publishing reports about us or our business.

We may be at an increased risk of securities class action litigation.

Historically, securities class action litigation has often been brought against a company following a decline in the market price of its securities. This risk is especially relevant for us because biotechnology and pharmaceutical companies have experienced significant stock price volatility in recent years. If we were to be sued, it could result in substantial costs and a diversion of management's attention and resources, which could harm our business. We maintain director and officer insurance that we regard as reasonably adequate to protect us from potential claims; however, we are responsible for meeting certain deductibles under the policies and, in any event, we cannot assure you that the insurance coverage will adequately protect us from claims made. Further, the costs of insurance may increase and the availability of coverage may decrease. As a result, we may not be able to maintain our current levels of insurance at a reasonable cost, or at all.

Our charter documents and Delaware law may inhibit a takeover that stockholders consider favorable.

Provisions of our amended and restated certificate of incorporation and amended and restated bylaws and applicable provisions of Delaware law may delay or discourage transactions involving an actual or potential change in control or change in our management, including transactions in which stockholders might otherwise receive a premium for their shares, or transactions that our stockholders might otherwise deem to be in their best interests. The provisions in our amended and restated certificate of incorporation and amended and restated bylaws:

- limit who may call stockholder meetings;
- restrict our stockholders from bringing matters before our annual meeting of stockholders or from making nominations for directors at our annual meeting of stockholders if the proper procedures are not followed;
- do not provide for stockholder action by written consent;
- do not provide for cumulative voting rights; and
- provide that all board vacancies may be filled by the affirmative vote of a majority of directors then in office, even if less than a quorum.

Section 203 of the DGCL may limit our ability to engage in any business combination with a person who beneficially owns 15% or more of our outstanding voting stock unless certain conditions are satisfied. This restriction lasts for a period of three years following the share acquisition. These provisions may have the effect of entrenching our management team and may deprive you of the opportunity to sell your shares to potential acquirers at a premium over prevailing prices. This potential inability to obtain a control premium could reduce the price of our common stock.

General Risk Factors

Changes in accounting standards and subjective assumptions, estimates and judgments by management related to complex accounting matters may materially impact reporting of our financial condition and results of operations.

Accounting principles generally accepted in the United States and related accounting pronouncements, implementation guidelines, and interpretations we apply to a wide range of matters that are relevant to our business, such as accounting for long-lived asset impairment and share-based compensation, are complex and involve subjective assumptions, estimates and judgments by our management. Changes in these rules or their interpretation or changes in underlying assumptions, estimates or judgments by our management could significantly change or add significant volatility to our reported or expected financial performance.

A potential failure to maintain effective internal control over financial reporting in accordance with Section 404 of the Sarbanes-Oxley Act could have a material adverse effect on our business, financial condition, and results of operations.

Our management is responsible for establishing and maintaining adequate internal control over financial reporting. Internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements in accordance with U.S. generally accepted accounting principles, or GAAP. Under standards established by the Public Company Accounting Oversight Board, or PCAOB, a deficiency in internal control over financial reporting exists when the design or operation of a control does not allow management or personnel, in the normal course of performing their assigned functions, to prevent or detect misstatements on a timely basis. The PCAOB defines a material weakness as a deficiency, or combination of deficiencies, in internal control over financial reporting, such that there is a reasonable possibility that a material misstatement of annual or interim financial statements will not be prevented, or detected and corrected, on a timely basis.

We are required, pursuant to Section 404 of the Sarbanes-Oxley Act, to furnish a report by management on, among other things, the effectiveness of our internal control over financial reporting for our second annual report on Form 10-K filed with the SEC and in each year thereafter. Our auditors will also need to attest to the effectiveness of our internal control over financial reporting at such time as we are an accelerated filed or large accelerated filer and no longer an emerging growth company or smaller reporting company. If we are unable to assert that our internal control over financial reporting is effective, or when required in the future, if our independent registered public accounting firm is unable to express an unqualified opinion as to the effectiveness of our internal control over financial reporting, investors may lose confidence in the accuracy and completeness of our financial reports, the market price of our common stock could be adversely affected, and we could become subject to litigation or investigations by the stock exchange on which our common stock are listed, the SEC or other regulatory authorities, which could require additional financial and management resources and could have a material adverse effect on our business, financial condition, and results of operations.

The limited amount of public company experience of our management team could adversely impact our ability to comply with the reporting requirements of U.S. securities laws, which could have a materially adverse effect on our business.

Our officers have limited public company experience, which could impair our ability to comply with legal and regulatory requirements such as those imposed by Sarbanes-Oxley Act. Such responsibilities include complying with federal securities laws and making required disclosures on a timely basis. Any such deficiencies, weaknesses or lack of compliance could have a materially adverse effect on our ability to comply with the reporting requirements of the Securities Exchange Act of 1934, or the Exchange Act, which is necessary to maintain our public company status. If we were to fail to fulfill those obligations, our ability to continue as a U.S. public company would be in jeopardy in which event you could lose your entire investment in our Company.

We identified material weaknesses in our internal control over financial reporting, and we may identify additional material weaknesses in the future that may cause us to fail to meet our reporting obligations or result in material misstatements of our financial statements. If we fail to remediate any material weaknesses or if we otherwise fail to establish and maintain effective control over financial reporting, our ability to accurately and timely report our financial results could be adversely affected.

Effective internal controls over financial reporting are necessary for us to provide reliable financial reports and, together with adequate disclosure controls and procedures, are designed to prevent fraud. Any failure to implement required new or improved controls, or difficulties encountered in their implementation, could cause us to fail to meet our reporting obligations. In addition, any testing by us conducted in connection with Section 404 of the Sarbanes-Oxley Act, or the subsequent testing by our independent registered public accounting firm when required, may reveal deficiencies in our internal controls over financial reporting that are deemed to be material weaknesses or that may require prospective or retrospective changes to our financial statements or identify other areas for further attention or improvement. Inferior internal controls could also cause investors to lose confidence in our reported financial information, which could have a negative effect on the trading price of our shares of common stock. There is also a risk that neither we nor our independent registered public accounting firm (when applicable in the future) will be able to conclude within the prescribed timeframe that internal controls over financial reporting is effective as required by Section 404. As a result, investors could lose confidence in our financial and other public reporting, which would harm our business and the trading price of our common stock.

During the preparation of our financial statements included in this report, we and our independent registered public accounting firm identified a material weakness as it relates to a lack of adequate segregation of accounting functions. We are in the process of implementing measures designed to improve our internal control over financial reporting and remediate this material weakness. We intend to increase staffing within our accounting infrastructure sufficient to facilitate proper segregation of accounting functions.

We may identify future material weaknesses in our internal controls over financial reporting or fail to meet the demands that will be placed upon us as a public company, including the requirements of the Sarbanes-Oxley, and we may be unable to accurately report our financial results, or report them within the timeframes required by law or stock exchange regulations. We cannot assure that our existing material weakness will be remediated or that additional material weaknesses will not exist or otherwise be discovered, any of which could adversely affect our reputation, financial condition and results of operations.

We have and will continue to incur significant increased costs as a result of being a public company that reports to the SEC and our management will be required to devote substantial time to meet compliance obligations.

As a public company reporting to the SEC, we will continue to incur significant legal, accounting and other expenses that we did not incur as a private company. We are subject to reporting requirements of the Exchange Act and the reporting and governance provisions of the Sarbanes-Oxley Act and the Dodd-Frank Wall Street Reform and Protection Act, as well as rules subsequently implemented by the SEC, that impose significant requirements on public companies, including requiring establishment and maintenance of effective disclosure and financial controls and changes in corporate governance practices. There are significant corporate governance and reporting provisions in these laws that will increase our legal and financial compliance costs, make some activities more difficult, time-consuming or costly and may also place undue strain on our personnel, systems and resources. Our management and other personnel will need to devote a substantial amount of time to these regulations. In addition, we expect these rules and regulations to make it more difficult and more expensive for us to obtain director and officer liability insurance, and we may be required to accept reduced policy limits and coverage or incur substantially higher costs to obtain the same or similar coverage. As a result, it may be more difficult for us to attract and retain qualified people to serve on our Board our Board committees or as executive officers.

Unfavorable geopolitical and macroeconomic developments could adversely affect our business, financial condition or results of operations.

Our business could be adversely affected by conditions in the U.S. and global economies, the United States and global financial markets and adverse geopolitical and macroeconomic developments, including rising inflation rates, the continuing adverse impacts of the COVID-19 pandemic, the Ukrainian/Russian and Israeli/Palestinian conflicts and related sanctions, bank failures, and economic uncertainties related to these conditions.

For example, inflation rates, particularly in the United States, have increased recently to levels not seen in years, and increased inflation may result in increases in our operating costs (including our labor costs), reduced liquidity and limits on our ability to access credit or otherwise raise capital on acceptable terms, if at all. In response to rising inflation, the U.S. Federal Reserve has raised, and may again raise, interest rates, which, coupled with reduced government spending and volatility in financial markets, may have the effect of further increasing economic uncertainty and heightening these risks.

Additionally, financial markets around the world experienced volatility following the invasion of Ukraine by Russia in February 2022 and the eruption of the Israeli/Palestinian conflict in October 2023, including as a result of economic sanctions and export controls against Russia and countermeasures taken by Russia. The full economic and social impact of these sanctions and countermeasures, in addition to the ongoing military conflicts in Ukraine and Gaza, which could conceivably expand, remains uncertain; however, both the conflicts and related sanctions have resulted and could continue to result in disruptions to trade, commerce, pricing stability, credit availability, and/or supply chain continuity, in both Europe and globally, and has introduced significant uncertainty into global markets. While we do not currently operate in Russia, Ukraine or the Middle East, as the adverse effects of these conflicts continue to develop our business and results of operations may be adversely affected.

Item 1B. Unresolved Staff Comments

Not applicable.

Item 1C. Cybersecurity

Risk Management and Strategy. We employ processes for assessing, identifying, and managing material risks from cybersecurity threats. In conjunction with EBM, Inc., we employ best in class Endpoint Detection and Response with 24/7 SOC at the Endpoints. We also utilize MFA and Geolocation enforcement where available. We continuously monitor and maintain our network infrastructure including consistent vulnerability monitoring and remediation. We also engage in quarterly phishing campaigns as well as cybersecurity awareness training to our end users to keep them vigilant in being able to detect threats.

Although we develop and maintain systems and controls designed to prevent cybersecurity threats from occurring, and we have a process to identify and mitigate threats, the development and maintenance of these systems, controls and processes is costly and requires ongoing monitoring and updating as technologies change and efforts to overcome security measures become increasingly sophisticated. Moreover, despite our efforts, the possibility of these events occurring cannot be eliminated entirely. As we outsource more of our information systems to vendors, engage in more electronic transactions with service providers and patients, and rely more on cloud-based information systems, the related security risks will increase and

we will need to expend additional resources to protect our technology and information systems. In addition, there can be no assurance that our internal information technology systems or those of our third-party contractors, or our consultants' efforts to implement adequate security and control measures, will be sufficient to protect us against breakdowns, service disruption, data deterioration or loss in the event of a system malfunction, or prevent data from being stolen or corrupted in the event of a cyberattack, security breach, industrial espionage attacks or insider threat attacks which could result in financial, legal, business or reputational harm.

As of the date of this report, we are not aware of any risks from cybersecurity threats, including as a result of any previous cybersecurity incidents, that have materially affected or are reasonably likely to materially affect us, including our business strategy, results of operations, or financial condition.

Governance. Our senior management team conducts the regular assessment and management of material risks from cybersecurity threats, including review with our IT team and third-party service providers. All employees and consultants are directed to report to our senior management any irregular or suspicious activity that could indicate a cybersecurity threat or incident. The Audit Committee of our Board of Directors evaluates our cybersecurity assessment and management policies, including quarterly interviews with our senior officers and independent registered accounting firm.

Item 2. Properties

Our executive offices are located in approximately 12,030 square feet of leased office and laboratory space at 21 Business Park Drive, Branford, Connecticut 06405. The lease expires in 2027, subject to our option to extend the lease for two additional five-year terms. We currently pay $14,385 per month under the lease, which will increase to $14,745 in 2025, plus our pro rata share of certain operating expenses of the property.

We also lease approximately 1,093 square feet of additional laboratory space, which is located at 93 Shennecossett Road, Groton, Connecticut 06340. The lease expires in April 2025, subject to our option to extend the lease for an additional one-year term. We pay $7,235 per month under the lease plus our pro rata share of certain operating expenses of the property.

We also lease approximately 1,868 square feet of office and laboratory space, which is located at 500 Cartier Boulevard, Laval, Quebec, Canada. We pay $6,882 per month under the lease. The lease expires in April 2026, subject to our option to extend the lease for an additional one-year term.

We believe that our facilities are adequate to meet our current needs and that additional space can be obtained on commercially reasonable terms as needed.

Item 3. Legal Proceedings

As of the date of this report, there are no legal proceedings to which we or our properties are subject. We may be involved, from time to time, in legal proceedings and claims arising in the ordinary course of its business. Such matters are subject to many uncertainties and outcomes and are not predictable with assurance.

Item 4. Mine Safety Disclosures

Not applicable.

PART II

Item 5. Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Repurchases of Equity Securities

Market Information

Our common stock has trades on the NYSE American Stock Exchange under the symbol "AZTR."

Holders of Record

As of February 24, 2025, there were 34 holders of record of our common stock.

Dividend Policy

We have never declared or paid cash dividends on our common stock. We presently intend to retain earnings to finance the operation and expansion of our business.

Equity Compensation Plan Information

We have adopted the Azitra, Inc. 2016 Stock Incentive Plan, or 2016 Plan, providing for the grant of non-qualified stock options and incentive stock options to purchase shares of our common stock and for the grant of restricted and unrestricted share grants and restricted stock units. We currently have reserved 7,457 shares of our common stock under the 2016 Plan. The purpose of the 2016 Plan is to provide eligible participants with an opportunity to acquire an ownership interest in our company. All officers, directors, employees and consultants to our company are eligible to participate under the 2016 Plan. The 2016 Plan provides that options may not be granted at an exercise price less than the fair market value of our shares of common stock on the date of grant.

In March 2023, our Board and stockholders approved and adopted the Azitra, Inc. 2023 Stock Incentive Plan, or 2023 Plan, providing for the grant of non-qualified stock options and incentive stock options to purchase shares of our common stock and for the grant of restricted and unrestricted share grants and restricted stock units. We currently have reserved 1,209,735 shares of our common stock under the 2023 Plan. On October 3, 2024, the Company's Board of Directors approved amendments to the 2023 Plan that, subject to stockholder approval, would (i) increase the number of shares of Common Stock that may be issued under the 2023 Plan by 1,144,401 shares and (ii) adopt an evergreen provision to the 2023 Plan providing for an automatic 5% annual increase in the shares of Common Stock available for issuance under the 2023 Plan over the next 10 years commencing on January 1, 2026. Both amendments were approved by the Company's stockholders at the Company's annual stockholder meeting held on November 20, 2024. The purpose of the 2023 Plan is to provide eligible participants with an opportunity to acquire an ownership interest in our company. All officers, directors, employees and consultants to our company are eligible to participate under the 2023 Plan. The 2023 Plan provides that options may not be granted at an exercise price less than the fair market value of our shares of common stock on the date of grant.

The following table sets forth certain information as of December 31, 2024 about our 2016 Plan and 2023 Plan under which our equity securities are authorized for issuance.

Plan Category	(a) Number of Securities to be Issued Upon Exercise of Outstanding Options	(b) Weighted-Average Exercise Price of Outstanding Options	(c) Number of Securities Remaining Available for Future Issuance Under Equity Compensation Plans (Excluding Securities Reflected In Column (a))
Equity compensation plans approved by security holders	41,608	$ 41.60	1,209,735
Equity compensation plans not approved by security holders	—	—	—
Total	41,608	$ 41.60	1,209,735

Unregistered Sales of Equity Securities

Unregistered Sale of Equity Securities

None.

Item 6. Reserved

Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations Cautionary Statement

The following discussion and analysis should be read in conjunction with our statements and the related notes thereto contained elsewhere in this report. The information contained in this annual report on Form 10-K is not a complete description of our business or the risks associated with an investment in our common stock. We urge you to carefully review and consider the various disclosures made by us in this report and in our other filings with the Securities and Exchange Commission, or SEC, including the "Risk Factors" section in this report.

In this report we make, and from time to time we otherwise make written and oral statements regarding our business and prospects, such as projections of future performance, statements of management's plans and objectives, forecasts of market trends, and other matters that are forward-looking statements within the meaning of Section 27A of the Securities Act of 1933 and Section 21E of the Securities Exchange Act of 1934. Statements containing the words or phrases "will likely result," "are expected to," "will continue," "is anticipated," "estimates," "projects," "believes," "expects," "anticipates," "intends," "target," "goal," "plans," "objective," "should" or similar expressions identify forward-looking statements, which may appear in our documents, reports, filings with the SEC, and news releases, and in written or oral presentations made by officers or other representatives to analysts, stockholders, investors, news organizations and others, and in discussions with management and other of our representatives.

