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

FORM 10-K

(Mark One)

☒ ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934 For the fiscal year ended December 31, 2022

or

☐ 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 001-39279

Old Ayala, Inc.
(Exact name of Registrant as specified in its Charter)

Delaware	82-3578375
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification No.)
Oppenheimer 4 Rehovot, Israel	7670104
(Address of principal executive offices)	(Zip Code)

(857) 444-0553
(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, $0.01 par value per share	N/A	N/A

* Form 25 filed by Nasdaq Global Market on January 19, 2023. By operation of law, Old Ayala's securities will remain registered under Section 12(b) until April 19, 2023.

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 Section 15(d) of the 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 (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit such files). YES ☒ NO ☐

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, 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 ☒

The aggregate market value of the voting and non-voting common equity held by non-affiliates of the registrant, based on the closing price of the shares of common stock on The Nasdaq Stock Market on June 30, 2022 was approximately $37.4 million.

The number of shares of Registrant's Common Stock outstanding as of March 30, 2023 was 1.

DOCUMENTS INCORPORATED BY REFERENCE

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EXPLANATORY NOTE

As previously disclosed on October 19, 2022, Old Ayala, Inc. ("Old Ayala") entered into an Agreement and Plan of Merger (the "Merger Agreement"), dated as of October 18, 2022, by and among Ayala Pharmaceuticals, Inc., (f/k/a Advaxis Inc.) a Delaware corporation ("Advaxis" and or "New Ayala") and Doe Merger Sub, Inc., a Delaware corporation and a wholly-owned subsidiary of Advaxis ("Merger Sub"). On January 19, 2023 (the "Closing Date"), pursuant to the Merger Agreement, Merger Sub merged with and into Old Ayala, with Old Ayala continuing as the surviving company and a wholly-owned subsidiary of Advaxis (the "Merger"). As a result of the Merger, Advaxis was renamed "Ayala Pharmaceuticals, Inc." The Merger Agreement and additional information on the details of the Merger may be found in the Current Report on Form 8-K filed with the Securities and Exchange Commission ("SEC") by Old Ayala on October 19, 2022.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K contains forward-looking statements.. All statements other than statements of historical facts contained in this Annual Report, including without limitation statements relating to our development of AL101 and AL102, our ability to continue as a going concern, our future capital needs and our need to raise additional funds, the promise and potential impact of our preclinical or clinical trial data, the timing of and plans to initiate additional clinical trials of AL101 and AL102, and the timing and results of any clinical trials or readouts, , are forward-looking statements. These statements involve known and unknown risks, uncertainties and other important factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements.

In some cases, you can identify forward-looking statements by terms such as "may," "will," "should," "expect," "plan," "anticipate," "could," "intend," "target," "project," "contemplate," "believe," "estimate," "predict," "potential", or "continue" or the negative of these terms or other similar expressions, although not all forward-looking statements are identified by these terms or expressions. The forward-looking statements in this Annual Report are only predictions. We have based these forward-looking statements largely on our current expectations and projections about future events and financial trends that we believe may affect our business, financial condition and results of operations. These forward-looking statements speak only as of the date of this Annual Report and are subject to a number of important factors that could cause actual results to differ materially from those in the forward-looking statements, including the factors described under the sections in this Annual Report titled and "Management's Discussion and Analysis of Financial Condition and Results of Operations."

Moreover, we operate in an evolving environment. New risk factors and uncertainties may emerge from time to time, and it is not possible for management to predict all and uncertainties.

You should read this Annual Report and the documents that we reference in this Annual Report completely and with the understanding that our actual future results may be materially different from what we expect. We qualify all of our forward-looking statements by these cautionary statements. Except as required by applicable law, we do not plan to publicly update or revise any forward-looking statements contained herein, whether as a result of any new information, future events, changed circumstances or otherwise.

PART I

Item 1. Business.

Introductory Note

The following discussion relates to the business of New Ayala as it existed prior to the Merger. Following the Merger, New Ayala has combined such existing business and the business of Old Ayala. In accordance with Rule 12b-23 under the Securities Exchange Act of 1934, as amended (the "Exchange Act"), we are incorporating into this Item 1 the description of the business of Old Ayala set forth in pages 233-273 of the Definitive Proxy Statement of Old Ayala for the Special Meeting of Stockholders of Old Ayala held on January 13, 2023, which was filed with the Commission on December 12, 2022 and which pages are set forth on Exhibit 99.1 to this Annual Report on Form 10-K. Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations as well as the Finical Statements refers to Old Ayala.

General

Prior to the Merger, New Ayala was a clinical-stage biotechnology company that was focused on the development and commercialization of proprietary *Listeria* monocytogenes, or *Lm*, Technology antigen delivery products based on a platform technology that utilizes live attenuated *Lm* bioengineered to secrete antigen/adjuvant fusion proteins. These *Lm*-based strains are believed to be a significant advancement in immunotherapy as they integrate multiple functions into a single immunotherapy and are designed to access and direct antigen presenting cells to stimulate anti-tumor T cell immunity, activate the immune system with the equivalent of multiple adjuvants, and simultaneously reduce tumor protection in the Tumor Microenvironment, or TME, to enable T cells to eliminate tumors. The Company believes that *Lm* Technology immunotherapies can complement and address significant unmet needs in the current oncology treatment landscape. Specifically, the Company's product candidates have the potential to optimize the clinical impact of checkpoint inhibitors while having a generally well-tolerated safety profile. The Company's passion for the clinical potential of *Lm* Technology is balanced by focus and fiscal discipline which is directed towards improving treatment options for cancer patients and increasing shareholder value.

Prior to the Merger, New Ayala was focused on multiple antigen delivery products which are in various stages of clinical development. All of the Company's products are anchored in the Company's *Lm* Technology™, a unique platform designed for its ability to target various cancers in multiple ways. As an intracellular bacterium, *Lm* is an effective vector for the presentation of antigens through both the Major Histocompatibility Complex, or MHC, I and II pathways, due to its active phagocytosis by Antigen Presenting Cells, or APCs. Within the APCs, *Lm* produces virulence factors which allow survival in the host cytosol and potently stimulate the immune system.

Through a license from the University of Pennsylvania and through its own development efforts, New Ayala has exclusive access to a proprietary formulation of attenuated *Lm* that is called *Lm* Technology. *Lm* Technology is designed to optimize this natural system, and one of the keys to the enhanced immunogenicity of *Lm* Technology is the *tLLO*-fusion protein, which is made up of tumor associated antigen, or TAA, fused to a highly immunogenic bacterial protein that triggers potent cellular immunity. The *tLLO*-fusion protein is also designed to help reduce immune tolerance in the TME and to promote antigen spreading, thereby improving activity in the TME. Multiple copies of the *tLLO*-fusion protein within each construct may increase antigen presentation and TME impact.

As the field of immunotherapy continues to evolve, the flexibility of the *Lm* Technology platform allowed New Ayala to develop highly innovative products. To date, *Lm* Technology has demonstrated preclinical synergy with multiple checkpoint inhibitors, co-stimulatory agents and radiation therapy. The safety profile of all *Lm* Technology constructs seen to date across over 470 patients has been generally predictable and manageable, consisting mostly of mild to moderate flu-like symptoms that have been transient and associated with infusion.

The New Ayala Corporate Strategy and Strategic Considerations

Prior to the Merger, New Ayala's strategy was to advance the *Lm* Technology platform and leverage its unique capabilities to design and develop an array of cancer treatments. We are currently conducting clinical studies of *Lm* Technology immunotherapies in early prostate cancer. We identified and worked with collaborators and potential licensees for these programs and others for first-generation *Lm* immunotherapies like ADXS-HPV for HPV-associated cancer and ADXS-HER-2 for pediatric osteosarcoma.

New Ayala mainly concentrated on its disease-focused, hotspot/"off-the-shelf" neoantigen-directed therapies called ADXS-HOT. ADXS-HOT is a program that leverages the Company's proprietary *Lm* technology to target hotspot mutations that commonly occur in specific cancer types. ADXS-HOT drug candidates are designed to target acquired shared or "public" mutations in tumor driver genes along with other cancer-associated antigens that also commonly occur in specific cancer types.

Prior to the Merger, New Ayala expected to continue investing exclusively in the HOT construct ADXS-504 in early prostate cancer through an ongoing Investigator Sponsored Trial (IST) at Columbia University in NYC. The study with ADXS-503 immunotherapy in non-small cell lung cancer was stopped due to the difficulty in enrolling additional patients. The *Lm* Technology platform is protected by a range of patents, covering both product and process, some of which we believe can be maintained into 2039.

In October 2022, we announced that we had entered into the Merger Agreement with Old Ayala, pursuant to which Old Ayala is to merge with and into Merger Sub, a direct, wholly-owned subsidiary of Old Ayala, with New Ayala continuing as the surviving company and a wholly-owned subsidiary of the Merger. The Merger closed on January 19, 2023.

***Lm* Technology and the Immunotherapy Landscape**

The challenge of cancer immunotherapy has been to find the best overall balance between efficacy and side effects when mobilizing the body's immune system to fight against cancer. The development of immune checkpoint inhibitors was a significant step forward, particularly with anti-PD-1 therapies, and brought with it impressive clinical activity in many different types of cancers, including melanoma, lung, head and neck and urothelial cancers. However, a literature review published in *Science* in 2018 noted that anti-PD-1 monotherapy response rates are only in the 15-25% range, and rise to ≥50% only in selected groups of patients with desmoplastic melanoma, Merkel carcinoma or tumors with mismatch-repair deficiency. Development of secondary resistance with disease progression is yet another common limitation of these therapies. Therefore, for most cancer patients, there is room for improvement. Checkpoint inhibitors can expand existing cancer fighting cells that may already be present in low numbers and support their activity against cancer cells, but if the right cancer-fighting cells are not present, checkpoint inhibitors may not provide clinical benefit. Similarly, there are many mechanisms of immune tolerance that are distinct from the checkpoints which may also be blocking the immune system from fighting cancer. Based on both pre-clinical and early clinical data, New Ayala believes that checkpoint inhibitors, when combined with treatments such as *Lm* Technology, can have an amplified anti-tumor effect. *Lm* Technology incorporates several complementary elements that include innate immune stimulation, potent generation of cancer-targeted T cells, ability to boost immunity through multiple treatments, enhancing lymphocyte infiltration into tumors, reduction of non-checkpoint mediated immune tolerance within the tumor microenvironment, and promotion of antigen spreading which may amplify the effects of treatment. These results provide rationale for further testing of *Lm* Technology agents alone and in combination with checkpoint inhibitors.

Traditional cancer vaccines were another development within immunotherapy and have a history beginning over 30 years ago. Unfortunately, these vaccines have largely been unsuccessful for a variety of potential reasons. These include poor selection of targets, imbalanced antigen presentation by inclusion of certain immune enhancing agents (adjuvants), failure to consider the blocking actions of immune tolerance, and choice of vaccine vectors. In some cases, patients may develop neutralizing antibodies, preventing further treatments. In contrast to traditional cancer vaccines, *Lm* Technology takes advantage of a natural pathway in the immune system that evolved to protect us against *Listeria* infections, that also happens to generate the same type of immunity that is required when fighting cancer. The live but weakened (attenuated) bacteria stimulate a balanced concert of innate immune triggers and present the tumor antigen target precisely where it needs to be able to generate potent cancer fighting cells from within the immune system itself. The multitude of accompanying signals serves to broadly mobilize most of the immune system in support of fighting what seems to be a *Listeria* infection, and is then "re-directed" against cancer cell targets. Additionally, the unique intracellular lifecycle of *Listeria* avoids the creation of neutralizing antibodies, thereby allowing for repeat administration as a chronic therapy with a sustained enhancing of tumor antigen-specific T cell immunity.