Our future results, including results related to forward-looking statements, involve a number of risks and uncertainties, including those risks included in the "Risk Factors" section in this report. No assurance can be given that the results reflected in any forward-looking statements will be achieved. Any forward-looking statement speaks only as of the date on which such statement is made. Our forward-looking statements are based upon assumptions that are sometimes based upon estimates, data, communications and other information from suppliers, government agencies and other sources that may be subject to revision. Except as required by law, we do not undertake any obligation to update or keep current either (i) any forward-looking statement to reflect events or circumstances arising after the date of such statement or (ii) the important factors that could cause our future results to differ materially from historical results or trends, results anticipated or planned by us, or which are reflected from time to time in any forward-looking statement.

General

We were formed in January 2014 as a biopharmaceutical company focused on developing innovative therapies for precision dermatology using engineered proteins and live biotherapeutic products. We are an early-stage clinical biopharmaceutical company and have not commenced commercial operations.

To date, we have capitalized our operations primarily through a series of private placements of our convertible preferred stock and convertible promissory notes and our initial public offering, IPO, of common stock which closed on June 21, 2023 and subsequent offerings. In connection with our IPO, we issued 1.5 million shares of our common stock at a public offering price of $5 per share. Concurrent with the close of our IPO, all of our outstanding shares of convertible preferred stock and convertible promissory notes converted into a total of 8,951,526 shares of our common stock. In July 2024, we completed a follow-on public offering in which we issued 6,665,000 shares of our common stock at a price of $1.50 per share and Class A Warrants exercisable for an aggregate 13,330,000 shares of common stock. The net proceeds received by us from the follow-on public offering were $9.1 million, after deducting underwriting discounts, commissions and other offering expenses. The Class A Warrants had an initial exercise price of $1.50 that was adjusted to $0.7043 in accordance with a reset price provision determined 30 days following the issuance date. In January 2025, we completed a public offering of 4,857,780 shares of our common stock, at an offering price of $0.30 per share, in which we received net proceeds of approximately $1.3 million, after deducting underwriter discounts and offering expenses, and in February 2025 we completed a registered direct offering of 2,495,5818 shares of our common stock, at an offering price of $0.2785 per share, in which we received net proceeds of approximately $695 thousand, after deducting placement agent commissions and offering expenses.

As of February 24, 2025, we had 14,979,354 shares of our common stock issued and outstanding. Except as otherwise indicated, all share and share price amounts in this report gives effect to a forward stock split effected on May 17, 2023 at a ratio of 7.1-for-1, and the reverse stock split effected on July 1, 2024 at a ratio of 1-for-30.

Overview

We focused on developing innovative therapies for precision dermatology using engineered proteins and topical live biotherapeutic products. We have built a proprietary platform that includes a microbial library comprised of approximately 1,500 unique bacterial strains that can be screened for unique therapeutic characteristics. The platform is augmented by an artificial intelligence and machine learning technology that analyzes, predicts and helps screen our library of strains for drug like molecules. The platform also utilizes a licensed genetic engineering technology, which can enable the transformation of previously genetically intractable strains. Our initial focus is on the development of genetically engineered strains of *Staphylococcus epidermidis, or S. epidermidis*, which we consider to be an optimal therapeutic candidate species for engineering of dermatologic therapies. The particular species demonstrates a number of well-described properties in the skin. As of the date of this report, we have identified among our microbial library over 60 distinct bacterial species that we believe are capable of being engineered to create living organisms or engineered proteins with significant therapeutic effect.

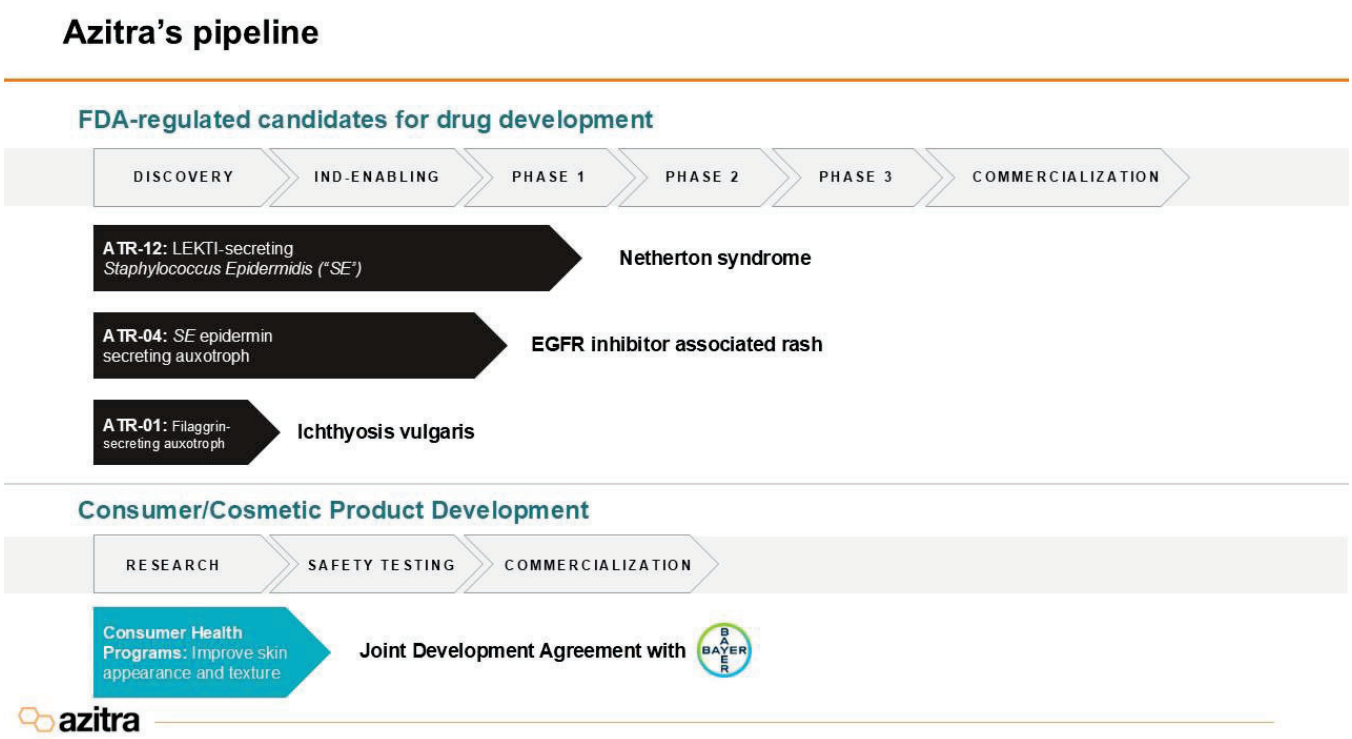
We are a pioneer in genetically engineered bacteria for therapeutic use in dermatology. Our goal is to leverage our platforms and internal microbial library bacterial strains to create new therapeutics that are either engineered living organisms or engineered proteins or peptides to treat skin diseases. Our initial focus is on the development of our current product candidates, including:

- **ATR-12**, a genetically modified strain of *S. epidermidis* for treating the orphan disease, Netherton syndrome, a chronic and sometimes fatal disease of the skin estimated to affect approximately one to nine in every 100,000, but its prevalence may be underestimated due to misdiagnosis caused by similarities to other skin diseases. We received Pediatric Rare Disease Designation for ATR-12 by the United States Food and Drug Administration, or FDA, in 2019. In December 2022, we submitted an investigational new drug application, or IND, for a Phase 1b clinical trial of ATR-12 in adult Netherton syndrome patients, and on January 27, 2023 we received notification from the FDA that the "study may proceed" with respect to the proposed Phase 1b clinical trial. After submitting post-IND manufacturing reports, we have commenced operating activities for our Phase 1b clinical trial in December 2023, and we have dosed our first patient in August 2024. We expect to report initial safety results in the first half of 2025.

- **ATR-04**, a genetically modified strain of *S. epidermidis* for treating the papulopustular rash experienced by cancer patients undergoing epidermal growth factor receptor inhibitor, or EGFRi, targeted therapy. In August 2024, we obtained IND clearance from the FDA to commence a Phase 1/2 clinical trial in certain cancer patients undergoing EGFRi targeted therapy. In September 2024, we obtained Fast Track designation by the FDA in this indication. We expect to dose the first patient in the Phase 1/2 clinical trial in the first half of 2025.

- **ATR-01**, a genetically modified strain of *S. epidermidis* that expresses an engineered recombinant human filaggrin protein for treating ichthyosis vulgaris, a chronic, xerotic (abnormally dry), scaly skin disease with an estimated incidence and prevalence of 1 in 250, which suggests a total patient population of 1.3 million in the United States. We are planning to perform lead optimization and IND-enabling studies in 2025 to support an IND filing.

- Two separate strains of bacterial microbes are being investigated and developed by us and Bayer Consumer Care AG, the consumer products division of Bayer AG, or Bayer, the international life science company. We entered into a Joint Development Agreement, or JDA, with Bayer in December 2019. Under the terms of the JDA, we are responsible for testing our library of bacterial strains and their natural products for key preclinical properties. After screening through hundreds of strains, we and Bayer have selected two particular strains to move forward into further development. Bayer holds the exclusive option to license the patent rights to these strains.



We also have established partnerships with teams from Carnegie Mellon University and the Fred Hutchinson Cancer Center, or Fred Hutch, two of the premier academic centers in the United States. Our collaboration with the Carnegie Mellon based team also takes advantage of the power of whole genome sequencing. This partnership is mining our proprietary library of bacterial strains for novel, drug like peptides and proteins. The artificial intelligence/machine learning technology developed by this team predicts the molecules made by microbes from their genetic sequences. The system then compares the predictions to the products actually made through tandem mass spectroscopy and/or nuclear magnetic resonance imaging to refine future predictions. The predictions can be compared to publicly available 2D and 3D protein databases to select drug like structures.

We hold an exclusive, worldwide license from Fred Hutch regarding the use of its patented SyngenicDNA Minicircle Plasmid, or SyMPL, technologies for all fields of genetic engineering, including to discover, develop and commercialize engineered microbial therapies and microbial-derived peptides and proteins for skin diseases. We are utilizing our licensed patent rights to build plasmids in order to make genetic transformations that have never been previously achieved. To date, our team has successfully engineered our lead therapeutic candidates without the SyMPL technology. However, we believe that SyMPL will open up the ability to make genetic transformations of an expanded universe of microbial species, and we expect that some or all of our future product candidates will incorporate the SyMPL technology. Our collaboration with Fred Hutch is led by Dr. Christopher Johnston, an expert in microbial engineering, and the innovator behind the SyMPL technology.

Our Strategy

Beyond our three lead product candidates and collaboration with Bayer, our goal is to develop a broad portfolio of product candidates focused on expanding the application of our platforms for precision dermatology. We believe that we have established a unique position in advancing the development of biologics for precision dermatology.

We intend to create a broad portfolio of product candidates for precision dermatology through our development of genetically engineered proteins selected from our proprietary microbial library of approximately 1,500 unique bacterial strains. Our strategy is as follows:

- ***Build a sustainable precision dermatology company.*** Our goal is to build a leading precision dermatology company with a sustainable pipeline of product candidates. To that end, we are focused on rapidly advancing our current pipeline of live biotherapeutic candidates while actively developing additional product candidates. Each of our current product candidates are proprietary and subject to pending patent applications. We expect that most, if not all, genetically engineered product candidates we develop will be eligible for patent protection.

- ***Advance our lead product candidates, ATR-12 and ATR-04, through clinical trials.*** In 2022, we obtained pre-IND correspondence with the FDA for purposes of discussing our proposed regulatory pathway for ATR-12 and obtaining guidance from the FDA on the preclinical plan leading to the filing and acceptance of an IND for ATR-12. In December 2022, we filed an IND for a first-in-human trial of ATR-12 in Netherton syndrome patients. On January 27, 2023, we received notification from the FDA that the "study may proceed" with respect to the proposed Phase 1b clinical trial, and in August 2024 we initiated dosing the first patient in its Phase 1b clinical trial evaluating ATR-12. In August 2024, we received IND clearance from the FDA for a first-in-human Phase 1b/2a clinical trial in patients with EGFRi-associated rash, and in September 2024, the FDA granted Fast Track designation for ATR-04. We commenced a Phase 1b trial of our ATR-04 in certain cancer patients undergoing EGFRi therapy in the fourth quarter of 2024. We expect to dose the first patient in the Phase 1/2 clinical trial with ATR-04 in the first half of 2025. We expect to report initial safety results of the first patients dosed in our Phase 1b clinical trial for our ATR-12 in Netherton syndrome patients in early 2025 with full results anticipated in the second half of 2025.

- ***Broaden our platform by selectively exploring strategic partnerships that maximize the potential of our precision dermatology programs.*** We intend to maintain significant rights to all of our core technologies and product candidates. However, we will continue to evaluate partnering opportunities in which a strategic partner could help us to accelerate development of our technologies and product candidates, provide access to synergistic combinations, or provide expertise that could allow us to expand into the treatment of different types of skin diseases. We may also broaden the reach of our platform by selectively in-licensing technologies or product candidates. In addition, we will consider potentially out-licensing certain of our proprietary technologies for indications and industries that we are not ourselves pursuing. We believe our genetic engineering techniques and technologies have applicability outside of the field of medicine, including cosmetics and in the generation of clean fuels and bioremediation.

- ***Leverage our academic partnerships.*** We currently have partnerships with investigators at the Fred Hutchinson Cancer Center, Yale University, Jackson Laboratory for Genomic Medicine, and Carnegie Mellon University. We expect to leverage these partnerships and potentially expand them or form other academic partnerships to bolster our engineering platforms and expand our research and development pipeline.

- ***Expand on our other potential product candidates.*** Beyond our three lead product candidates, our goal is to develop a broad portfolio of product candidates focused on expanding the application of our platforms for precision dermatology. We have a proprietary platform for discovering and developing therapeutic products for precision dermatology. Our platform is built around a microbial library comprised of approximately 1,500 unique bacterial strains to allow screening for unique therapeutic characteristics and utilizes a microbial genetic technology that analyzes, predicts and engineers the proteins, peptides and molecules made by skin microbes. Our ability to genetically engineer intractable microbial species is uniquely leveraged by our exclusive license to the SyMPL technology.

Results of Operations

We are an early-stage clinical biopharmaceutical company, formed in January 2014, and have limited operating history. We have not commenced revenue-producing operations apart from limited service revenue derived through our JDA with Bayer. Under the terms of the JDA, we are responsible for testing our library of microbial strains and their natural products for key preclinical properties and Bayer reimburses us for our development costs. To date, our operations have consisted of the development of our proprietary microbial library, the identification, characterization and testing of certain bacterial species from our microbial library that we believe are capable of being engineered to provide significant therapeutic effect and the development of our initial product candidates.

Year Ended December 31, 2024 **Compared to** Year Ended December 31, 2023

The following table summarizes our results of operations with respect to the items set forth below for the years ended December 31, 2024 and 2023 together with the percentage change for those items.

	Year Ended December 31,			
	2024	2023	$ Change	% Change
Service revenue - related party	$ 7,500	$ 686,000	$ (678,500)	(99)%
Total revenue	7,500	686,000	(678,500)	(99)%
Operating expenses:				
General and administrative	6,269,262	4,493,332	1,775,930	40%
Research and development	4,723,378	3,643,214	1,080,164	30%
Total operating expenses	10,992,640	8,136,546	2,856,094	35%
Loss from operations	(10,985,140)	(7,450,546)	(3,534,594)	47%
Non operating income (expense)				
Interest income	122,553	1,577	120,976	7671%
Interest expense	(12,160)	(167,726)	155,566	(93)%
Change in fair value of convertible note	—	(3,630,100)	3,630,100	(100)%
Change in fair value of warrants	4,034,072	34,930	3,999,142	(100)%
Loss on issuance of common stock	(2,132,800)	—	(2,132,800)	(100)%
Other income (expense)	15,014	(54,608)	69,622	(127)%
Total other income (expense)	2,026,679	(3,815,927)	5,842,606	(153)%
Loss before income taxes	(8,958,461)	(11,266,473)	2,308,012	(20)%
Income tax expense	(9,031)	(17,308)	8,277	(48)%
Net loss	(8,967,492)	(11,283,781)	2,316,289	(21)%
Dividends on preferred stock	—	(1,355,347)	1,355,347	(100)%
Net loss attributable to common shareholders	$ (8,967,492)	$ (12,639,128)	$ 3,671,636	(29)%

Service Revenue - Related Party

We generated $7,500 of service revenue under the Bayer JDA during the year ended December 31, 2024 compared to service revenue of $686,000 under the JDA for the year ended December 31, 2023. The decrease of $(678,500) in service revenue is attributable to a decrease in the amount of reimbursable development costs in 2024, and the Company does not expect any significant future revenue under the Bayer JDA.

General and Administrative

General and administrative costs during the year ended December 31, 2024 increased by $1.8 million, or 40%, to $6.3 million from the prior year. The increase was primarily related to the costs incurred following, and a result of, our emergence as a public company in June 2023, including $1.2 million of salaries and benefits primarily attributable to hiring our CFO and COO, an increase of $111,000 primarily related to the achievement of a milestone for our CEO's performance based options, an increase of $172,000 in public relations, an increase of $162,000 of insurance costs and a net increase of $111,000 in other overhead expenses.