Looking back on the last two decades, there have been promising technology advancements to harness and activate killer T cells against cancers and every day more is learned about the interplay between immunity and cancer that can lead to improved treatments. However, there are still significant unmet needs in the immunotherapy landscape that New Ayala, feels *Lm* Technology may be able to address and complement. Specifically, *Lm* Technology has the potential to optimize and expand checkpoint inhibitor activity in combination. It also avoids many of the limitations of previous cancer vaccine attempts by tapping into the pathway reserved for defense against *Listeria* infection while incorporating the best cancer targets science can identify, including neoantigens that result from mutations in the cancer. Moreover, these immunotherapies could be effectively used as adjuvant therapies for patients who have had clinical response to radical therapy, in order to prevent emergence of new metastases and disease progression. To date, *Lm* Technology products have a manageable safety profile, do not generate neutralizing antibodies lending themselves to retreatments, and most of the products are designed to be immediately available for treatment without the complication and expense of modifying a patient's own cells in a laboratory.

***Lm* Technology: An optimized *Listeria* -based antigen delivery system**

New Ayala's *Listeria* -based immunotherapies are designed for antigen delivery through a process of insertion of multiple copies of the proprietary *tLLO*-fusion protein into each extrachromosomal protein expression and secretion plasmid that makes and secretes the target protein right inside the patient's antigen presenting cells to initiate and/or boost their immune response. The *tLLO*-fusion protein approach was developed at the University of Pennsylvania as an improvement over insertion of a single copy of the target gene, as an ACT-A (or other *Lm* peptide) fusion, within the bacterial genome for four key reasons:

1. Multiple copies of the DNA in the plasmids per bacteria can result in larger amounts of *tLLO* -fusion protein being expressed simultaneously, versus a single copy. This is designed to improve antigen presentation and immunologic priming and increases the number of T cells generated for a particular treatment.

2. tLLO expressed on plasmids (with or without a tumor target protein attached) has been shown preclinically to reduce numbers and immune suppressive function of Tregs and myeloid-derived suppressor cells, or MDSCs, in the tumor microenvironment. Presented preclinical data demonstrates that Tregs are destroyed as soon as five days after the first Lm Technology treatment and that suppressive M2 tumor-associated macrophages, or TAMs, are replaced by M1 macrophages which support antigen presentation and adoptive immunity.

3. The extrachromosal DNA plasmids themselves also contain CpG sequence patterns that trigger TLR-9, which confers additional innate immune stimulation beyond a Listeria without the plasmids.

4. The multiple copies of bacterial DNA plasmids (up to 80-100 per bacteria) confers additional stimulation of the STING receptor within APC's which has been associated with enhancing anti-cancer immunity in patients.

Clinical Pipeline

Prior to the Merger, New Ayala was focused on the development and commercialization of proprietary *Lm* Technology antigen delivery products. New Ayala is currently winding down or has wound down clinical studies of *Lm* Technology immunotherapies in four program areas:

- Non-small cell lung cancer (ADXS-503)
- Human Papilloma Virus ("HPV")-associated cancers
- Personalized neoantigen-directed therapies
- Human epidermal growth factor receptor-2 (HER-2) associated cancers

All these clinical program areas are anchored in the Company's *Lm* Technology™, a unique platform designed for its ability to safely and effectively target various cancers in multiple ways. The Phase 1/2 study with ADXS-PSA ± pembrolizumab in metastatic castration-resistant prostate cancer patients was closed on January 25, 2021. The MEDI Phase 2 combo study (AZ) with AXAL ± durvalumab in Cervical and Head and Neck Cancer and the AIM2CERV Phase 3 clinical trial with ADXS-HPV (AXAL) in cervical cancer were closed on August 22, 2019 and June 11, 2021, respectively. The study with personalized neoantigen-directed therapies (ADXS-NEO) was closed on May 22, 2020 and the NEO program-IND inactivation request was submitted to the FDA on May 10, 2021. On October 18, 2022, New Ayala announced that it would begin the orderly wind down of its ADXS-503 product in the 4Q 2022 to focus primarily on the Old Ayala product line and its other products.

While we are currently winding down clinical studies of *Lm* Technology immunotherapies in these program areas, our license agreements continue with OS Therapies, LLC, for ADXS-HER2, and with GBP for the exclusive license for the development and commercialization of ADXS-HPV or AXAL in Asia, Africa, and the former USSR territory, exclusive of India and certain other countries.

New Ayala Pipeline of Product Candidates

Disease-focused hotspot/'off -the-shelf' neoantigen therapies (ADXS-HOT)

Prior to the Merger, New Ayala created a new group of immunotherapy constructs for major solid tumor cancers that combines our optimized *Lm* Technology vector with promising targets designed to generate potent anti-cancer immunity. The ADXS-HOT program is a series of novel cancer immunotherapies that will target somatic mutations, or hotspots; cancer testis antigens, or CTAs; and oncofetal antigens, or OFAs. These three types of targets form the basis of the ADXS-HOT program because they are designed to be more capable of generating potent, tumor-specific, and high-strength killer T cells, versus more traditional over-expressed native sequence tumor associated antigens. Most hotspot mutations and OFA/CTA proteins play critical roles in oncogenesis; targeting both at once could significantly impair cancer proliferation. The ADXS-HOT products will combine many of the potential high avidity targets that are expressed in all patients with the target disease into one "off-the-shelf," ready-to-administer treatment. The ADXS-HOT technology has a strong intellectual property, or IP, position, with potential protection into 2037, and an IP filing strategy provides for broad coverage opportunities across multiple disease platforms and combination therapies. New Ayala entered into an agreement with Columbia University Irving Medical Center in April 2021 to fund a phase 1 clinical study evaluating ADXS-504 in patients with biochemically recurrent prostate cancer. The study started early in 3Q 2021 and was the first clinical evaluation of ADXS-504, New Ayala's off-the-shelf neoantigen immunotherapy drug candidate for early prostate cancer.

Nearly 248,530 men in the United States will be diagnosed with prostate cancer in 2021. It has been estimated that ~135,000 new cases undergo radical prostatectomy (RP) or radiotherapy (RT). Of these cases, 20–40% of pts with RP and 30–50% with RT will experience rising prostate specific antigen (PSA) levels following local therapy (BCR) within 10 years, a condition known as biochemical recurrence (BCR). BCR is not typically associated with imminent death, and biochemical progression may occur over a prolonged period. Clinicians treating men with BCR thus face a difficult set of decisions in attempting to delay the onset of metastatic disease and death while avoiding over-treating patients whose disease may never affect their overall survival or quality of life.

The phase 1 open-label study is evaluating the safety and tolerability of ADXS-504 monotherapy, administered via infusion, in 9-18 patients with biochemically recurrent prostate cancer, i.e., those with elevation of prostate-specific antigen (PSA) in the blood after radical prostatectomy or radical radiotherapy (external beam or brachytherapy) and who are not currently receiving androgen ablation therapy. The study will also evaluate if the body's immune system can control the prostate cancer following treatment with ADXS-504 monotherapy.

HPV-Related Cancers

The Company conducted several studies evaluating axalimogene filolisbac, or AXAL, for HPV-related cancers. AXAL is an *Lm*-based antigen delivery product directed against HPV and designed to target cells expressing HPV.

In June 2019, the Company announced the closing of its AIM2CERV Phase 3 clinical trial with axalimogene filolisbac (AXAL) in high-risk locally advanced cervical cancer. Company estimates showed that the remaining cost to complete the AIM2CERV trial ranged from $80 million to $90 million, and initial efficacy data was not anticipated for at least three years. Therefore, results from the clinical trial were not the basis for the decision to close the study, nor was safety as the trial recently underwent its third Independent Data Monitoring Committee (IDMC) review with no safety issues noted. The Company has unblinded the AIM2CERV clinical data generated to date and currently has no plans to present it at any medical conference as the data set is incomplete and inconclusive. The Company's clinical study report of the AIM2CERV Phase 3 study was completed on January 3, 2022 and submitted to the FDA.

In 2014, New Ayala granted Global BioPharma, or GBP, an exclusive license for the development and commercialization of AXAL in Asia, Africa, and the former USSR territory, exclusive of India and certain other countries. GBP is responsible for all development and commercial costs and activities associated with the development in their territories.

Personalized Neoantigen-directed Therapies (ADXS-NEO)

ADXS-NEO is an individualized *Lm* Technology antigen delivery product developed using whole-exome sequencing of a patient's tumor to identify neoantigens. ADXS-NEO is designed to work by presenting a large payload of neoantigens directly into dendritic cells within the patient's immune system and stimulating a T cell response against cancerous cells. In October 2019, the Company announced that it has dosed its last patient in Part A, in monotherapy, and does not intend to continue into Part B, in combination with a checkpoint inhibitor. As a result, New Ayala has closed this study. The Company has completed the clinical study report from Part A of the ADXS-NEO study and the NEO program-IND inactivation request has been submitted to FDA.

Prostate Cancer (ADXS-PSA)

According to the American Cancer Society, prostate cancer is the second most common type of cancer found in American men and is the second leading cause of cancer death in men, behind only lung cancer. More than 160,000 men are estimated to be diagnosed with prostate cancer in 2018, with approximately 30,000 deaths each year. Unfortunately, in about 10-20% of cases, men with prostate cancer will go on to develop castration-resistant prostate cancer, or CRPC, which refers to prostate cancer that progresses despite androgen deprivation therapy. Metastatic CRPC, or mCRPC, occurs when the cancer spreads to other parts of the body and there is a rising prostate-specific antigen, PSA, level. This stage of prostate cancer has an average survival of 9-13 months, is associated with deterioration in quality of life, and has few therapeutic options available.

Recent data regarding checkpoint inhibitor monotherapy has shown some antitumor activity that provides disease control in a subset of patients with bone predominant mCRPC previously treated with next generation hormonal agents and docetaxel. Data from the KEYNOTE-199 trial in bone predominant-mCRPC patients treated with KEYTRUDA®, or pembrolizumab, was updated at the ASCO GU meeting in 2019. In this trial, the total stable disease/disease stabilization rate was 39% with no responses reported so far, and only one patient with ≥50% decrease in the post-baseline PSA value. It is hypothesized that the limited activity in mCRPC may be due to 1) the inability of the checkpoint inhibitor to infiltrate the tumor microenvironment and 2) the presence of an immunosuppressive tumor micro-environment, or TME. The combination therapy with agents—like *Lm* constructs—that induce T cell infiltration within the tumor and decrease negative regulators in the TME may improve performance of checkpoints in prostate cancer.