Research and Development

Research and development expenses include salaries and benefits of all research personnel, payments to contract research organizations, payments to research consultants, and the purchase of lab supplies. These expenses are offset by income earned from government grant payments.

During the year ended December 31, 2024, research and development expenses increased by $1.1 million, or 30%, to $4.7 million from the prior year period. The increase was primarily related to an increase of $450,000 in payroll related costs, $500,000 in research and development related costs attributable to our efforts in moving our EGFR program forward, an increase of $37,000 in moving our Netherton program forward, and a net increase of $113,000 of other costs. There was no government and nonprofit grant revenue received by us during fiscal year 2024 or 2023, and do not expect any future grant revenue at this time.

We expect our research and development expenses to significantly increase in the future due primarily to our planned clinical trial activity and continued development of product candidates.

Non-operating income (expense)

Our non-operating income (expense) consists of refundable research and development credits, change in the valuation of warrants carried at fair market value, loss on the issuance of stock, loss on disposal of equipment, loss on foreign currency translation, change in fair value of the convertible note, interest income, and interest expense. During the year ended December 31, 2024, non-operating income (expense) increased by $5.8 million, or (153)%, compared to the comparable period in fiscal 2023. The increase was primarily attributable to a $3.6 million decrease in fair value of the convertible note and an increase of $4.0 million attributable to the decrease in valuation of the warrants. This was offset by a one-time $2.1 million loss attributable to the issuance of stock, and a a net increase of $0.3 million attributable to other income (expense).

Financial Condition

As of December 31, 2024, we had total assets of approximately $7.4 million and working capital of approximately $3.9 million. As of December 31, 2024, our liquidity included approximately $4.6 million of cash and cash equivalents. In January 2025, we completed a public offering of shares of our common stock for the net proceeds of approximately $1.3 million, and in February 2025 we completed a registered direct offering of shares of our common stock for the net proceeds of approximately $695 thousand. After giving effect to both offerings, we believe that our cash on-hand as of the date of this report will be not sufficient to cover our proposed plan of operations beyond six months from the date of this report. We intend to seek additional funds through various financing sources, including the sale of our equity and debt securities, licensing fees for our technology and joint ventures with industry partners. In addition, we will consider alternatives to our current business plan that may enable us to achieve revenue producing operations and meaningful commercial success with a smaller amount of capital. However, there can be no guarantees that such funds will be available on commercially reasonable terms, if at all. If such financing is not available on satisfactory terms, we may be required to scale back our proposed plan of operations and we may be unable to continue operations.

To the extent that we raise additional capital through the sale of equity or convertible debt securities, our common stockholders' ownership interests will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect rights as a common stockholder. Debt financing and preferred equity financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making acquisitions or capital expenditures or declaring dividends. If we raise additional funds through collaborations, strategic alliances or marketing, distribution or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates, or grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings or other arrangements when needed, we may be required to delay, limit, reduce or terminate our research, product development or future commercialization efforts, or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

Due to our accumulated deficit, recurring and negative cash flow from operations there is substantial doubt about our ability to continue as a going concern. Our financial statements include disclosure with respect to a substantial doubt about our ability to continue as a going concern and the report of our independent auditor includes an explanatory paragraph with respect to that substantial doubt.

Cash Flows

The following table shows a summary of our cash flows for the periods indicated:

	December 31,	
	2024	**2023**
Net cash used in operating activities	$ (10,183,740)	$ (7,362,375)
Net cash used in investing activities	$ (379,246)	$ (318,259)
Net cash provided by financing activities	$ 13,321,716	$ 5,983,967
Net decrease in cash	$ 2,758,730	$ (1,696,667)

Operating Activities

During the year ended December 31, 2024, operating activities used $10.2 million of cash primarily driven by our net loss of $9.0 million and by non-cash items of $1.2 million. During fiscal 2023, operating activities used $7.4 million of cash primarily driven by our net loss of $11.3 million offset by non-cash items of $3.9 million.

Investing Activities

During the year ended December 31, 2024, investing activities used $0.4 million of cash primarily driven by $0.4 million of deferred patent costs and patent and trademark costs. During fiscal 2023, investing activities used $0.3 million of cash primarily driven by $0.3 million of deferred patent costs and patent and trademark costs.

Financing Activities

During the year ended December 31, 2024, financing activities provided $13.3 million in cash primarily driven by proceeds from our follow-on public offerings. During fiscal 2023, financing activities provided $6.0 million in cash primarily driven by the proceeds from our initial public offering.

Critical Accounting Estimates

Our management's discussion and analysis of our financial condition and results of operations are based on our consolidated financial statements, which have been prepared in accordance with U.S. generally accepted accounting principles. The preparation of these consolidated financial statements requires us to make judgments and estimates that affect the reported amounts of assets, liabilities, 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 are believed to be reasonable under the circumstances. Actual results may differ from these estimates under different assumptions or conditions. On an ongoing basis, we evaluate our judgments and estimates in light of changes in circumstances, facts and experience. The effects of material revisions in estimates, if any, will be reflected in the consolidated financial statements prospectively from the date of change in estimates.

Item 7A. Quantitative and Qualitative Disclosures About Market Risk Disclosures

Not applicable.

Item 8. Financial Statements and Supplementary Data

Index to Financial Statements

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Board of Directors and Stockholders of Azitra, Inc.
Branford, CT

Opinion on the Financial Statements

We have audited the accompanying balance sheets of Azitra, Inc. (the "Company") as of December 31, 2024 and 2023, and the related statements of operations, stockholders' equity, and cash flows for the years then ended, and the related notes (collectively referred to as the financial statements). In our opinion, the financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2024 and 2023, and the results of its operations and its cash flows for the years then ended, in conformity with accounting principles generally accepted in the United States of America.

Substantial Doubt Regarding the Company's Ability to Continue as a Going Concern

The accompanying financial statements have been prepared assuming that Azitra, Inc., will continue as a going concern. As discussed in Note 1 to the financial statements, the Company's significant operating losses raise substantial doubt regarding the entity's ability to continue as a going concern. Management's evaluation of the events and conditions, and management's plans regarding those matters, are also described in Note 1. The financial statements do not include any adjustments that might result from the outcome of this uncertainty. Our opinion is not modified with respect to this matter.

Basis for Opinion

These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's 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 audit to obtain reasonable assurance about whether the 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 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 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 financial statements. We believe that our audits provide a reasonable basis for our opinion.

GRASSI & CO., CPAs, P.C.
We have served as the Company's auditor since 2022.
Jericho, New York
February 24, 2025

AZITRA, INC.

BALANCE SHEETS

	December 31, 2024	December 31, 2023
ASSETS		
Current assets:		
Cash and cash equivalents	$ 4,554,719	$ 1,795,989
Accounts receivable	233	8,255
Accounts receivable - related party	—	90,000
Tax credits receivable	101,663	118,383
Income tax receivable	—	6,836
Deferred offering costs	4,106	67,859
Prepaid expenses	567,569	448,257
Total current assets	**5,228,290**	**2,535,579**
Property and equipment, net	653,957	710,075
Financing lease right-of-use asset	24,522	40,002
Operating lease right-of-use asset	527,393	828,960
Intangible assets, net	246,420	210,881
Deferred patent costs	593,802	742,229
Deferred issuance costs	37,477	—
Other assets	46,941	47,760
Total assets	**$ 7,358,802**	**$ 5,115,486**
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities:		
Accounts payable	490,255	897,272
Income tax payable	11,572	—
Current financing lease liability	16,066	14,600
Current operating lease liability	255,177	307,655
Accrued expenses	602,787	383,668
Total current liabilities	**1,375,857**	**1,603,195**
Long-term financing lease liability	10,105	26,169
Long-term operating lease liability	274,161	537,523
Warrant liability	381	35,453
Total liabilities	**1,660,504**	**2,202,340**
Commitments and contingencies (Note 13)		
Stockholders' equity		
Preferred stock; $0.0001 par value; 10,000,000 shares authorized at December 31, 2024 and December 31, 2023; 0 shares issued at December 31, 2024 and December 31, 2023	—	—
Common stock; $0.0001 par value, 100,000,000 shares authorized at December 31, 2024 and December 31, 2023, 7,626,056 and 403,246 shares issued and outstanding at December 31, 2024 and December 31, 2023, respectively	763	40
Additional paid-in capital	63,263,360	51,510,269
Accumulated deficit	(57,565,825)	(48,597,163)
Total stockholders' equity	**5,698,298**	**2,913,146**
Total liabilities and stockholders' equity	**$ 7,358,802**	**$ 5,115,486**

The accompanying notes are an integral part of these financial statements.

AZITRA, INC.

STATEMENTS OF OPERATIONS

	For the Year Ended December 31, 2024	2023
Service revenue - related party	$ 7,500	$ 686,000
Total revenue	7,500	686,000
Operating expenses:		
General and administrative	6,269,262	4,493,332
Research and development	4,723,378	3,643,214
Total operating expenses	10,992,640	8,136,546
Loss from operations	(10,985,140)	(7,450,546)
Other income (expense):		
Interest income	122,553	1,577
Interest expense	(12,160)	(167,726)
Change in fair value of convertible note	—	(3,630,100)
Change in fair value of warrants	4,034,072	34,930
Loss on issuance of common stock	(2,132,800)	—
Other income (expense)	15,014	(54,608)
Total other income (expense)	2,026,679	(3,815,927)
Loss before income taxes	(8,958,461)	(11,266,473)
Income tax expense	(9,031)	(17,308)
Net loss	(8,967,492)	(11,283,781)
Dividends on preferred stock	—	(1,355,347)
Net loss attributable to common shareholders	$ (8,967,492)	$ (12,639,128)
Net loss per share, basic and diluted	$ (2.37)	$ (54.98)
Weighted average common stock outstanding, basic and diluted	3,784,482	229,866

The accompanying notes are an integral part of these financial statements.

AZITRA, INC.

STATEMENTS OF CHANGES IN STOCKHOLDERS' EQUITY (DEFICIT)

	Series A Convertible Preferred Stock		Series A-1 Convertible Preferred Stock		Series B Convertible Preferred Stock		Common Stock		Additional Paid-in-	Accumulated	Total Stockholders'
	Shares	Amount	Shares	Amount	Shares	Amount	Shares	Amount	Capital	Deficit	Equity (Deficit)
Balance - December 31, 2022	**205,385**	**$ 3,272,944**	**380,657**	**$ 14,100,533**	**391,303**	**$ 16,321,065**	**34,791**	**$ 3**	**$ 1,054,239**	**$ (37,314,552)**	**$ (36,260,310)**
Issuance of Series B Convertible Preferred Stock	—	—	—	—	23,432	1,124,759	—	—	—	—	—
Conversion of convertible notes payable	—	—	—	—	—	—	61,534	6	9,495,066	—	9,495,072
Conversion of preferred stock	(205,385)	(3,272,944)	(380,657)	(14,100,533)	(414,735)	(17,445,824)	256,921	26	34,819,275	—	34,819,301
Initial public offering, net of issuance costs of $1,508,641	—	—	—	—	—	—	50,000	5	5,991,354	—	5,991,359
Stock-based compensation	—	—	—	—	—	—	—	—	151,505		151,505
Net loss	—	—	—	—	—	—	—	—	—	(11,283,781)	(11,283,781)
Balance - December 31, 2023	**—**	**$ —**	**—**	**$ —**	**—**	**$ —**	**403,246**	**$ 40**	**$51,511,439**	**$ (48,598,333)**	**$ 2,913,146**
Exercise of stock options	—	—	—	—	—	—	1,333	—	19,100	—	19,100
Follow-on public offering, net of issuance costs of $709,426	—	—	—	—	—	—	555,567	56	4,290,618	—	4,290,674
Follow-on public offering issuance costs adjustment	—	—	—	—	—	—	—	—	(227)	—	(227)
Follow-on public offering, net of issuance costs of $933,960	—	—	—	—	—	—	6,665,000	667	9,062,873	—	9,063,540
Reclass of warrant liability	—	—	—	—	—	—		—	(1,866,200)	—	(1,866,200)
Exercise of Warrants	—	—	—	—	—	—	1,000	—	704	—	704
Partial Share Cancellation Reverse Stock Split	—	—	—	—	—	—	(90)	—	—	—	—
Stock based compensation expense	—	—	—	—	—	—	—	—	245,053	—	245,053
Net loss	—	—	—	—	—	—	—	—	—	(8,967,492)	(8,967,492)
Balance - December 31, 2024	**—**	**$ —**	**—**	**$ —**	**—**	**$ —**	**7,626,056**	**$ 763**	**$63,263,360**	**$ (57,565,825)**	**$ 5,698,298**

The accompanying notes are an integral part of these financial statements.

AZITRA, INC.

STATEMENTS OF CASH FLOWS

	For the Year Ended December 31,	
	2024	**2023**
Cash flows from operating activities:		
Net loss	$ (8,967,492)	$ (11,283,781)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization	131,188	129,653
Amortization of right-of-use assets	317,047	295,896
Change in foreign currency rates on remeasurement of Canadian fixed assets	(14,198)	—
Accrued interest on convertible notes	—	166,019
Stock based compensation	245,053	151,505
Change in fair value of warrant liability	(4,034,072)	(34,830)
Loss on issuance of common stock	2,132,800	—
Change in fair value of convertible notes	—	3,630,100
Forgiveness of accounts payable	—	(56,285)
Loss on disposal of property and equipment	4,859	41,417
Impairment of intangible assets and deferred patent costs	442,793	351,360
Changes in operating assets and liabilities:		
Accounts receivable	98,022	84,565
Prepaid expenses	(119,312)	(288,124)
Other assets	819	(253)
Tax credits receivable	16,720	(48,717)
Income tax receivable	18,408	6,886
Accounts payable and accrued expenses	(140,535)	(68,684)
Operating lease liability	(315,840)	(283,102)
Contract liabilities	—	(156,000)
Net cash used in operating activities	(10,183,740)	(7,362,375)
Cash flows from investing activities:		
Purchases of property and equipment	(8,569)	(26,544)
Deferred patent costs	(370,677)	(214,152)
Capitalization of licenses	—	(77,563)
Net cash used in investing activities	(379,246)	(318,259)
Cash flows from financing activities		
Payment of deferred issuance costs	(37,477)	—
Principal payments on finance leases	(14,598)	(7,392)
Proceeds from public offerings, net	13,354,691	5,991,359
Proceeds from exercise of stock options	19,100	—
Net cash provided by financing activities	13,321,716	5,983,967
Net change in cash and cash equivalents	2,758,730	(1,696,667)
Cash and cash equivalents at beginning of period	1,795,989	3,492,656
Cash and cash equivalents at end of period	$ 4,554,719	$ 1,795,989
Supplemental disclosure of non-cash investing and financing information:		
Obtaining a right-of-use asset in exchange for financing lease liability	$ —	$ 46,452
Conversion of note to common stock	$ —	$ 9,495,066
Conversion of note to Series B Convertible Preferred Stock	$ —	$ 1,124,759
Purchases of fixed assets in accounts payable	$ 45,999	$ —
Conversion of Series A, A-1, B Convertible Preferred Stock to Common Stock	$ —	$ 34,819,301

The accompanying notes are an integral part of these financial statements.

1. Organization and Nature of Operations

Azitra, Inc. (the "Company") was founded on January 2, 2014. It is a synthetic biology company focused on screening and genetically engineering microbes of the skin. The mission is to discover and develop novel therapeutics to create a new paradigm for treating skin disease. The Company's discovery platform is screened for naturally occurring bacterial cells with beneficial effects. These microbes are then genomically sequenced and engineered to make cellular therapies, recombinant therapeutic proteins, peptides and small molecules for precision treatment of dermatology diseases. On May 17, 2023, the Company changed its name to from "Azitra Inc" to "Azitra, Inc."

The Company maintains a location in Montreal, Canada for certain research activities. The Company also opened a manufacturing and laboratory space in Groton, Connecticut during 2021.

Stock Splits, Change in Par Value, and Initial and Follow-on Public Offerings

In June 2023, the Company completed its initial public offering (IPO) in which it issued and sold 50,000 shares of its common stock at a price to the public of $150.00 per share. The shares began trading on the NYSE American on June 16, 2023 under the symbol "AZTR". The net proceeds received by the Company from the offering were $6.0 million, after deducting underwriting discounts, commissions and other offering expenses.

Immediately prior to the effectiveness of the Company's registration statement, the Company effected a 7.1-for-1 forward stock split (the "Forward Stock Split") of its issued and outstanding shares of common stock (the Forward Stock Split). On May 17, 2023, the Company changed the par value of its capital stock from $0.01 to $0.0001. Accordingly, all share and per share amounts for all periods presented in the accompanying audited financial statements and notes thereto have been adjusted retroactively, unless otherwise noted, to reflect the effect of the Forward Stock Split. Refer to Note 7 for additional details relating to the Forward Stock Split.

In February 2024, the Company completed a follow-on public offering in which it issued and sold 555,567 shares of its common stock at a price to the public of $9.00 per share. The net proceeds received by the Company from the follow-on public offering were $4.3 million, after deducting underwriting discounts, commissions and other offering expenses.

On July 1, 2024, the Company effected a 30-for-1 reverse stock split of its issued and outstanding shares of common stock (the "Reverse Stock Split") and began trading on a split-adjusted basis the same day. There was no change in par value. Accordingly, all share and per share amounts for all periods presented in the accompanying audited financial statements and notes thereto have been adjusted retroactively, where applicable, to reflect the effect of the Reverse Stock Split. Refer to Note 7 for additional details relating to the Reverse Stock Split.

In July 2024, the Company completed a follow-on public offering in which it issued and sold 6,665,000 shares of its common stock at a price of $1.50 per share and Class A Warrants exercisable for an aggregate 13,330,000 shares of common stock. The net proceeds received by the Company from the follow-on public offering were $9.1 million, after deducting underwriting discounts, commissions and other offering expenses. The Class A Warrants had an initial exercise price of $1.50 that was adjusted to $0.7043 in accordance with a reset price provision determined 30 days following the issuance date. Refer to Note 7 for additional details relating to the follow-on offering.

Going Concern Matters

The financial statements have been prepared on the going concern basis, which assumes that the Company will continue in operation for the foreseeable future, and which contemplates the realization of assets and liquidation of liabilities in the normal course of business. However, management has identified the following conditions and events that created an uncertainty about the ability of the Company to continue as a going concern. As of and for the for the year ended December 31, 2024, the Company has an accumulated deficit of $57.6 million, a loss from operations of $11.0 million, used $10.2 million to fund operations and had $3.9 million of working capital. These factors among others raise substantial doubt about the Company's ability to continue as a going concern.

The Company will require a significant amount of additional funds to complete the development of its product and to fund additional losses which the Company expects to incur over the next few years. The Company is still in its pre-commercialization phase and therefore does not yet have product revenue. Management plans to continue to raise funds through equity and debt financing to fund operating and working capital needs, however, there can be no assurance that the Company will be successful in securing additional financing, if needed, to meet its operating needs.

These conditions and events create substantial doubt about the ability of the Company to continue as a going concern for twelve months from the date that the financial statements are available to be issued. The financial statements do not include any adjustments that might be necessary should the Company be unable to continue as a going concern.

2. Summary of Significant Accounting Policies

Basis of Accounting

The financial statements of the Company are prepared in accordance with United States generally accepted accounting principles ("U.S. GAAP").

Reclassification and Revision of Prior Period Financial Statements

Certain prior period amounts and disclosures have been reclassified to conform to the current period's financial presentation. During the year ended December 31, 2024, the Company identified an immaterial error in the statements of operations for the periods ended December 31, 2024 and 2023 relating to a misclassification between Other income (expense) and Research and development expenses resulting from the forgiveness of accounts payable in the amount of $56,285. The Company determined the error was not material to any previously issued financial statements; however, the Company decided to revise the prior periods impacted. The prior period revisions had no impact on our previously reported net loss; however, the revision decreased our Research and development expenses and Total operating expenses, and increased our Other income (expense).

Use of Estimates

The preparation of the financial statement in conformity with U.S. GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities at the date of the balance sheet. While management believes the estimates and assumptions used in the preparation of the financial statement are appropriate, actual results could differ from those estimates.

Cash and Cash Equivalents

For purposes of the balance sheets and statements of cash flows, the Company considers all cash on hand, demand deposits and all highly liquid investments with original maturities of three months or less to be cash equivalents.

Property and Equipment

Property and equipment are recorded at cost. Depreciation is computed using the straight-line method over the estimated useful lives, which range from 3 to 10 years. Expenditures for maintenance and repairs, which do not extend the economic useful life of the related assets, are charged to operations as incurred. Gains or losses on disposal of property and equipment are reflected in the statements of operations in the period of disposal.

Accounts Receivable

The Company carries its accounts receivable at cost less an allowance for credit losses. The Company had accounts receivable of $175,000 at December 31, 2022. On a periodic basis, the Company evaluates its accounts receivable and establishes an allowance for credit losses based on a history of past write-offs, collections and current conditions. There was no allowance for credit losses at December 31, 2024 and 2023. Accounts receivable are written off when deemed uncollectible. Recoveries of accounts receivable previously written off are recorded when received.

Deferred Offering Costs

The Company capitalized deferred offering costs, which primarily consisted of direct, incremental legal, professional, accounting, and other third-party fees relating to the Company's initial public offering and follow-on offerings. In June 2023 the Company consummated its IPO. In February and July 2024, the Company consummated its follow-on offerings. The Company recorded these amounts against the gross proceeds of these offerings within the statements of stockholders' equity during the periods ended December 31, 2024 and 2023.

In July 2024, the Company also filed a Form S-3 Registration Statement and recorded deferred issuance costs as a long-term asset and will reclass a portion of these costs against gross proceeds upon such time the proceeds are raised.

Leases

The Company elected to account for non-lease components as part of the lease component to which they relate. Lease accounting involves significant judgments, including making estimates related to the lease term, lease payments, and discount rate. In accordance with the guidance, the Company recognized ROU assets and lease liabilities for all leases with a term greater than 12 months. Leases are classified as either operating or financing leases based on the economic substance of the agreement.

The Company has 3 operating leases for buildings with a ROU asset and lease liability totaling $1,418,502. The basis, terms and conditions of the leases are determined by the individual agreements. The Company's option to extend certain leases ranges from 36 – 52 months. All options to extend have been included in the calculation of the ROU asset and lease liability. The leases do not contain residual value guarantees, restrictions, or covenants that could incur additional financial obligations to the Company. There are no subleases, sale-leaseback, or related party transactions.

At December 31, 2024, the Company had operating right-of-use assets with a net value of $527,393 and current and long-term operating lease liabilities of $255,177 and $274,161, respectively.

In 2023, the Company entered into a lease for the use of certain equipment that is classified as a finance lease. The finance lease has a term of 36 months. At December 31, 2024, the Company had financing right-of-use assets with a net value of $24,522 and current and long-term operating lease liabilities of $16,066 and $10,105, respectively.

Intangible Assets

Intangible assets consist of trademarks and patents. All costs directly related to the filing and prosecution of patent and trademark applications are capitalized. Patents are amortized over their respective remaining useful lives upon formal approval. Trademarks have an indefinite life.

The Company accounts for other indefinite life intangible assets in accordance ASC Topic 350, *Goodwill and Other Intangible Assets* (ASC 350). ASC 350 requires that intangible assets that have indefinite lives are required to be tested at least annually for impairment or whenever events or changes in circumstances indicate that the carrying amount may not be recoverable. Intangible assets that have finite lives will continue to be amortized over their useful lives.

Deferred Patent Costs

Deferred patent costs represent legal and filing expenses incurred related to the submission of patent applications for patents pending approval. These deferred costs will be reclassed to intangible assets and begin to be amortized over their estimated useful lives upon the formal approval of the patent. If the patent is not issued, the costs associated with the patent will be expensed in the year the patent was rejected. Deferred patent costs are reviewed for impairment at each reporting period. The costs associated with any impairment are expensed in the period the deferred patent costs are determined to be impaired. The Company recorded impairment expenses of $442,793 and $351,360 during the years ended December 31, 2024 and 2023, respectively.

Impairment of Long-Lived Assets

In accordance with ASC Topic 360-10, Accounting for the Impairment or Disposal of Long-Lived Assets (ASC 360-10), the Company's policy is to review its long-lived assets for impairment whenever events or changes in circumstances indicate that the carrying amount of an asset may not be recoverable. In connection with this review, the Company also reevaluates the periods of depreciation for these assets. The Company recognizes an impairment loss when the sum of the undiscounted expected future cash flows from the use and eventual disposition of the asset is less than its carrying amount. If an asset is considered to be impaired, the impairment to be recognized is measured by the amount by which the carrying amount of the asset exceeds the fair value of the asset, which is determined using the present value of the net future operating cash flows generated by the asset.

Accrued Expenses

The Company accrues expenses related to development activities performed by third parties based on an evaluation of services received and efforts expended pursuant to the terms of the contractual arrangements. Payments under some of these contracts depend on research and non-clinical trial milestones. There may be instances in which payments made to the Company's vendors will exceed the level of services provided and result in a prepayment of expense. In accruing service fees, the Company estimates the period 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, the Company will adjust the accrual or prepaid expense accordingly. The Company has not experienced any material differences between accrued costs and actual costs incurred since its inception.

Convertible Debt and Warrant Accounting

Warrants

The Company accounts for warrants as either equity-classified or liability-classified instruments based on an assessment of the warrant's specific terms and applicable authoritative guidance in ASC 480, *Distinguishing Liabilities from Equity* ("ASC 480") and ASC 815, *Derivatives and Hedging* ("ASC 815"). The assessment considers whether the warrants are freestanding financial instruments pursuant to ASC 480, meet the definition of a liability pursuant to ASC 480, and whether the warrants meet all of the requirements for equity classification under ASC 815, including whether the warrants are indexed to the Company's own common stock, among other conditions for equity classification. This assessment, which requires the use of professional judgment, is conducted at the time of warrant issuance and as of each subsequent quarterly period end date while the warrants are outstanding.

For issued warrants that meet all of the criteria for equity classification, the warrants are required to be recorded as a component of additional paid-in capital at the time of issuance. For issued warrants that do not meet all the criteria for equity classification, the warrants are required to be recorded at their initial fair value on the date of issuance, and each balance sheet date thereafter. Changes in the estimated fair value of the warrants are recognized as a non-cash gain or loss on the statements of operations under Other Income/loss.

Convertible debt

When the Company issues debt with a conversion feature, it first assesses whether the debt should be accounted for in accordance with ASC 480. If the debt does not meet the criteria of an ASC 480 liability, the note's conversion features require bifurcation in accordance with ASC 815. If the Company determines the embedded conversion feature requires bifurcation in accordance with ASC 815, the Company also considers if it can elect the fair value option. If the fair value option is elected, the Company records the note at its initial fair value with any subsequent changes in fair value recorded in earnings. As noted in Note 6, the Company has elected the fair value option for the 2022 Convertible Notes and will record the notes at their initial fair values with any subsequent changes in fair value recorded in earnings. The Convertible Notes were converted into the Company's common stock on the Closing Date of the Company's IPO.

Convertible Preferred Stock

As the Convertible Preferred stockholders have liquidation rights in the event of a deemed liquidation event that, in certain situations, are not solely within the control of the Company and would require the redemption of the then-outstanding Convertible Preferred Stock, the Company classifies the Convertible Preferred Stock in mezzanine equity on the balance sheet.

As noted in Note 8, at the Closing Date of the Company's IPO, the Convertible Preferred stock converted into shares of the Company's common stock.

Revenue

The Company follows the *five* steps to recognize revenue from contracts with customers under ASC 606, Revenue from Contracts with Customers ("ASC 606"), which are:

- Step *1*: Identify the contract(s) with a customer
- Step *2*: Identify the performance obligations in the contract
- Step *3*: Determine the transaction price
- Step *4*: Allocate the transaction price to the performance obligations in the contract
- Step *5*: Recognize revenue when (or as) a performance obligation is satisfied

The Company generates service revenue through a joint development agreement with a research partner. The Company recognizes revenue related to the research and development aspects of the agreement over time using the input method as work is performed on the contract.

The Company also generates grant revenue, which represents monies received on contracts with various federal agencies and nonprofit research institutions for general research conducted by the Company to further their product development and are therefore considered contributions to the Company. The contracts are generally for periods of one year or more and can be cancelled by either party. The Company concluded that the grant arrangements do not meet the criteria to be treated as a collaborative arrangement under FASB ASC Topic 808 as the Company is the only active participant in the arrangement. The grant arrangements also do not meet the criteria for revenue recognition under Topic 606, as the U.S. Government would not meet the definition of a customer.

Amounts earned under these grant contracts are recorded as a reduction to research and development expense when eligible expenses are incurred and the right to payment is realizable or realized and earned. The Company believes this policy is consistent with Topic 606, to ensure that recognition reflects the transfer of promised goods or services to customers in an amount that reflects the consideration that the Company expects to be entitled to in exchange for those goods or services, even though there is no exchange as defined in Topic 606. Additionally, the Company has determined that the recognition of amounts received as costs are incurred and amounts become realizable is analogous to the concept of transfer of control of a service over time under Topic 606.

Receipts of grant awards in advance, which are payable back to the funding agency if not used in accordance with conditions in the grants related to allowable costs or receipt of funding from research partners related to service revenue arrangements before work is performed on the contract, are classified as contract liabilities in the accompanying balance sheets.

Research and Development

The Company accounts for research and development costs in accordance with Accounting Standards Codification (ASC) subtopic 730-10, *Research and Development*. Accordingly, research and development costs are expensed as incurred. Research and development costs consist of costs related to labor, materials and supplies. Research and development costs incurred were $4,723,378 and $3,643,214 during the years ended December 31, 2024 and 2023, respectively.

At December 31, 2024 and 2023, the Company had state tax credit receivables of $65,676 and $86,778, respectively, for pending refunds related to the selling of research and development tax credits back to the State of Connecticut. At December 31, 2024 and 2023, the Company had $27,666 and $20,040, respectively, for pending refunds related to Canadian Scientific Research and Experimental Development (SRED) credits. At December 31, 2024 and 2023, the Company had recorded $8,321 and $11,565, respectively, related to refunds of Canadian Goods and Services Tax (GST) and Quebec Sales Tax (QST). Receipts of refunds are recorded in research and development on the statements of operations.

Stock-Based Compensation

The Company accounts for stock-based compensation in accordance with ASC 718, *Compensation-Stock Compensation* (ASC 718). ASC 718 requires employee stock options and rights to purchase shares under stock participation plans to be accounted for at fair value. ASC 718 requires that compensation costs related to share-based payment transactions be recognized as operating expenses in the financial statements. Under this method, compensation costs for all awards granted or modified are measured at estimated fair value at date of grant and are included as compensation expense over the vesting period during which an employee provides service in exchange for the award. For awards with a performance condition that affects vesting, the Company recognizes compensation expense when it is determined probable that the performance condition will be achieved. The Company recognized the effect of forfeitures when the forfeitures occur.

The Company uses a Black-Scholes option pricing model to determine fair value of its stock options. The Black-Scholes model includes various assumptions, including the value of the underlying common stock, the expected life of stock options, the expected volatility and the expected risk-free interest rate. These assumptions reflect the Company's best estimates, but they involve inherent uncertainties based on market conditions generally outside of the control of the Company. As a result, if other assumptions had been used, stock-based compensation cost could have been materially impacted. Furthermore, if the Company uses different assumptions for future grants, stock-based compensation cost could be materially impacted in future periods.

The Company accounts for equity instruments issued to non-employees in accordance with the provisions of ASC 718 as updated by Accounting Standards Update (ASU) No. 2018-07, *Improvements to Nonemployee Share-Based Payment Accounting*, which expands the scope of ASC 718 to include share-based payment transactions to non-employees.

The following assumptions are used in valuing options issued using the Black-Scholes option pricing model:

Expected Volatility. The expected volatility of the Company's shares is estimated based on the average volatility of peer companies.

Expected Term. The expected term of options is estimated using the simplified method which is based on the vesting period and contractual term for each grant, or for each vesting-tranche for awards with graded vesting.

Underlying Common Stock Value. The underlying common stock value of the Company's shares is estimated by a third-party valuation expert up until the Company's IPO, at which time the Company utilized its trading price on the NYSE American on the date of grant.

Risk-free Interest Rate. The Company bases the risk-free interest rate on the implied yield available on a U.S. Treasury note with terms equal to the expected term of the underlying grant.

Dividend Yield. The Black-Scholes valuation model calls for a single expected dividend yield as an input. The Company has not paid dividends on Common stock in the past nor does it expect to pay dividends on Common stock in the near future. As such, the Company uses a dividend yield percentage of zero.

Income Taxes

The Company uses the liability method of accounting for income taxes, as set forth in ASC 740, Accounting for Income Taxes. Under this method, deferred tax assets and liabilities are recognized for the expected future tax consequence of temporary differences between the carrying amounts and the tax basis of assets and liabilities and net operating loss carry forwards, all calculated using presently enacted tax rates.

Management has evaluated the effect of ASC guidance related to uncertain income tax positions and concluded that the Company has no significant financial statement exposure to uncertain income tax positions at December 31, 2024 and 2023. The Company's income tax returns have not been examined by tax authorities through December 31, 2023.

Certain Risks and Uncertainties

The Company's activities are subject to significant risks and uncertainties including the risk of failure to secure additional funding to properly execute the Company's business plan. The Company is subject to risks that are common to companies in the pharmaceutical industry, including, but not limited to, development by the Company or its competitors of new technological innovations, dependence on key personnel, reliance on third party manufacturers, protection of proprietary technology, and compliance with regulatory requirements.

Fair Value Measurements

The Company carries certain liabilities at fair value on a recurring basis. A fair value hierarchy that consists of three levels is used to prioritize the inputs to fair value valuation techniques:

- Level 1 – Inputs are based upon observable or quoted prices for identical instruments traded in active markets.

- Level 2 – Inputs are based upon quoted prices for similar instruments in active markets, quoted prices for identical or similar instruments in markets that are not active, and model-based valuation techniques for which all significant assumptions are observable in the market or can be corroborated by observable market data for substantially the full term of the assets or liabilities.