Lm Technology constructs demonstrated the ability to induce anti-tumor T cell responses and T cell infiltration in the TME and to reduce the number and suppressive function of Tregs and MDSCs in the TME. For example, destruction of Tregs in the TME has been documented as soon as five days after dosing *Lm* constructs in models. This reduction of immune suppression in the tumors has been attributed to our proprietary *tLLO*-fusion peptides expressed by multiple copies of the plasmids in each bacteria. Because of all these effects, it is hypothesized that *Lm* constructs can turn "cold prostate tumors" into "hot tumors" that better respond to checkpoint inhibitors. Advaxis believes that the combination of ADXS-PSA, its immunotherapy designed to target the PSA antigen, with a checkpoint inhibitor may provide an alternative treatment option for patients with mCRPC.

New Ayala entered into a clinical trial collaboration and supply agreement with Merck to evaluate the safety and efficacy of ADXS-PSA as monotherapy and in combination with KEYTRUDA®, Merck's anti PD-1 antibody, in a Phase 1/2, open-label, multicenter, dose determination and expansion trial in patients with previously treated metastatic, castration-resistant prostate cancer (KEYNOTE-046). ADXS-PSA was tested alone or in combination with KEYTRUDA in an advanced and heavily pretreated patient population who had progressed on androgen deprivation therapy. A total of 13 and 37 patients were evaluated on monotherapy and combination therapy, respectively. For the ADXS-PSA monotherapy dose escalation and determination portion of the trial, cohorts were started at a dose of 1×10^9 cfu (n=7) and successfully escalated to higher dose levels of 5×10^9 cfu (n=3) and 1×10^{10} cfu (n=3) without achieving a maximum tolerated dose. TEAEs noted at these higher dose levels were generally consistent with those observed at the lower dose level (1×10^9 cfu) other than a higher occurrence rate of Grade 2/3 hypotension. The Recommended Phase II Dose of ADXS-PSA monotherapy was determined to be 1×10^9 cfu based on a review of the totality of the clinical data. This dose was used in combination with 200mg of pembrolizumab in a cohort of six patients to evaluate the safety of the combination before moving into an expanded cohort of patients. The safety of the combination was confirmed and enrollment in the expansion cohort phase was initiated. Enrollment in the study was completed in January 2017.

At the final data cutoff of September 16, 2019, median overall survival for 37 patients in the combination arm was 33.6 months (95% CI, range 15.4-33.6 months). This updated median overall survival is an increase from the previous data presented at the American Association for Cancer Research Annual Meeting in April 2019, where median overall survival was 21.1 months in the combination arm. The combination of ADXS-PSA with KEYTRUDA®, might be associated with prolonged OS in this population, particularly in patients with unmet medical needs like visceral metastasis (16.4 months, range 4.0 - not reached) and those with prior docetaxel (16 months, range 6.4-34.6). The majority of TEAEs consisted of transient and reversible Grade 1-2 chills/rigors, fever, hypotension, nausea and fatigue. The combination of ADXS-PSA and KEYTRUDA® has appeared to be well-tolerated to date, with no additive toxicity observed. The Company presented these new data at the ASCO Genitourinary Cancers Symposium in San Francisco, CA. on February 2020 and the final results were published in the peer-reviewed journal "The Oncologist" in 2022. New Ayala has also completed the clinical study report for the ADXS-PSA study.

Other Lm Technology Products

HER2 Expressing Solid Tumors

HER2 is overexpressed in a percentage of solid tumors including osteosarcoma. According to published literature, up to 60% of osteosarcomas are HER2 positive, and this overexpression is associated with poor outcomes for patients. ADXS-HER2 is an *Lm* Technology antigen delivery product candidate designed to target HER2 expressing solid tumors including human and canine osteosarcoma. ADXS-HER2 has received FDA and EMA ODD for osteosarcoma and has received Fast Track designation from the FDA for patients with newly-diagnosed, non-metastatic, surgically-resectable osteosarcoma.

A phase 1B dose escalation study of ADXS31-164 in subjects with HER-2 expressing tumors was completed, and the database lock was completed in November 2018. Overall, ADXS31-164 IV infusion at the dose of 1×10^9 CFU appeared to be safe and well tolerated in 12 subjects treated and evaluable. No objective responses were observed in this late stage heavily pre-treated patient cohort. The results of this study were primarily intended to describe the safety and tolerability of ADXS31-164. This study was not intended to contribute to the evaluation of the effectiveness of ADXS31-164 for the treatment of patients with a history of HER2 expressing tumors. New Ayala has completed the clinical study report and it has been transferred along with the ADXS31-164 program-IND to OS Therapies, as described below.

In September 2018, the Company announced that it had granted a license to OS Therapies, LLC, or OS Therapies, for the use of ADXS31-164, also known as ADXS-HER2, for evaluation in the treatment of osteosarcoma in humans. Under the terms of the license agreement, OS Therapies, in collaboration with the Children's Oncology Group, will be responsible for the conduct and funding of a clinical study evaluating ADXS-HER2 in recurrent, completely resected osteosarcoma. In December 2020 and January 2021, we received an aggregate of $1,415,000 from OS Therapies upon achievement of the $1,550,000 funding milestone set forth in the license agreement. In April 2021, the Company achieved the second milestone set forth in the license agreement for evaluation in the treatment of osteosarcoma in humans and received the amount due from OS Therapies of $1,375,000 in May 2021. For more information, see Note 12, "*Licensing Agreements*" of the "*Notes to the Consolidated Financial Statements*" included in Item 8.