- Level 3 – Inputs are generally unobservable and typically reflect management's estimates of assumptions that market participants would use in pricing the asset or liability. The fair values are therefore determined using model-based techniques that include option pricing models, discounted cash flow models, and similar techniques

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In determining fair value, the Company utilizes valuation techniques that maximize the use of observable inputs and minimize the use of unobservable inputs to the extent possible as well as considers counterparty credit risk in its assessment of fair value.

Financial Instruments

The Company's financial instruments are primarily comprised of accounts receivable, accounts payable, accrued liabilities, and long-term debt. For accounts receivable, accounts payable and accrued liabilities, the carrying amount approximates fair value due to the short-term maturities of such instruments. The estimated fair value of the Company's long-term debt approximates carrying value.

Recent Accounting Pronouncements

In November 2024, the FASB issued ASU 2024-03, "Income Statement: Reporting Comprehensive Income— Expense Disaggregation Disclosures," which requires more detailed information about specified categories of expenses (purchases of inventory, employee compensation, depreciation, amortization, and depletion) included in certain expense captions presented on the face of the income statement, as well as disclosures about selling expenses. This ASU is effective for fiscal years beginning after December 15, 2026 and for interim periods within fiscal years beginning after December 15, 2027. Early adoption is permitted. The amendments may be applied either (1) prospectively to financial statements issued for reporting periods after the effective date of this ASU or (2) retrospectively to all prior periods presented in the financial statements. The Company is currently evaluating this guidance to determine the impact it may have on its consolidated financial statements disclosures.

Management does not believe that any other recently issued, but not yet effective, accounting standards could have a material effect on the accompanying financial statements. As new accounting pronouncements are issued, the Company will adopt those that are applicable under the circumstances.

3. Property and Equipment

Property and equipment consisted of the following at:

	December 31, 2024	December 31, 2023
Laboratory equipment	$ 1,070,032	$ 1,013,134
Computers and office equipment	30,825	30,825
Furniture and fixtures	24,316	24,316
Leasehold improvements	28,855	28,855
Building equipment	14,932	14,932
Total property and equipment	1,168,960	1,112,062
Less accumulated depreciation & amortization	(515,003)	(401,987)
Total property and equipment, net	$ 653,957	$ 710,075

Depreciation and amortization expense was $120,026 and $122,010 for the years ended December 31, 2024 and 2023, respectively. Fixed assets are reviewed for impairment each reporting period. The Company recorded losses on disposal of assets of $4,859 and $41,417 for the years ended December 31, 2024 and 2023, respectively.

4. Intangible Assets

Intangible assets consisted of the following at:

December 31, 2024:

	Estimated Useful Life	Gross Amount	Accumulated Amortization	Impairment	Net Amount
Trademarks	Indefinite	$ 60,244	$ —	$ —	$ 60,244
Patents	17 years	213,122	26,946	—	186,176
Intangible assets		$ 273,366	$ 26,946	$ —	$ 246,420

December 31, 2023:

	Estimated Useful Life	Gross Amount	Accumulated Amortization	Impairment	Net Amount
Trademarks	Indefinite	$ 57,474	$ —	$ —	$ 57,474
Patents	17 years	169,190	15,783	—	153,407
Intangible assets		$ 226,664	$ 15,783	$ —	$ 210,881

During the years ended December 31, 2024 and 2023, amortization expense related to intangible assets was $11,162 and $7,643, respectively.

5. Accrued Expenses

Accrued expenses consisted of the following at:

	December 31, 2024	December 31, 2023
Employee payroll and bonuses	$ 410,781	$ 207,556
Vacation	32,969	31,074
Research and development projects	75,047	85,767
Professional fees	82,762	35,624
Other	1,228	23,647
Total accrued expenses	$ 602,787	$ 383,668

6. Convertible Debt

Effective January 5, 2021, the Company entered into a Note Purchase Agreement to issue up to $2,000,000 of convertible promissory notes. On the same date, the Company entered into a convertible promissory note (2021 Convertible Note) with one investor for $1,000,000. The 2021 Convertible Note bears interest at a rate of 6% per annum and is due and payable in full on January 5, 2023. The 2021 Convertible Note automatically converts upon a qualified equity financing, as defined in the note agreement to the number of preferred shares equal to all principal and accrued interest divided by the conversion price of $48.00 on a basis unadjusted for the Forward Stock Split and the Reverse Stock Split, which is subject to adjustment as defined in the note agreement. The 2021 Convertible Note is also optionally convertible as defined in the note agreement for certain non-qualified financing, a change in control, or upon the maturity date of the 2021 Convertible Note. The Company incurred issuance costs of $15,613 related to the 2021 Convertible Note, which has been recorded as a debt discount and will be amortized over the term of the 2021 Convertible Note.

In September 2022, the Company entered into a Convertible Note Purchase Agreement (the Agreement) to issue up to $4,500,000 convertible promissory notes. On the same day, the Company entered into convertible promissory notes (2022 Convertible Notes) with three investors totaling $4,350,000. The 2022 Convertible Notes mature on January 13, 2023 or the occurrence of an Event of Default (as defined) and bear interest at a rate of 8% per annum which shall accrue but is not due and payable until conversion or full repayment of outstanding principal. The principal and interest outstanding under the 2022 Convertible Notes is automatically converted a) upon the closing of a Qualified Financing resulting in gross proceeds to the Company of at least $20 million into securities issued in connection with the Qualified Financing, at a discount of 30% per share; b) upon the closing of a Change of Control event into shares of capital stock of the Company or Series B preferred stock; and c) upon the closing of a Public Company Event, into shares of capital stock being issued to investors equal to two-times (2x) the amount of the outstanding principal and accrued interest then outstanding divided by the public offering price per share. The principal and interest outstanding under the 2022 Convertible Notes is convertible, at the option of the holders, at the maturity date into a new class of Company's Preferred Stock (Series C Preferred) equal to the quotient of the outstanding principal amount plus interest divided by the Capped Price, which is defined as the price per share equal to the Valuation Cap of $30 million divided by the Company Capitalization, as defined in the Agreement.

In January 2023, the Company elected to convert the 2021 Convertible Note, including interest accrued but not yet paid of $124,759 at a conversion price of $48.00 into 23,432 shares of its Series B Preferred Stock on a basis unadjusted for the Forward Stock Split and the Reverse Stock Split in accordance with the terms outlined in the Note Purchase Agreement.

In February 2023, the 2022 Convertible Notes were amended to extend the maturity date to March 31, 2023 and to change the conversion price upon a Qualified Financing or Change in Control event to $30 million divided by the number of shares of the Company's common stock issued and outstanding, on a fully diluted basis, immediately prior to the close of the Qualified Financing or Change in Control event.

During April and June 2023, the 2022 Convertible Notes were further amended to extend the maturity date to September 30, 2023 and allow for the sale of additional notes of $500,000 for a total aggregate principal of $4,850,000.

Effective June 21, 2023, the 2022 Convertible Notes were converted to 61,534 shares of the Company's common stock equal to $9,495,066. During the years ended December 31, 2024 and 2023, the Company recorded a loss on the change in the fair value of Convertible Notes of $0 and $(3,630,100), respectively.

Interest expense was $0 and $166,019 during the years ended December 31, 2024 and 2023, respectively.

7. Stockholders' Equity

On May 17, 2023, the Company effected a 7.1-for-1 Forward Stock Split of its issued and outstanding shares of common stock and a proportional adjustment to the existing conversion ratios for each series of the Company's preferred stock. The par value of the common stock was adjusted as a result of the Forward Stock Split from $0.01 to $0.0001 and the authorized shares were increased to 100,000,000 shares of common stock in connection with the Forward Stock Split. In lieu of any fractional shares issued as a result of the split the Company paid a cash amount to the holder of such fractional share. The accompanying financial statements and notes to the financial statements give retroactive effect to the Forward Stock Split for all periods presented. Shares of common stock underlying outstanding stock-based awards and other equity instruments were proportionately increased and the respective per share value and exercise prices, if applicable, were proportionately decreased in accordance with the terms of the agreements governing such securities.

On February 16, 2024, the Company completed a follow-on offering of an aggregate of 555,567 shares of its common stock at a public offering price of $9.00 per share. The gross proceeds from the offering, before deducting the placement agent's fees and other offering expenses, were approximately $5.0 million.

As consideration for ThinkEquity LLC serving as the placement agent for the offering (the "Placement Agent"), the Company paid the Placement Agent a cash fee of 7.5% of the aggregate gross proceeds of the Offering and reimbursed the Placement Agent for certain expenses and legal fees for a total of $537,559. The Company also issued warrants to designees to the Placement Agent (the "Placement Agent Warrants") exercisable for an aggregate of 22,223 shares of Common Stock (the "Placement Agent Shares") at an exercise price of $11.40 per share (125% of the $9.00 offering price of the Common Share), have an initial exercise date of August 14, 2024 and expire on February 16, 2029. The Placement Agent Warrants were evaluated in accordance with ASC 718 and recorded within stockholders' equity.

On July 1, 2024, the Company effected a 30-for-1 Reverse Stock Split of its issued and outstanding shares of common stock and began trading on a split-adjusted basis the same day. There was no change to the par value of the common stock. In lieu of any fractional shares issued as a result of the split the Company paid a cash amount to the holder of such fractional share. The accompanying financial statements and notes to the financial statements give retroactive effect to the Reverse Stock Split for all periods presented unless otherwise noted. Shares of common stock underlying outstanding stock-based awards and other equity instruments were proportionately decreased and the respective per share value and exercise prices, if applicable, were proportionately increased in accordance with the terms of the agreements governing such securities.

On July 25, 2024, the Company completed a follow-on offering of an aggregate of 6,665,000 shares of its common stock and Class A warrants to purchase 13,330,000 shares of common stock, at a combined public offering price of $1.50. The Class A warrant had an initial exercise price of $1.50 per share, are exercisable immediately upon issuance, and will expire on the fifth anniversary of the original issuance date. However, if on the date that was 30 calendar days immediately following the date of issuance of the Class A Warrants, or August 24, 2024 (the "Reset Date"), the Reset Price, as defined below, was less than the exercise price at such time, the exercise price would be decreased to the Reset Price. "Reset Price" is defined as 100% of the trailing five-day VWAP immediately preceding the Reset Date, provided, that in no event would the Reset Price be less than $0.32 (subject to adjustment for reverse and forward stock splits, recapitalizations and similar transactions), which represented 20% of the most recent closing price for the Common Stock at the time of execution of the placement agent agreement with respect to the offering. The Reset Price of the Class A Warrants as calculated on the Reset Date was $0.7043. The number of shares of Common Stock issuable upon exercise of the Class A Warrants has not been proportionately adjusted due to the reset of the exercise price.

In consideration for Maxim Group LLC serving as the placement agent of the offering (the "Placement Agent"), the Company paid the Placement Agent a cash fee equal to 7% of the aggregate gross proceeds of the Offering and reimbursed the Placement Agent for certain expenses and legal fees for a total of $809,825. The Company also issued warrants to designees of the Placement Agent (the "Placement Agent Warrants") exercisable for an aggregate of 266,600 shares of Common Stock (the "Placement Agent Warrant Shares"). The Placement Agent Warrants have substantially the same terms as the Class A Warrants, except that the Placement Agent Warrants have an exercise price equal to $1.875 per share (125% of the $1.50 offering price of the Common Share and accompanying Class A Warrants), have an initial exercise date of January 23, 2025 and expire on July 23, 2029. The Placement Agent Warrants were evaluated in accordance with ASC 718 and recorded within stockholders' equity.

The gross proceeds from the offering, before deducting the placement agent's fees and other offering expenses, were approximately $10.0 million.

Common Stock

At December 31, 2024 and 2023, per the Company's amended and restated Certificate of Incorporation, the Company was authorized to issue 100,000,000 shares of $0.0001 par value common stock.

Each share of common stock entitles the holder to one vote on all matters submitted to a vote of the Company's stockholders.

The Company currently has 13,670,222 shares of common stock reserved for future issuance for the potential exercise of stock options and warrants outstanding at December 31, 2024.

Preferred Stock

At December 31, 2024 and 2023, per the Company's amended and restated Certificate of Incorporation, the Company has authorized 10,000,000 shares of $0.0001 par value preferred stock.

Upon the close of the Company's IPO in June 2023, all of the then outstanding preferred stock converted to common stock, resulting in the issuance of shares of common stock in exchange for outstanding Series A (48,608 shares), Series A-1 (98,828 shares), and Series B Preferred Stock (109,485 shares), respectively. There was no gain or loss upon conversion.

8. Warrants

The Company issued warrants to purchase 1,596 shares of common stock in 2018 in conjunction with convertible debt financing that have a redemption provision providing the holder the right to have the Company redeem all or any portion of the warrant (or shares it has converted into) at a purchase price equal to the fair market value of the shares as determined by the board of directors or an independent appraiser. As a result of this redemption provision, the warrants have been classified as a liability in the financial statements based on ASC 480. These warrants have an exercise price of $14.40 per share and a term of 10 years. The warrants are marked to market each reporting period. The fair value was $381 and $35,453 at December 31, 2024 and 2023, respectively.

The Company issued 2,000 warrants to its underwriters as part of our initial public offering in fiscal 2023. In fiscal 2024, the Company issued an additional 22,223 warrants in February, and 266,600 warrants in July to its underwriters as part of our follow-on offerings in fiscal 2024. The underwriter warrants have a term of 5 years.

The Company also issued warrants in fiscal years 2019, 2023, and 2024 which did not meet the criteria under ASC 480 to be classified as a liability, and instead meet the equity classification criteria.

Additionally, the Company issued 13,330,000 Class A Warrants to shareholders who participated in the Company's July 2024 follow-on public offering. The Class A Warrants had an initial exercise price of $1.50 per share of Common Stock, however on August 24, 2024 the exercise price was reset to $0.7043. See Note 7. The number of shares of Common Stock issuable upon exercise of the Class A Warrants were not proportionately adjusted in connection with the reset of the exercise price.

The Class A Warrants are exercisable upon issuance and expire five years from the date of issuance. The Class A Warrants contain ownership limitations pursuant to which a holder does not have the right to exercise any portion of their warrants if it would result in the holder (together with its affiliates) beneficially owning more than 4.99% (or, at the election of the holder, 9.99%) of the Company's outstanding Common Stock. The Class A Warrants are issued pursuant to a Warrant Agent Agreement dated July 25, 2024 ("Warrant Agent Agreement") between the Company and VStock Transfer LLC, as warrant agent.

In connection with the July 2024 follow-on public offering, the Company evaluated the Class A Warrants and determined they met the criteria for liability classification as they met the criteria in ASC 815 - Derivatives and Hedging due to the reset provision. The Class A Warrants had an initial fair value of $12.1 million. The gross proceeds of $10.0 million from the July 2024 follow-on public offering was allocated to the Class A Warrants resulting in a loss on issuance of common stock of approximately $2.1 million recorded in Other income (expenses). Upon the reset of the Class A Warrant exercise price, the Class A Warrants no longer met the criteria for liability classification pursuant to ASC 815; at which time the Company recorded a gain in Other income (expenses) - Change in fair value of Class A warrants of $4.0 million, and reclassified $1.9 million to equity representing the difference between the change in the fair value, and the loss upon issuance of our common stock.

The Class A Warrants were valued utilizing a probability weighted scenario method with a Monte Carlo simulation model and Black-Scholes Model. The significant assumptions in the Monte Carlo simulation model include a stay public assumption of 90%, and a fundamental transaction assumption of 10%. The significant assumptions utilized in estimating the fair value of the Class A Warrants at issuance include (i) a per share price of common stock range of $1.14 - $1.40; (ii) a dividend yield of 0%; (iii) a risk-free rate range of 4.13% - 4.14%; (iv) expected volatility of 119%; (v) projected stock price and volume weighted average price as of the Reset Date of $1.14; (vi) a strike price range of $1.40 - $1.50; and (vii) expected term of 4.92.

The following table summarizes information about warrants outstanding at December 31, 2024:

		Warrants Outstanding			Warrant Exercisable		
Year Granted	Exercise Price	Number of Warrants at 12/31/2024	Weighted Average Remaining Contractual Life	Weighted Average Exercise Price	Number of Warrants at 12/31/2024	Weighted Average Remaining Contractual Life	Weighted Average Exercise Price
2018	$ 14.40	1,596	3.3 years	$ 14.40	1,596	3.3 years	$ 14.40
2019	$ 158.40	7,195	1.1 years	$ 158.40	7,195	1.1 years	$ 158.40
2023	$ 187.50	2,000	3.5 years	$ 187.50	2,000	3.5 years	$ 187.50
2024	$ 11.40	22,223	4.2 years	$ 11.40	22,223	4.2 years	$ 11.40
2024	$ 0.70	13,329,000	4.6 years	$ 0.70	13,329,000	4.6 years	$ 0.70
2024	$ 1.88	266,600	4.6 years	$ 1.88	—	0 years	$ —
		13,628,614		$ 0.85	13,362,014		$ 0.83

9. Stock Options

In March 2023, the Company's Board of Directors and stockholders approved the 2023 Stock Incentive Plan ("2023 Plan"). The 2023 Plan allows the Compensation Committee to grant up to 1,211,068 shares of Common Stock in the form of incentive and non-statutory stock options, restricted stock awards, restricted stock units, and other stock-based awards to employees, directors, and non-employees. As of December 31, 2024, options to purchase 1,333 shares of common stock had been granted and were outstanding under the 2023 Plan and 1,209,735 shares of common stock were available for grant under the plan. On October 3, 2024, the Company's Board of Directors approved amendments to the 2023 Plan that, subject to stockholder approval, would (i) increase the number of shares of Common Stock that may be issued under the 2023 Plan by 1,144,401 shares and (ii) adopt an evergreen provision to the 2023 Plan providing for an automatic 5% annual increase in the shares of Common Stock available for issuance under the 2023 Plan over the next 10 years. Both amendments were approved by the Company's stockholders at the Company's annual stockholder meeting held on November 20, 2024.