Canine Osteosarcoma

On March 19, 2014, we entered into a definitive Exclusive License Agreement, or Aratana Agreement, with Aratana Therapeutics, Inc., or Aratana, where we granted Aratana an exclusive, worldwide, royalty-bearing license, with the right to sublicense, certain of our proprietary technology that enables Aratana to develop and commercialize animal health products that will be targeted for treatment of osteosarcoma and other cancer indications in animals. A product license request was filed by Aratana for ADXS-HER2 (also known as AT-014 by Aratana) for the treatment of canine osteosarcoma with the United States Department of Agriculture, or USDA. Aratana received communication in December 2017 that the USDA granted Aratana conditional licensure for AT-014 for the treatment of dogs diagnosed with osteosarcoma, one year of age or older. Initially, Aratana plans to make the therapeutic available for purchase at approximately two dozen veterinary oncology practice groups across the United States who participate in the study. Aratana received communication in December 2017 that the USDA granted Aratana conditional licensure for AT-014 for the treatment of dogs diagnosed with osteosarcoma, one year of age or older. Aratana is currently conducting an extended field study which is a requirement for full USDA licensure. Initially, Aratana plans to make the therapeutic available for purchase at approximately two dozen veterinary oncology practice groups across the United States who participate in the study.

Under the terms of the Aratana Agreement, Aratana paid an upfront payment to New Ayala in the amount of $1,000,000 upon signing of the Aratana Agreement. Aratana will also pay New Ayala: (a) up to $36.5 million based on the achievement of milestone relating to the advancement of products through the approval process with the USDA in the United States and the relevant regulatory authorities in the European Union, or E.U., in all four therapeutic areas and up to an additional $15 million in cumulative sales milestones based on achievement of gross sales revenue targets for sales of any and all products for use in non-human animal health applications, or the Aratana Field, (regardless of therapeutic area), and (b) tiered royalties starting at 5% and going up to 10%, which will be paid based on net sales of any and all products (regardless of therapeutic area) in the Aratana Field in the United States. Royalties for sales of products outside of the United States will be paid at a rate equal to half of the royalty rate payable by Aratana on net sales of products in the United States (starting at 2.5% and going up to 5%). Royalties will be payable on a product-by-product and country-by-country basis from first commercial sale of a product in a country until the later of (a) the 10th anniversary of first commercial sale of such product by Aratana, its affiliates or sub licensees in such country or (b) the expiration of the last-to-expire valid claim of our patents or joint patents claiming or covering the composition of matter, formulation or method of use of such product in such country. Aratana will also pay us 50% of all sublicense royalties received by Aratana and its affiliates. In fiscal year 2019, the Company received approximately $8,000 in royalty revenue from Aratana. Additionally, in July 2019, Aratana announced that their shareholders approved a merger agreement with Elanco Animal Health, or Elanco, whereby Elanco is now the majority shareholder of Aratana. On October 6, 2020, the Company received a notice from Aratana, dated September 17, 2020, indicating that Aratana was terminating the Exclusive License Agreement effective December 21, 2020. The Company did not incur any early termination penalties as a result of the termination. Aratana was required to make all payments to the Company that were otherwise payable under the Exclusive License Agreement through the effective date of termination.

Corporate Information

We were originally incorporated in the State of Colorado on June 5, 1987 under the name Great Expectations, Inc. We were a publicly-traded "shell" company without any business until November 12, 2004 when we acquired New Ayala, a Delaware corporation, through a Share Exchange and Reorganization Agreement, dated as of August 25, 2004, which we refer to as the Share Exchange, by and among New Ayala, the stockholders of New Ayala and us. As a result of the Share Exchange, New Ayala became our wholly-owned subsidiary and our sole operating company. On December 23, 2004, we amended and restated our articles of incorporation and changed our name to New Ayala. On June 6, 2006, our stockholders approved the reincorporation of our company from Colorado to Delaware by merging the Colorado entity into our wholly-owned Delaware subsidiary. Our date of inception, for financial statement purposes, is March 1, 2002 and the Company was listed on The Nasdaq Capital Market ("Nasdaq") in 2014. In December 2021, the Company was delisted from Nasdaq and accepted onto the OTCQX. Shares of New Ayala's common stock are currently quoted on the OTCQX under the symbol "ADXS." We have filed an application for listing on Nasdaq, and intend to undertake the actions necessary to allow our common stock to be uplisted from the OTCQX to Nasdaq.

Our principal executive offices are located at 9 Deer Park Drive, Suite K-1, Monmouth Junction, New Jersey 08852, and our telephone number is (609) 452-9813. We maintain a corporate website at www.ayalapharma.com which contains descriptions of our technology, our product candidates and the development status of each drug. We make available free of charge through our internet website our annual reports on Form 10-K, quarterly reports on Form 10-Q and Current Reports on Form 8-K, and any amendments to these reports, as soon as reasonably practicable after we electronically file such material with, or furnish such material to, the SEC. We are not including the information on our website as a part of, nor incorporating it by reference into, this report. The SEC maintains a website that contains annual, quarterly, and current reports, proxy statements, and other information that issuers (including us) file electronically with the SEC. The SEC's website address is http://www.sec.gov.

Intellectual Property

Protection of our intellectual property is important to our business. We have a robust patent portfolio that protects our product candidates and *Lm* -based immunotherapy technology. Currently, we own or have rights to several hundred patents and applications, which are owned, licensed from, or co-owned with University of Pennsylvania, or Penn, Merck, National Institute of Health, or NIH, and/or Augusta University. We aggressively prosecute and defend our patents and proprietary technology. Our patents and applications are directed to the compositions of matter, use, and methods thereof, of our *Lm*-LLO immunotherapies for our product candidates, including AXAL, ADXS-PSA, ADXS-HOT, ADXS-HER2. We have and may continue to abandon prosecuting certain patents that are not strategically aligned with the direction of the Company.