During 2016, the Company established the Azitra Inc. 2016 Stock Incentive Plan ("2016 Plan") which provides for the grant up to 49,687 shares of Common Stock in the form of stock options and restricted shares to the Company's employees, officers, directors, advisors and consultants. As of December 31, 2024, options to purchase 40,275 shares of common stock had been granted and 7,457 shares of common stock were available for grant under the 2016 Plan.

At December 31, 2024, there was $81,386 of unamortized compensation expense that will be amortized over the remaining vesting period. At December 31, 2024 and 2023, there were 0 and 3,105 performance-based options outstanding, respectively with fair values of $0 and $109,551, respectively. During the year ended December 31, 2024, the Company recognized compensation expense of $109,551 for performance-based options. The Company determined the options qualified as plain vanilla under the provisions of SAB 107 and the simplified method was used to estimate the expected option life.

Stock-based compensation expense recognized for options was as follows:

	December 31	
	2024	2023
Research and development	$ 2,505	$ 25,947
General and administrative	242,548	125,558
Total	$ 245,053	$ 151,505

The following table summarizes information about options outstanding and exercisable at December 31, 2024:

	Options Outstanding			Options Exercisable		
Exercise Price	Number of Options at December 31, 2024	Weighted Average Remaining Contractual Life	Weighted Average Exercise Price	Number of Options at December 31, 2024	Weighted Average Remaining Contractual Life	Weighted Average Exercise Price
$ 14.32	6,871	1.0 year	$ 14.32	6,871	1.0 year	$ 14.32
$ 27.80	6,735	1.0 year	$ 27.80	6,735	1.0 year	$ 27.80
$ 51.08	26,669	6.3 years	$ 51.08	25,571	6.2 years	$ 51.08
$ 62.10	1,333	8.7 years	$ 62.10	472	8.7 years	$ 62.10
	41,608			39,649		

Total stock option activity for the year ended December 31, 2024, is summarized as follows:

	Options	Weighted Average Exercise Price	Weighted Average Remaining Contractual Term (years)	Aggregate Intrinsic Value (in thousands)
Outstanding at December 31, 2023	42,941	$ 41.10	5.5 years	—
Granted	—	—		
Exercised	(1,333)	14.32		
Forfeited	—	—		
Outstanding at December 31, 2024	41,608	$ 41.60	4.6 years	—
Vested and Exercisable at December 31, 2024	39,649	38.41	4.4 years	—

The weighted-average fair value of the options granted during the years ended December 31, 2024 and 2023 was $— and $1.65 per share, respectively.

10. Fair Value Measurements

The following tables summarize the fair values and levels within the fair value hierarchy in which the fair value measurements fall for assets and liabilities measured on a recurring basis as of:

December 31, 2024

Description	Level 1	Level 2	Level 3	Total
Liabilities				
Common stock warrants	$ —	$ —	$ 381	$ 381
Total	$ —	$ —	$ 381	$ 381

December 31, 2023

Description	Level 1	Level 2	Level 3	Total
Liabilities				
Common stock warrants	$ —	$ —	$ 35,453	$ 35,453
Total	$ —	$ —	$ 35,453	$ 35,453

The following table presents the changes in Level 3 instruments measured on a recurring basis for the period ended December 31, 2024:

Balance at December 31, 2022	$	5,670,283
Changes in fair value of warrants		(34,830)
Changes in fair value of 2022 Convertible Notes		3,630,100
Conversion of 2022 Convertible Notes		(9,230,100)
Balance at December 31, 2023	$	35,453
Changes in fair value of warrants		(35,072)
Balance at December 31, 2024	$	381

At December 31, 2024 and 2023, the Company estimated the fair value of the warrants using the Black-Scholes option pricing model with the following assumptions:

	December 31, 2024	December 31, 2023
Underlying common stock value	$ 0.43	$ 27.60
Expected term (years)	3.29	4.29
Expected volatility	172%	99%
Risk free interest rate	4%	4%
Dividend yield	—%	—%

Fluctuations in the fair value of the Company's common stock, and the expected volatility are the primary drivers for the change in the common stock warrant liability valuation during each year. As the fair value of the common stock, and expected volatility increases the value to the holder of the instrument generally increases.

11. Net Loss Per Share

Basic and diluted net loss per share were calculated as follows:

The denominator for each respective period is as follows:

	December 31	
	2024	2023
Weighted average common stock outstanding, basic and diluted	3,784,482	229,627
$0.01 warrants	—	239
Total	3,784,482	229,866

The following potential common stock equivalents, presented based on amounts outstanding at each period end, were excluded from the calculation of diluted net loss per share for the periods indicated because including them would have had an anti-dilutive effect:

	December 31,	
	2024	2023
Options to purchase shares of common stock	41,608	42,942
Warrants outstanding	13,628,614	10,791
Total	13,670,222	53,733

12. Income Taxes

The provision for income taxes for the years ending December 31, 2024 and December 31, 2023 consists of:

	December 31, 2024	December 31, 2023
Current		
Federal	$ —	$ —
Foreign	9,031	17,308
State	—	—
Total current	9,031	17,308
Deferred		
Federal	—	—
Foreign	—	—
State	—	—
Total deferred	—	—
Total provision for income taxes	$ 9,031	$ 17,308

A reconciliation of income tax computed using the U.S. federal statutory tax rate compared to that reflected in operations for the years ending December 31, 2024 and December 31, 2023 consists of:

	2024		2023	
	Amount	**Percent**	**Amount**	**Percent**
Income taxes using U.S. statutory rate	$ (1,870,405)	21.00%	$ (2,401,761)	21.00%
Debt fair value adjustment	—	—%	762,321	(6.67)%
Warrant fair value adjustment	(847,155)	9.51%	(7,314)	0.06%
Loss on Issuance of Common Stock	447,888	(5.03)%	—	—%
State taxes, net of federal benefit	(704,887)	7.91%	(538,268)	4.71%
Research and development tax credit	(385,677)	4.33%	(356,237)	3.11%
Change in valuation allowance	3,263,544	(36.64)%	2,502,918	(21.88)%
Other, net	105,723	(1.19)%	55,649	(0.49)%
	$ 9,031	**(0.10)%**	**$ 17,308**	**(0.15)%**

Deferred income taxes are provided on temporary differences between the carrying amounts of assets and liabilities for financial reporting purposes and those for income tax reporting purposes. Deferred income tax assets / (liabilities) as of December 31, 2024 and 2023 are as follows:

	December 31, 2024	December 31, 2023
Deferred tax assets:		
Net operating loss carryforwards	$ 10,360,042	$ 8,755,690
Tax credits	2,632,663	2,155,118
Depreciation and amortization	3,566,210	2,372,070
Accrued expenses	89,324	89,462
Other	18,218	30,572
Total deferred tax assets	$ 16,666,457	13,402,912
Deferred tax liabilities:		
Depreciation and amortization	—	—
Total deferred tax liabilities	—	—
Valuation allowance	(16,666,457)	(13,402,912)
Net deferred tax assets	$ —	$ —

The Company has federal net operating loss carryforwards of approximately $38,488,000 and $32,529,000 for the tax years ending December 31, 2024 and 2023, respectively, of which $1,285,000 will expire in tax years 2036 through 2037 and approximately $37,203,000 which does not expire. The Company has state net operating loss carryforwards of approximately $38,441,000 and $32,484,000 for the tax years ending December 31, 2024 and 2023, respectively, which will expire in tax years 2037 through 2043.

The Company has federal research tax credits of approximately $1,884,000 and $1,524,000 for the tax years ending December 31, 2024 and 2023, respectively, which expire in tax years 2039 through 2043. The Company has state research tax credits of approximately $582,000 and $466,000 for the tax years ending December 31, 2024 and 2023, respectively, of which $437,000 will expire in tax year 2036 through 2038 and the remainder can be carried forward indefinitely. The Company has Canadian research tax credits of approximately $288,000 and $263,000 for the tax years ending December 31, 2024 and 2023, respectively, which expire in tax years 2039 through 2043.

The U.S. Internal Revenue Code Section 382 imposes an annual limit on the ability of a corporation that undergoes a greater than 50% ownership change to use its net operating loss carry forwards to reduce its tax liability. If in the future the Company undergoes an ownership change exceeding the 50% limitation threshold imposed by Section 382, the Company's net operating loss carryforwards may be significantly limited as to the amount of use in a particular year. In addition, all or a portion of the Company's net operating loss carryforwards incurred before 2018, may expire unutilized.

The realization of deferred tax assets is dependent upon the Company's ability to generate future taxable income during the periods in which the temporary differences become deductible. Based on the Company's recent earnings history and projected future U.S. earnings, management believes that it is more likely than not that its federal and state deferred tax assets will not be fully realized in the foreseeable future. As a result of this assessment, management believes that a full valuation allowance against its net federal and state deferred tax assets is required.

The Company applies the provisions of ASC 740-10 to account for uncertain tax positions. ASC 740-10 addresses the determination of whether tax benefits claimed or expected to be claimed on a tax return should be recorded in the financial statements. Under ASC 740-10, the Company may recognize the tax benefit from an uncertain tax position only if it is more likely that not that the tax position will be sustained on examination by the taxing authorities, based on the technical merits of the position. The Company has determined that it has no significant uncertain tax positions requiring recognition and measurement under ASC 740-10.

The Company is subject to U.S. federal income tax, Connecticut state income tax and Canada branch tax. The Company has not been audited by the IRS, state, or foreign tax authorities in connection with income taxes. The Company's tax years remain open to examination for all federal and state tax matters until its net operating loss carryforwards are utilized and the applicable statute of limitations have expired. The years 2021 to 2023 remain subject to examination by taxing authorities.

The Company will recognize interest and penalties related to unrecognized tax benefits, if applicable, as a component of income tax expense.

13. Commitments and Contingencies

Legal

The Company is subject to legal proceedings or claims which arise in the ordinary course of its business. Although occasional adverse decisions or settlements may occur, the Company believes that the final disposition of such matters should not have a material adverse effect on its financial position, results of operations or liquidity.

License Agreement

Effective January 26, 2022, the Company entered into an Exclusive License Agreement (the License Agreement) with an unrelated third party. Under the License Agreement, the Company is granted an exclusive license for certain patents and a non-exclusive license for certain know-how. The License Agreement continues until the later of the expiration of the last to expire licensed patent or ten years after the first commercial sale of the first licensed therapeutic or non-therapeutic product. The Company may terminate the License Agreement at any time by providing at least 30 days written notice to the third party. The License Agreement is also terminated upon breach of a material obligation under the agreement or bankruptcy. Upon any termination of the License Agreement, neither party is relieved of obligations incurred prior to the termination.

During the years ended December 31, 2024 and 2023, the Company capitalized payments made under this license agreement in the amount of $0 and $13,096, respectively.

Operating Leases

The Company leases office and lab space in Branford, CT, Groton, CT, and Montreal, Quebec. The Company's leases expire at various dates through May 31, 2027. Most leases are for a fixed term and for a fixed amount.

During 2019, the Company entered into a new lease agreement for office and laboratory space in Montreal, Quebec. The Montreal lease required monthly payments of $6,906, CAD which increases approximately 4% in each of the following years. The Montreal lease was increased to $8,130 CAD in 2021 upon leasing additional space. The Montreal lease was initially for a one-year term, renewable annually. The Montreal lease also requires the Company to pay additional common area maintenance.

During 2020, the Company entered into a new lease agreement for the Company's primary office and laboratory space in Branford, CT. The Branford lease requires monthly payments of $13,033 for the first year of the lease, which increases approximately 2% in each of the following years. The Branford lease also requires the Company to pay a pro-rata share of common area maintenance.

During May 2021, the Company entered into a new lease for office and laboratory space in Groton, CT. The Groton lease required monthly payments of $4,234, which was increased to $6,824 in September 2021 upon leasing additional space. In August 2024, the Company reassessed its needs and released certain lab space resulting in a decrease to the monthly payment to $5,216. The Groton lease is initially for a one-year term, renewable annually for up to three additional years.

Future minimum payments under non-cancelable operating leases with initial or remaining terms in excess of one year during each of the next five years follow:

2025	$	277,183
2026		204,131
2027		71,979
Total future undiscounted lease payments		553,293
Less interest		(23,955)
Present value of minimum lease payments	$	529,338

Rent expense for all operating leases was $338,856 and $338,856 for the years ended December 31, 2024 and 2023, respectively. The weighted average lease term for all operating leases is 2.1 years. The weighted average discount rate for all operating leases is 4.25%.

Finance Leases

During 2023, the Company entered into an agreement with Hewlett Packard to lease equipment. The lease requires monthly payments of $1,478, including tax. The lease is for a 3 years term with option of purchase or extension at term end. The remaining lease term is 1.6 years and the discount rate is 9.60%.

The following is a schedule showing the future minimum lease payments under finance leases by years and the present value of the minimum payments as of December 31, 2024.

2025	$	17,740
2026		10,351
Total future undiscounted lease payments		28,091
Less interest		(1,921)
Present value of minimum lease payments	$	26,170

Lease expense for the finance lease was $15,480 and $6,450 for the years ended December 31, 2024 and 2023, respectively. Interest expense for the finance lease was $3,129 and $1,707 for the years ended December 31, 2024 and 2023, respectively.

14. Retirement Plan

Effective January 1, 2019, the Company sponsors a 401(k) plan that covers substantially all employees. In order to be eligible to participate, an employee must complete two consecutive months of service and work a minimum of two hundred fifty hours or work 1,000 hours in their first year of service. Employees may make pre-tax deferrals upon meeting the Plan eligibility requirements. Effective January 1, 2020, the Plan was transitioned to a safe harbor plan in which highly compensated employees are not eligible for matching contributions and non-highly compensated employees earn 100% match on first 3% contributed and 50% on the next 2% contributed. Total employer matching contributions were $22,264 and $11,446 for the years ended December 31, 2024 and 2023, respectively.

15. Concentration of Credit Risk

Financial instruments that potentially subject the Company to credit risk consist principally of cash.

The cash balance identified in the balance sheet is held in an account with a financial institution and insured by the Federal Deposit Insurance Corporation (FDIC) up to $250,000. At times, cash maintained on deposit may be in excess of FDIC limits.

16. Related Parties

Total related party revenue was $7,500 and $686,000 for the years ended December 31, 2024 and 2023, respectively. Accounts receivable due from the related party was $0 and $90,000 at December 31, 2024 and 2023, respectively.

In September 2022, the Company entered into a convertible promissory note totaling $4,350,000 of which $4,000,000 was attributable to an entity who was also an investor in the Company's Series A, A-1, and B Preferred Stock financing (See Note 6). This entity received 1,697,490 shares of common stock on a basis unadjusted for a Forward Stock Split and a Reverse Stock Split, upon conversion of the promissory notes for principal and interest of $4,243,726.

In July 2024, Bayer was no longer considered a related party as their holdings in the Company no longer exceeded 5% of the total outstanding common stock, and the amounts disclosed above are accordingly presented while they were considered a related party.

17. Subsequent Events

The Company has evaluated events subsequent to the balance sheet date through February 24, 2025, the date these financial statements are issued.

On January 14, 2025, the Company completed a follow-on offering on an aggregate of 4,857,780 shares of its common stock at a public offering price of $0.30 per share. The shares were offered by the Company pursuant to a shelf registration statement on Form S-3 filed with the SEC on July 1, 2024, and a final prospectus supplement dated January15, 2025.

In consideration for Maxim Group LLC serving as the placement of the Offering (the "Placement Agent"), the Company paid the Placement Agent a cash fee equal to 7.0% of the aggregate gross proceeds raised in the Offering and the reimbursed the Placement Agent for certain expenses and legal fees of $60,000. The Company also issued warrants to designees of the Placement Agent (the "Placement Agent Warrants") exercisable for an aggregate of 194,311 shares of Common Stock (the "Placement Agent Shares"), which represent 4.0% of the aggregate number of Shares sold in the Offering, at an exercise price per share equal to 125% of the offering price of each Share, or $0.375. The Placement Agent Warrants are exercisable six months from the date of issuance and expire five years from the commencement of the sales in this Offering. The Placement Agent Warrant may be exercisable via cashless exercise in certain circumstances.

The gross proceeds from the offering, before deducting the placement's fees and other offering expenses were approximately $1.5 million.

On February 5, 2025, the Company completed a follow-on offering on an aggregate of 2,495,518 shares of its common stock at a public offering price of $0.2785 per share. The shares were offered by the Company pursuant to a shelf registration statement on Form S-3 filed with the SEC on July 1, 2024, and a final prospectus supplement dated February 6, 2025. In connection with the follow-on offering, the Company and investors entered into a letter agreement, pursuant to which the Company will issue warrants to purchase up to 2,245,967 shares of common stock. The warrants are exercisable on the six-month and one day anniversary of their issuance, and their exercise price is equal to the greater of the (1) book value of the common stock or (ii) market value of the common stock as determined by the NYSE American Rules.

In consideration for Maxim Group LLC serving as the placement of the Offering (the "Placement Agent"), the Company paid the Placement Agent a cash fee equal to 7.0% of the aggregate gross proceeds raised in the Offering and the reimbursed the Placement Agent for certain expenses and legal fees of $40,000.

The gross proceeds from the offering, before deducting the placement's fees and other offering expenses were approximately $695 thousand.

Item 9. Changes in and Disagreements with Accountants on Accounting and Financial Disclosure

Not applicable

Item 9A. Controls and Procedures

(a) Evaluation of Disclosure Controls and Procedures.

Our management, with the participation of our chief executive officer and chief financial officer evaluated the effectiveness of our disclosure controls and procedures pursuant to Rule 13a-15(e) under the Exchange Act as of December 31, 2023. In the course of that evaluation, we identified a material weakness as it relates to a lack of adequate segregation of accounting functions. We intend to increase staffing within our accounting infrastructure sufficient to facilitate proper segregation of accounting functions and to enable appropriate review of our internally prepared financial statements. Based upon the foregoing, our chief executive officer and chief financial officer concluded that our disclosure controls and procedures were not effective as of December 31, 2023.

(b) Changes in internal control over financial reporting.

There were no changes to our internal control over financial reporting, as defined in Rule 13a-15(f) under the Exchange Act that occurred during the quarter ended December 31, 2023 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

(c) Management's report on internal controls over financial reporting.

This annual report does not include a report of management's assessment regarding internal control over financial reporting or an attestation report of our registered public accounting firm due to a transition period established by rules of the Securities and Exchange Commission for newly public companies

Our management is responsible for establishing and maintaining adequate internal controls over financial reporting, as defined under Rule 13a-15(f) under the Exchange Act. Our management has assessed the effectiveness of our internal controls over financial reporting as of December 31, 2024 based on the framework established in Internal Control - Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 Framework) ("COSO"). Our internal control system was designed to provide reasonable assurance to our management and board of directors regarding the preparation and fair presentation of published financial statements. Our management assessed the effectiveness of our internal control over financial reporting as of December 31, 2024, and based on that evaluation, management concluded that our internal control over financial reporting were not effective as of December 31, 2024 due to a material weakness relating to a lack of segregation of accounting functions.

This report does not include an attestation report of our registered public accounting firm regarding internal control over financial reporting. Management's report was not subject to attestation by our registered public accounting firm pursuant to the rules of the Securities and Exchange Commission that permit us to provide only management's report in this Annual Report.

Item 9B. Other Information

None.

Item 9C. Disclosure Regarding Foreign Jurisdictions that Prevent Inspections

Not applicable.

PART III

Item 10. Directors, Executive Officers and Corporate Governance

Executive Officers and Directors

The following table sets forth the names, ages and positions of our current executive officers and directors.

Name	Age	Position
Francisco D. Salva	54	President, Chief Executive Officer and Director
Norman Staskey	55	Chief Financial Officer
Travis Whitfill	35	Chief Operating Officer and Director
Barbara Ryan	65	Independent Director
John Schroer	59	Independent Director

Information about our Executive Officers and Directors

Francisco D. Salva has served as our president and chief executive officer and a member of our Board since April 2021. Mr. Salva has over 15 years of experience in senior leadership roles in the biotechnology and pharmaceutical industries. Mr. Salva served as president and chief executive officer of Complexa, Inc., an inflammation and fibrosis focused biopharmaceutical company, from May 2018 to August 2020. From February 2011 to November 2016, Mr. Salva served as a co-founder and vice president of operations of Acerta Pharma B.V., Inc, a cancer and autoimmune focused biopharmaceutical company. Mr. Salva serves as a director of Vincerx Pharma, Inc. (Nasdaq: VINC). Prior to his operating roles, Mr. Salva served in various senior positions in the venture capital and investment banking industries focusing on healthcare, biotechnology and pharmaceuticals companies. Mr. Salva received a B.A. from Brown University and an MSc in economics and philosophy from the London School of Economics. We believe that Mr. Salva's experience as a senior executive, venture capitalist and investment banker in the biotech and pharmaceutical industries qualifies him to serve on our Board.

Norman Staskey has served as our chief financial officer since October 2022. Since May 15, 2021, Mr. Staskey has also served as a senior director of Danforth Advisors, a national consulting firm providing financial, accounting and reporting services to the life science industry. From September 2014 to May 2021, Mr. Staskey was employed by EY (formally Ernst & Young), most recently as a managing director in EY's Financial Accounting and Advisory services practice.

Travis Whitfill is a co-founder of Azitra and has served on our Board since inception. Mr. Whitfill has served in various roles at Azitra, including chief scientific officer from January 2014 to September 2019 and director of advanced technology since September 2019, and as chief operating officer since June 2023. Mr. Whitfill served as a partner at Bios Equity Partners, LP, a biotechnology-focused venture capital firm, from October 2015 to June 2023 and a senior analyst at Bios Research from September 2014 to June 2023. He has also served as an associate research scientist and assistant professor adjunct at Yale University from July 2016 to March 2022 and since March 2022, respectively, with appointments in the Departments of Pediatrics and Emergency Medicine. Mr. Whitfill has served on the board of directors of IN8Bio, Inc. (Nasdaq: INAB) since March 2018, 410 Medical from September 2017 to July 2019 and SIRPant Immunotherapeutics from September 2021 to June 2023. Mr. Whitfill has led numerous grant-funded projects, holds several patents and has co-authored over 60 publications. Mr. Whitfill received a B.S. from Dallas Baptist University, an MPH from Yale University and an MPhil from University College London. We believe that Mr. Whitfill's strong background in entrepreneurship and in the biotech and healthcare industries qualifies him to serve on our Board.

Barbara Ryan has served as a member of our Board since June 2023. Ms. Ryan founded Barbara Ryan Advisors, a capital markets and communications firm, in 2012 following a more than 30-year career on Wall Street as a sell-side research analyst covering the U.S. pharmaceutical industry. Ms. Ryan has deep experience in equity and debt financings, M&A, valuation, SEC reporting, financial analysis and corporate strategy across a broad range of life sciences companies. Ms. Ryan worked on several of the industry's largest M&A transactions, including Shire's defense versus a hostile takeover attempt by Abbvie, Shire's takeover of Baxalta, Allergan's defense against Valeant and Perrigo's defense versus Mylan Ms. Ryan served as an executive team member and on the disclosure committee for Radius Health from January 2014 to December 2017. Previously, Ms. Ryan was a managing director at Deutsche Bank/Alex Brown and head of the company's pharmaceutical research team for 19 years and began her research career covering the pharmaceutical industry at Bear Stearns in 1982. Ms. Ryan currently serves as a director on the board of MiNK Therapeutics, Inc. (Nasdaq: INKT), where she chairs the audit committee, INVO Bioscience, Inc, (Nasdaq: INVO), Invidior, PLC (LON:INDV) and The Red Door Community (formerly Gilda's Club NYC), a non-profit organization. Ms. Ryan is the founder of Fabulous Pharma Females, a non-profit whose

mission is to advance women in the biopharma industry, is a member of the editorial advisory board of Pharmaceutical Executive Magazine, a faculty member of the GLG Institute and a member of the Prix Galien executive advisory board. We believe that Ms. Ryan is qualified to serve as a member of our Board because of her experience and knowledge of corporate finance, mergers and acquisitions, corporate governance, as well as other operational, financial and accounting matters gained as a past and present executive officer and/or director of other public and private companies.

John Schroer has served as a member of our Board since June 2023. Mr. Schroer has served as chief financial officer of Alumis, Inc., a publicly traded biotechnology company developing precision immunology therapies, since March 2022. Mr. Schroer was chief financial officer of Arsenal Biosciences, Inc., a privately held biotechnology company developing programmable cell therapy for solid tumors, from February 2021 to February 2022. Mr. Schroer was chief financial officer of Translate Bio, Inc., a biotechnology company developing mRNA therapeutics and vaccines acquired by Sanofi in September 2021 for $3.2 billion, from May 2018 to December 2020. Previously, Mr. Schroer was Sector Head – Global Health Care for Allianz Global Investors, an international asset management firm, from January 2014 to May 2018. Mr. Schroer received his B.S. and M.B.A from the University of Wisconsin – Madison. We believe that Mr. Schroer's strong background holding leadership positions in the biotechnology industry and almost 30 years of investing in the life sciences sector qualifies him to serve on our Board.

Family Relationships

There are no family relationships among any of our executive officers or directors.

Corporate Governance

Audit Committee

Our audit committee consists of John Schroer, and Barbara Ryan, with Mr. Schroer serving as chairperson. Our Board has determined that each member meets the independence requirements of the Sarbanes-Oxley Act, Rule 10A-3 under the Exchange Act and the applicable listing standards of the NYSE American. In addition, our Board has determined that Mr. Schroer qualifies as an audit committee financial expert within the meaning of SEC regulations and meets the financial sophistication requirements of the NYSE American listing rules. Each member of our audit committee can read and understand fundamental financial statements in accordance with the SEC and NYSE American audit committee requirements. In arriving at this determination, the Board has examined each audit committee member's scope of experience and the nature of their prior and/or current employment. Both our independent registered public accounting firm and management periodically meet with our Audit Committee.

Process for Stockholders to Send Communications to our Board of Directors

Because we have always maintained open channels of communication with our stockholders, we do not have a formal policy that provides a process for stockholders to send communications to our Board. However, if a stockholder would like to send a communication to our Board, please address the letter to the attention of our corporate secretary, Travis Whitfill, and it will be distributed to each director.

Section 16(A) Beneficial Ownership Reporting Compliance

Rules adopted by the SEC under Section 16(a) of the Exchange Act require our officers and directors, and persons who own more than 10% of the issued and outstanding shares of our equity securities, to file reports of their ownership, and changes in ownership, of such securities with the SEC on Forms 3, 4 or 5, as appropriate. Such persons are required by the regulations of the SEC to furnish us with copies of all forms they file pursuant to Section 16(a).

Based solely upon a review of Forms 3, 4 and 5 and amendments thereto furnished to us during our most recent fiscal year, and any written representations provided to us, we believe that all of the officers, directors, and owners of more than 10% of the outstanding shares of our common stock complied with Section 16(a) of the Exchange Act for the year ended December 31, 2024.

Code of Ethics

We have adopted a Code of Ethics applicable to all of our employees, executive officers and directors. The Code of Ethics is available on our website at www.azitrainc.com. The audit committee of our Board is responsible for overseeing the Code of Ethics and must approve any waivers of the Code of Ethics for employees, executive officers and directors. In addition, we have posted on our website all disclosures that are required by law or the listing standards of the applicable stock exchange concerning any amendments to, or waivers from, any provision of the Code of Ethics.

Insider Trading Policy

We have adopted an Insider Trading Policy governing the purchase, sale, and other dispositions of our securities by our directors, officers, employees and consultants, including those persons serving in similar positions with our subsidiaries. Our Insider Trading Policy is reasonably designed to promote compliance with insider trading laws, rules and regulations, and any listing standards applicable to us and our directors, officers, employees and consultants. A copy of our Insider Trading Policy is filed as an exhibit to this report.

Item 11. Executive Compensation

Summary Compensation Table

The following table sets forth the compensation awarded to or earned by our chief executive officer and our two other highest paid executive officers for the years ended December 31, 2024 and 2023. In reviewing the table, please note that Travis Whitfill was appointed to serve as our chief operating officer in June 2023.

	Year	Salary ($)	Bonus ($)	Option Awards $ [1]	All Other Compensation [2]	Total
Francisco Salva,.....	2024	$ 440,000	$ —	$ —	$ 1,080	$ 441,080
Pres. and CEO	2023	$ 420,000	$ —	$ —	$ 7,030	$ 427,030
Norman Staskey,.....	2024	$ —	$ —	$ —	$ 457,560	$ 457,560
CFO	2023	$ —	$ —	$ 20,700	$ 314,025	$ 334,725
Travis Whitfill, ...	2024	$ 380,000	$ —	$ —	$ 4,460	$ 384,460
COO	2023	$ 158,846	$ —	$ 20,700	$ 2,767	$ 182,313

(1) The dollar amounts in the Option Awards columns above reflect the values of options as of the grant date for the years ended December 31, 2024 and 2023, in accordance with ASC 718, *Compensation-Stock Compensation* ("ASC 718") and, therefore, do not necessarily reflect actual benefits received by the individuals. Assumptions used in the calculation of these amounts are included in Note 9 to our audited financial statements.

(2) All other compensation includes commuter benefits, vacation payouts, relocation reimbursements, 401K match contributions, and life insurance premiums, plus consulting fees paid for Mr. Staskey's services as chief financial officer and consulting fees paid to Mr. Whitfill prior to his appointment as chief operating officer.

Narrative Disclosure to Officer Compensation Table

All of our current named executive officers are at-will employees and set forth below is a summary of the current terms of their compensatory arrangements.

Francisco D. Salva

We have entered into an executive employment agreement dated April 22, 2021 with Mr. Salva, pursuant to which Mr. Salva serves as our president and chief executive officer. We have agreed to pay Mr. Salva an annual base salary of $420,000 under the agreement. Mr. Salva is also eligible to receive a bonus of up to 35% of his base salary based on performance parameters set by our Board. Mr. Salva's executive employment agreement entitles him to participate in health insurance and other benefits, at our expense, made available to other executive officers. In the event of Mr. Salva's termination by us without cause or his resignation for good reason, as such terms are defined in the executive employment agreement, Mr. Salva will be entitled to the continuation of his base salary and health insurance coverage for a period of 12 months and a prorated amount of his annual bonus for the year in which the termination occurred, subject to the achievement of applicable performance targets. Mr. Salva's executive employment agreement is an "at will" agreement subject to termination by either party at any time and for any reason, subject to certain notice requirements. The agreement contains customary provisions relating to intellectual property assignment, confidentiality and indemnification.

In connection with our execution of the executive employment agreement, we granted to Mr. Salva an option to purchase up to 15,525 shares of our common stock at an exercise price of $51.08 per share under the 2016 Plan. The options vest and become exercisable as follows: 80% of the options, or options to purchase 12,420 shares of our common stock, are subject to time-based vesting, with options to purchase 3,105 shares (25%) vesting on the first anniversary of the grant and options to purchase 9,315 shares (75%) vesting in equal monthly installments over the 36 months following the first anniversary; 20% of the options, or options to purchase 3,105 shares of our common stock, shall vest upon patient dosing in the first in-human clinical trial of ATR-12 or a substitute live biotherapeutic product, as determined by our Board in its reasonable discretion. The options expire on the ten-year anniversary of the date of grant.

Norman Staskey

Mr. Staskey serves as our chief financial officer pursuant to a Consulting Agreement dated October 12, 2002 between us and Danforth Advisors, LLC. Pursuant to the Consulting Agreement, Danforth Advisors provides to us certain strategic and financial advice and support services, including Mr. Staskey's services as chief financial officer, at hourly rates between $135 and $575 per hour, depending on the level of service and the seniority of the service provider. The Consulting Agreement is subject to termination by either party on 30 days written notice and contains customary provisions relating to intellectual property assignment, confidentiality and indemnification.

On September 8, 2023, we granted to Mr. Staskey an option to purchase up to 333 shares of our common stock at an exercise price of $62.01 per share under the 2023 Plan. The options are subject to time-based vesting, with options to purchase 83 shares (25%) vesting on the first anniversary of the grant and options to purchase 250 shares (75%) vesting in equal monthly installments over the 36 months following the first anniversary; The options expire on the ten-year anniversary of the date of grant.

Travis Whitfill

We have entered into an executive employment agreement dated July 5, 2023 with Mr. Whitfill, pursuant to which Mr. Whitfill serves as our chief operating officer. We have agreed to pay Mr. Whitfill an annual base salary of $350,000 under the agreement. Mr. Whitfill is also eligible to receive a bonus of up to 30% of his base salary based on performance parameters set by our Board. Mr. Whitfill's executive employment agreement entitles him to participate in health insurance and other benefits, at our expense, made available to other executive officers. In the event of Mr. Whitfill's termination by us for any reason other than cause or his incapacity, as such terms are defined in the executive employment agreement, Mr. Whitfill will be entitled to the continuation of his base salary for a period of six months and, if unpaid at the time of termination, his annual bonus for the year prior to the year in which the termination occurred. Mr. Whitfill's executive employment agreement is an "at will" agreement subject to termination by either party at any time and for any reason, subject to certain notice requirements. The agreement contains customary provisions relating to intellectual property assignment, confidentiality and indemnification.

On September 8, 2023, we granted to Mr. Whitfill an option to purchase up to 333 shares of our common stock at an exercise price of $62.10 per share under the 2023 Plan. The options are subject to time-based vesting, with options to purchase 83 shares (25%) vesting on the first anniversary of the grant and options to purchase 250 shares (75%) vesting in equal monthly installments over the 36 months following the first anniversary; The options expire on the ten-year anniversary of the date of grant.