Our approach to the intellectual property portfolio is to create, maintain, protect, enforce and defend our proprietary rights for the products we develop from our immunotherapy technology platform. We endeavor to maintain a coherent and aggressive strategic approach to building our patent portfolio with an emphasis in the field of cancer vaccines. Issued patents which are directed to AXAL, ADXS-PSA, and ADXS-HER2 in the United States, will expire between 2021 and 2032. Issued patents directed to our product candidates AXAL, ADXS-PSA, and ADXS-HER2 outside of the United States, will expire in 2032. Issued patents directed to our *Lm* -based immunotherapy platform in the United States, will expire between 2021 and 2031. Issued patents directed to our *Lm*-based immunotherapy platform outside of the United States, will expire between 2021 and 2033.

We have pending patent applications directed to our product candidates AXAL, ADXS-PSA, ADXS-HER2, and ADXS-HOT that, if issued would expire in the United States and in countries outside of the United States between 2021 and 2037. We have pending patent applications directed to methods of using of our product candidates AXAL, ADXS-PSA, ADXS-HOT, ADXS-HER2 directed to the following indications and others: prostate cancer and her2/neu-expressing cancer, that, if issued would expire in the United States and in countries outside of the United States between 2021 and 2037, depending on the specific indications.

We will be able to protect our technology from unauthorized use by third parties only to the extent it is covered by valid and enforceable patents or is effectively maintained as trade secrets. Patents and other proprietary rights are an essential element of our business.

Our success will depend in part on our ability to obtain and maintain proprietary protection for our product candidates, technology, and know-how, to operate without infringing on the proprietary rights of others, and to prevent others from infringing our proprietary rights. Our policy is to seek to protect our proprietary position by, among other methods, filing U.S. and foreign patent applications related to our proprietary technology, inventions, and improvements that are important to the development of our business. We also rely on trade secrets, know-how, continuing technological innovation, and in-licensing opportunities to develop and maintain our proprietary position.

Any patent applications which we have filed or will file or to which we have or will have license rights may not issue, and patents that do issue may not contain commercially valuable claims. In addition, any patents issued to us or our licensors may not afford meaningful protection for our products or technology, or may be subsequently circumvented, invalidated, narrowed, or found unenforceable. Our processes and potential products may also conflict with patents which have been or may be granted to competitors, academic institutions or others. As the pharmaceutical industry expands and more patents are issued, the risk increases that our processes and potential products may give rise to interferences filed by others in the U.S. Patent and Trademark Office, or to claims of patent infringement by other companies, institutions or individuals. These entities or persons could bring legal actions against us claiming damages and seeking to enjoin clinical testing, manufacturing and marketing of the related product or process. In recent years, several companies have been extremely aggressive in challenging patents covering pharmaceutical products, and the challenges have often been successful. If any of these actions are successful, in addition to any potential liability for damages, we could be required to cease the infringing activity or obtain a license in order to continue to manufacture or market the relevant product or process. We may not prevail in any such action and any license required under any such patent may not be made available on acceptable terms, if at all. Our failure to successfully defend a patent challenge or to obtain a license to any technology that we may require to commercialize our technologies or potential products could have a materially adverse effect on our business. In addition, changes in either patent laws or in interpretations of patent laws in the United States and other countries may materially diminish the value of our intellectual property or narrow the scope of our patent protection.

We also rely upon unpatented proprietary technology, and in the future may determine in some cases that our interests would be better served by reliance on trade secrets or confidentiality agreements rather than patents or licenses. We may not be able to protect our rights to such unpatented proprietary technology and others may independently develop substantially equivalent technologies. If we are unable to obtain strong proprietary rights to our processes or products after obtaining regulatory clearance, competitors may be able to market competing processes and products.

Others may obtain patents having claims which cover aspects of our products or processes which are necessary for, or useful to, the development, use or manufacture of our services or products. Should any other group obtain patent protection with respect to our discoveries, our commercialization of potential therapeutic products and methods could be limited or prohibited.

The Drug Development Process

The product candidates in our pipeline are at various stages of clinical development. The path to regulatory approval includes multiple phases of clinical trials in which we collect data that will ultimately support an application to regulatory authorities to allow us to market a product for the treatment, of a specific type of cancer. There are many difficulties and uncertainties inherent in research and development of new products, resulting in high costs and variable success rates. Bringing a drug from discovery to regulatory approval, and ultimately to market, takes many years and significant costs.

The process required by the FDA before product candidates may be marketed in the United States generally involves the following:

- completion of preclinical laboratory tests, animal studies, and formulation studies in compliance with the FDA's Good Laboratory Practice, or GLP, regulations;
- submission to the FDA of an IND which must become effective before human clinical trials may begin at United States clinical trial sites;
- approval by an IRB for each clinical site, or centrally, before each trial may be initiated;
- adequate and well-controlled human clinical trials to establish the product candidate's safety, purity, and potency for its intended use, performed in accordance with GCPs;
- development of manufacturing processes to ensure the product candidate's identity, strength, quality, purity, and potency;
- submission to the FDA of a BLA;
- satisfactory completion of an FDA advisory committee review, if applicable;
- satisfactory completion of an FDA inspection of the manufacturing facility or facilities at which the products are produced to assess compliance with cGMPs and to assure that the facilities, methods, and controls are adequate to preserve the therapeutics' identity, strength, quality, purity, and potency as well as satisfactory completion of an FDA inspection of selected clinical sites and selected clinical investigators to determine GCP compliance; and
- FDA review and approval of the BLA to permit commercial marketing for particular indications for use.