Outstanding Equity Awards at December 31, 2024

Set forth below is information concerning the equity awards held by our named executive officers as of December 31, 2024.

	Option Awards			
Name	**Number of Securities Underlying Unexercised Options (#) Exercisable**	**Number of Securities Underlying Unexercised Options (#) Unexercisable**	**Option Exercise Price ($)**	**Option Expiration Date**
Francisco Salva.....	11,385	1,035[1]	$ 51.08	06/29/31
	3,105	0[2]	$ 51.08	06/29/31
Norman Staskey.....	111	222[3]	$ 62.10	09/08/33
Travis Whitfill	1,859	0	$ 14.32	01/01/26
	1,246	0	$ 51.08	12/16/30
	111	222[3]	$ 62.10	09/08/23

(1) Options continue to vest ratably over the remaining thirty-six months of continuous service.

(2) Options are performance based and vest upon the achievement of clinical milestones as defined in Mr. Salva's employment agreement.

(3) 25% of the option awards vest on the first anniversary of the grant date with the remaining shares vesting ratably each month during the remaining thirty-six months of continuous service.

Non-Employee Director Compensation

Set forth below is a summary of the compensation we paid to our non-executive directors during the year ended December 31, 2024. In reviewing the table, please note that Andrew McClary resigned from our Board in August 2024.

Name	Fees Earned or Paid in Cash ($)	Option Awards ($)	All Other Compensation ($)	Total ($)
Andrew D. McClary, MD	$ —	$ —	$ —	$ —
Barbara Ryan	$ 42,983	$ 4,128	$ —	$ 47,111
John Schroer	$ 45,301	$ 4,128	$ —	$ 49,429

The dollar amounts in the Option Awards columns above reflect the values of options as of the grant date for the years ended December 31, 2024, in accordance with ASC 718, Compensation-Stock Compensation and, therefore, do not necessarily reflect actual benefits received by the individuals. Assumptions used in the calculation of these amounts are included in Note 9 to our audited consolidated financial statements included in our 2024 Form 10-K.

We do not compensate any of our executive directors for their service as a director. Our Board, on the recommendation of the Compensation Committee, approved the following compensation policy for our non-executive directors commencing with the 2024 calendar year:

- An annual Board retainer of $25,000 for the non-executive directors;
- An annual retainer of $5,000 for the chairs of the Compensation Committee and Nominating and Corporate Governance Committee and an annual retainer of $7,500 for the chair of the Audit Committee; and
- An annual retainer of $3,500 for the other members of the Compensation Committee, Nominating and Corporate Governance Committee and Audit Committee.

All retainers are payable quarterly in arrears and shall be prorated for any portion of a year to which they apply for each outside director. We also reimburse our non-executive directors for their reasonable expenses incurred in connection with attending meetings of our Board and Board Committees. From time to time, we may engage our non-executive directors to provide consulting services on our behalf, although we have not engaged any non-executive directors in a consulting capacity as of the date of this Proxy Statement.

In addition to cash retainers, in September 2023, we granted to each of Mrs. Ryan and Mr. Schroer an option to purchase up to 333 shares of our common stock at an exercise price of $62.10 per share under the 2023 Plan. The options are subject to time-based vesting, with options to purchase 83 shares (25%) vesting on the first anniversary of the grant and options to purchase 250 shares (75%) vesting in equal monthly installments over the 36 months following the first anniversary, subject to their continued service on our Board. The options expire on the 10-year anniversary of the date of grant.

Stock Incentive Plans

We have adopted the Azitra, Inc. 2016 Stock Incentive Plan, or 2016 Plan, providing for the grant of non-qualified stock options and incentive stock options to purchase shares of our common stock and for the grant of restricted and unrestricted share grants and restricted stock units. We currently have reserved 7,457 shares of our common stock under the 2016 Plan. The purpose of the 2016 Plan is to provide eligible participants with an opportunity to acquire an ownership interest in our company. All officers, directors, employees and consultants to our company are eligible to participate under the 2016 Plan. The 2016 Plan provides that options may not be granted at an exercise price less than the fair market value of our shares of common stock on the date of grant. As of the date of this report, we have outstanding options granted under the 2016 Plan to purchase an aggregate of 40,275 shares of our common stock at an average exercise price of $40.20 per share.

In March 2023, our Board and stockholders approved and adopted the Azitra, Inc. 2023 Stock Incentive Plan, or 2023 Plan, providing for the grant of non-qualified stock options and incentive stock options to purchase shares of our Common Stock and for the grant of restricted and unrestricted share grants and restricted stock units. In November 2024, our stockholders approved amendments to the 2023 Plan that (i) increased the number of shares of Common Stock that may be issued under the

2023 Plan by 1,144,401 shares and (ii) adopted an evergreen provision to the 2023 Plan providing for an automatic 5% annual increase in the shares of Common Stock available for issuance under the 2023 Plan over the next 10 years, commencing on January 1, 2026. We currently have reserved 1,211,068 shares of our common stock under the 2023 Plan. The purpose of the 2023 Plan is to provide eligible participants with an opportunity to acquire an ownership interest in our company. All officers, directors, employees and consultants to our company are eligible to participate under the 2023 Plan. The 2023 Plan provides that options may not be granted at an exercise price less than the fair market value of our shares of common stock on the date of grant. As of the date of this report, we have outstanding options granted under the 2023 Plan to purchase an aggregate of 1,333 shares of our common stock at an average exercise price of $62.10 per share.

Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters

The following table sets forth certain information regarding the beneficial ownership of our shares of common stock as of the date of this report by:

- each person who is known by us to be the beneficial owner of more than five percent (5%) of our issued and outstanding shares of common stock;
- each of our executive officers and directors; and
- all of the aforementioned directors and executive officers as a group.

The beneficial ownership of each person was calculated based on 14,979,354 shares of common stock issued as of February 12, 2025. The SEC has defined "beneficial ownership" to mean more than ownership in the usual sense. For example, a person has beneficial ownership of a share not only if he owns it, but also if he has the power (solely or shared) to vote, sell or otherwise dispose of the share. Beneficial ownership also includes the number of shares that a person has the right to acquire within 60 days of February 12, 2025, pursuant to the exercise of options or warrants or the conversion of notes, debentures or other indebtedness. Two or more persons might count as beneficial owners of the same share.

Unless otherwise indicated, the address for each reporting person is c/o Azitra, Inc., 21 Business Park Drive, Branford, Connecticut 06405.

Name of Director and Executive Officer	Number of Shares	Percentage Owned
Francisco D. Salva[1]	26,802	*
Norman Staskey[2]	1,842	*
Travis whitfill[3]	14,394	*
Barbara Ryan [4]	153	*
John Schroer[5]	153	*
Directors and executive officers, as a group (5 persons)	43,344	*

Name and Address of Five Percent Stockholders	Number of Shares	Percentage Owned
L1 Capital Global Opportunities Master Fund, Ltd[6]	776,375	5.18%

* Represents less than 1% of the number of shares of our common stock outstanding.

(1) Includes 15,525 shares of our common stock issuable upon exercise of presently exercisable options.
(2) Includes 139 shares of our common stock issuable upon exercise of presently exercisable options.
(3) Includes 3,244 shares of our common stock issuable upon exercise of presently exercisable options.
(4) Includes 153 shares of our common stock issuable upon exercise of presently exercisable options.
(5) Includes 153 shares of our common stock issuable upon exercise of presently exercisable options.
(6) Includes 146,375 of Class A Warrants held, which are exercisable subject to a 9.99% beneficial ownership limitation.

Item 13. Certain Relationships and Related Transactions, and Director Independence

Related Party Transactions

Since January 1, 2023, we have not been a party to any transaction in which the amount involved in the transaction exceeded the lesser of $120,000 or one percent of the average of our total assets as of December 31, 2024 and 2023, and in which any of our directors, executive officers or, to our knowledge, beneficial owners of more than 5% of our voting securities or any member of the immediate family of any of the foregoing persons had or will have a direct or indirect material interest, other than compensation arrangements, which include equity and other compensation, termination, change in control and other arrangements, which are described under "Executive Compensation." We have adopted a policy that any transactions with directors, officers, beneficial owners of five percent or more of our common stock, any immediate family members of the foregoing or entities of which any of the foregoing are also officers or directors or in which they have a financial interest, will only be on terms consistent with industry standards and approved by a majority of the disinterested directors of our Board.

Indemnification Agreements

We have entered into indemnification agreements with each of our directors and executive officers that may be broader than the specific indemnification provisions contained in the DGCL. These indemnification agreements require us, among other things, to indemnify our directors and executive officers against liabilities that may arise by reason of their status or service. These indemnification agreements also require us to advance all expenses incurred by the directors and executive officers in investigating or defending any such action, suit, or proceeding. We believe that these agreements are necessary to attract and retain qualified individuals to serve as directors and executive officers.

Director Independence

Our Board may establish the authorized number of directors from time to time by resolution. Our Board currently consists of five (4) authorized members. Generally, under the listing requirements and rules of the NYSE American, independent directors must comprise a majority of a listed company's board of directors. Our Board has undertaken a review of its composition, the composition of its committees and the independence of each director. Our Board has determined that, other than Mr. Salva and Mr. Whitfill, by virtue of their executive officer positions, none of our director has a relationship that would interfere with the exercise of independent judgment in carrying out the responsibilities of a director and that each is "independent" as that term is defined under the applicable rules and regulations of the SEC and the listing requirements and rules of the NYSE American. In making this determination, our Board considered the current and prior relationships that each nonemployee director nominee has with our Company and all other facts and circumstances our Board deemed relevant in determining their independence, including the beneficial ownership of our capital stock by each nonemployee director nominee. Accordingly, a majority of our directors are independent, as required under applicable NYSE American rules, as of the date of this report.

Item 14. Principal Accountant Fees and Services

Fees Incurred for Services by Principal Accountant

The following table sets forth the aggregate fees billed to us for services rendered to us for the years ended December 31, 2024 and 2023 by our independent registered public accounting firm, Grassi & Co., CPAs, P.C. (in thousands).

	2024	2023
Audit Fees [(A)]	$ 245,000	$ 195,929
Audit - Related Fees	—	—
Tax Fees	$ —	—
	$ 245,000	$ 195,929

(A) The audit fees consisted of fees for the audit of our financial statements, the review of the interim financial statements included in our quarterly reports on Form 10-Q, and other professional services provided in connection with the statutory and regulatory filings or engagements and capital market financings.

Pre-Approval Policies and Procedures

The Audit Committee has responsibility for selecting, appointing, evaluating, compensating, retaining and overseeing the work of the independent registered public accounting firm. In recognition of this responsibility, the Audit Committee has established policies and procedures in its charter regarding pre-approval of any audit and non-audit service provided to the Company by the independent registered public accounting firm and the fees and terms thereof.

The Audit Committee considered the compatibility of the provision of other services by its registered public accountant with the maintenance of their independence. The Audit Committee approved all audit services provided by Grassi & Co. in 2024 and 2023. Grassi & Co. did not perform any non-audit or tax services in 2024 or 2023.

PART IV

Item 15. Exhibits and Financial Statement Schedules

(a) Financial statements

Reference is made to the Index and Financial Statements under Item 8 in Part II hereof where these documents are listed.

(b) Financial statement schedules

Financial statement schedules are either not required or the required information is included in the consolidated financial statements or notes thereto filed under Item 8 in Part II hereof.

(c) Exhibits

The exhibits to this Annual Report on Form 10-K are set forth below. The exhibit index indicates each management contract or compensatory plan or arrangement required to be filed as an exhibit.

Number	Exhibit Description	Method of Filing
3.1	Second Amended and Restated Certificate of Incorporation of the Registrant	Incorporated herein by reference to the Company's Current Report on Form 8-K filed on June 21, 2023.
3.2	Second Amended and Restated Bylaws of the Registrant	Incorporated herein by reference to the Company's Current Report on Form 8-K filed on June 21, 2023.
3.3	Certificate of Amendment dated June 27, 2024 to Amended and Restated Certificate of Incorporation	Incorporated herein by reference to the Company's Form S-3 filed on July 1, 2024.
3.4	Amendment to Second Amended and Restated Bylaws of the Registrant	Incorporated herein by reference to the Company's Current Report on Form 8-K filed on August 12, 2024.
4.1	Specimen Certificate representing shares of Common Stock	Incorporated herein by reference to the Company's Form S-1 filed on June 13, 2023.
4.2	Form of Warrant issued to Private Placement investors	Incorporated herein by reference to the Company's Form S-1 filed on June 13, 2023.
4.3	Form of Representative's Warrant dated June 20, 2023 issued to ThinkEquity LLC	Incorporated herein by reference to the Company's Form S-1 filed on June 13, 2023.
4.4	Form of Representative's Warrant dated February 16, 2024 issued to ThinkEquity LLC (attached to Underwriting Agreement between the Registrant and ThinkEquity, LLC dated February 13, 2024)	Incorporated herein by reference to the Company's Current Report on Form 8-K filed on February 14, 2024.
4.5	Form of Class A Warrant issued in July 2024 offering	Incorporated herein by reference to the Company's Current Report on Form 8-K filed on July 26, 2024
4.6	Form of Placement Agent Warrant issued to Maxim Partners, LLC	Incorporated herein by reference to the Company's Current Report on Form 8-K filed on July 26, 2024
4.7	Warrant Agent Agreement dated July 25, 2024 between the Registrant and VStock Transfer LLC	Incorporated herein by reference to the Company's Current Report on Form 8-K filed on July 26, 2024
4.8	Form of Placement Agent Warrant issued to Maxim Partners, LLC	Incorporated herein by reference to the Company's Current Report on Form 8-K filed on January 16, 2025
4.9	Form of Letter Agreement Between the Registrant and investors in February 2025 Securities Offering	Incorporated herein by reference to the Company's Current Report on Form 8-K filed on February 6, 2025
4.10	Form of Warrant issued to Investors in February 2025 Securities Offering	Incorporated herein by reference to the Company's Current Report on Form 8-K filed on February 6, 2025
4.11	Description of Capital Stock	Incorporated herein by reference to the Company's Annual Report on Form 10-K filed on March 15, 2024
+10.10	Azitra Inc. 2016 Stock Incentive Plan	Incorporated herein by reference to the Company's Form S-1 filed on June 13, 2023.
+10.20	Azitra Inc. 2023 Stock Incentive Plan	Incorporated herein by reference to the Company's Form S-1 filed on June 13, 2023.
+10.30	Executive Employment Agreement dated April 22, 2021 between the Registrant and Francisco D. Salva	Incorporated herein by reference to the Company's Form S-1 filed on June 13, 2023.

Number	Exhibit Description	Method of Filing
+10.40	Executive Employment Agreement dated July 5, 2023 between the Registrant and Travis Whitfill	Incorporated herein by reference to the Company's Form S-1 filed on January 19, 2024.
+10.50	Form of Indemnity Agreement between the Registrant and each of its directors and executive officers	Incorporated herein by reference to the Company's Form S-1 filed on June 13, 2023.
10.6	Second Amended and Restated Investors' Rights Agreement dated September 10, 2020 between the Registrant and each of the investors named therein	Incorporated herein by reference to the Company's Form S-1 filed on June 13, 2023.
19.1	Azitra, Inc. Insider Trading Policy	Filed electronically herewith
21.1	List of Subsidiaries of the Registrant	Incorporated herein by reference to the Company's Form S-1 filed on March 20, 2023.
23.2	Consent of Grassi & Co., CPAs, P.C., Independent Registered Public Accounting Firm	Filed electronically herewith.
31.1	Certification under Section 302 of the Sarbanes-Oxley Act of 2002	Filed electronically herewith.
31.2	Certification under Section 302 of the Sarbanes-Oxley Act of 2002	Filed electronically herewith.
32.1	Certifications Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, 18 U.S.C. Section 1350	Filed electronically herewith.
97.1	Azitra, Inc. Executive Officer Clawback Policy	Incorporated herein by reference to the Company's Annual Report on Form 10-K filed on March 15, 2024.

+ Indicates management compensatory plan, contract or arrangement.

Item 16. Form 10-K Summary

Not provided

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the Registrant has duly caused this annual report on Form 10-K to be signed on its behalf by the undersigned, thereunto duly authorized.

AZITRA, INC.

Date: February 24, 2025

By: */s/ Francisco D. Salva*
Francisco D. Salva,
President and Chief Executive Officer
(Principal Executive Officer)

Date: February 24, 2025

By: */s/ Norman Staskey*
Norman Staskey
Chief Financial Officer
(Principal Financial Officer)

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed below by the following persons on behalf of the registrant and in the capabilities and on the dates indicated.

Signature	Title	Date
/s/ Francisco D. Salva Francisco D. Salva,	President, Chief Executive Officer and Director (Principal Executive Officer)	February 24, 2025
/s/ Norman Staskey Norman Staskey	Chief Financial Officer, and Treasurer (Principal Financial and Accounting Officer)	February 24, 2025
/s/ Travis Whitfill Travis Whitfill	Chief Operating Officer, Secretary, and Director	February 24, 2025
/s/ Barbara Ryan Barbara Ryan	Director	February 24, 2025
/s/ John Schroer John Schroer	Director	February 24, 2025