Preclinical studies include laboratory evaluation of chemistry, pharmacology, toxicity, and product formulation, as well as animal studies to assess potential safety and efficacy. Such studies must generally be conducted in accordance with the FDA's GLPs. Prior to commencing the first clinical trial at a United States investigational site with a product candidate, an IND sponsor must submit the results of the preclinical tests and preclinical literature, together with manufacturing information, analytical data, any available clinical data or literature, and proposed clinical study protocols among other things, to the FDA as part of an IND. An IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA notifies the applicant of safety concerns or questions related to one or more proposed clinical trials and places the trial on a clinical hold. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. Clinical holds also may be imposed by the FDA at any time before or during trials due to safety concerns or non-compliance. A separate submission to an existing IND must also be made for each successive clinical trial conducted during product development.

Clinical testing, known as clinical trials or clinical studies, is either conducted internally by pharmaceutical or biotechnology companies or managed on behalf of these companies by Clinical Research Organizations, or CROs. The process of conducting clinical studies is highly regulated by the FDA, as well as by other governmental and professional bodies. In a clinical trial, participants receive specific interventions according to the research plan or protocol created by the study sponsor and implemented by study investigators. Clinical trials must be conducted in accordance with federal regulations and GCP requirements, which include the requirements that all research subjects provide their informed consent in writing for their participation in any clinical trial, as well as review and approval of the study by an IRB. Additionally, some clinical trials are overseen by an independent data safety monitoring board, which reviews data and advises the study sponsor on study continuation. A protocol for each clinical trial, and any subsequent protocol amendments, must be submitted to the FDA as part of the IND.

Clinical trials may compare a new medical approach to a standard one that is already available or to a placebo that contains no active ingredients or to no intervention. Some clinical trials compare interventions that are already available to each other. When a new product or approach is being studied, it is not usually known whether it will be helpful, harmful, or no different than available alternatives. The investigators try to determine the safety and efficacy of the intervention by measuring certain clinical outcomes in the participants.

Phase 1. Phase 1 clinical trials begin when regulatory agencies allow initiation of clinical investigation of a new drug or product candidate. They typically involve testing an investigational new drug on a limited number of patients. Phase 1 studies determine a drug's basic safety, maximum tolerated dose, mechanism of action and how the drug is absorbed by, and eliminated from, the body. Typically, cancer therapies are initially tested on late-stage cancer patients.

Phase 2. Phase 2 clinical trials involve larger numbers of patients that have been diagnosed with the targeted disease or condition. Phase 2 clinical trials gather preliminary data on effectiveness (where the drug works in people who have a certain disease or condition) and to determine the common short-term side effects and risks associated with the drug. If Phase 2 clinical trials show that an investigational new drug has an acceptable range of safety risks and probable effectiveness, a company will continue to evaluate the investigational new drug in Phase 3 studies.

Phase 3. Phase 3 clinical trials are typically controlled multi-center trials that involve a larger number of patients to ensure the study results are statistically significant. The purpose is to confirm effectiveness and safety on a large scale and to provide an adequate basis for physician labeling. These trials are generally global in nature and are designed to generate clinical data necessary to submit an application for marketing approval to regulatory agencies. Typically, two Phase 3 trials are required for product approval. Under limited circumstances, however, approval may be based upon a single adequate and well-controlled clinical trial plus confirmatory evidence or a single large multicenter trial without confirmatory evidence.

The FDA may also consider additional kinds of data in support of a BLA, such as patient experience data and real-world evidence. For genetically targeted populations and variant protein targeted products intended to address an unmet medical need in one or more patient subgroups with a serious or life threatening rare disease or condition, the FDA may allow a sponsor to rely upon data and information previously developed by the sponsor or for which the sponsor has a right of reference, that was submitted previously to support an approved application for a product that incorporates or utilizes the same or similar genetically targeted technology or a product that is the same or utilizes the same variant protein targeted drug as the product that is the subject of the application.

Reports regarding clinical study progress must be submitted to the FDA and IRB on an annual basis. Additional reports are required if serious adverse events or other significant safety information is found. Certain reports may also be required to be submitted to the IBC. Investigational biologics must additionally be manufactured in accordance with cGMPs, imported in accordance with FDA requirements, and exported in accordance with the requirements of the receiving country as well as FDA.

Additionally, under the Pediatric Research Equity Act, or PREA, BLAs or BLA supplements for a new active ingredient, dosage form, dosage regimen, or route of administration, unless subject to the below requirement for molecularly targeted cancer products, must contain data to assess the safety and effectiveness of the product in all relevant pediatric subpopulations. The FDA may, however, grant deferrals or full or partial waivers of this requirement. PREA does not apply to orphan designated products approved solely for the orphan indication.

If a product is intended for the treatment of adult cancer and is directed at molecular targets that the FDA determines to be substantially relevant to the growth or progression of pediatric cancer, even if the product has orphan designation, the application sponsors must submit, reports from molecularly targeted pediatric cancer investigations designed to yield clinically meaningful pediatric study data, gathered using appropriate formulations for each applicable age group, to inform potential pediatric labeling. Like PREA, FDA may grant deferrals or waivers of some or all of this data requirement.

Certain gene therapy studies are also subject to the National Institutes of Health's Guidelines for Research Involving Recombinant DNA Molecules, or NIH Guidelines. The NIH Guidelines include the review of the study by a local institutional committee called an institutional biosafety committee, or IBC. The IBC assesses the compliance of the research with the NIH Guidelines, assesses the safety of the research and identifies any potential risk to public health or the environment.

In addition to the regulations discussed above, there are a number of additional standards that apply to clinical trials involving the use of gene therapy. The FDA has issued various guidance documents regarding gene therapies, which outline additional factors that the FDA will consider during product development. These include guidance regarding preclinical studies; chemistry, manufacturing, and controls; the measurement of product potency; how FDA will determine whether a gene therapy product is the same as another product for the purpose of the agency's orphan drug regulations; and long term patient and clinical study subject follow up and regulatory reporting.

To lessen the burden of subjects being required to travel to the clinic for an onsite visit during the *Lm* surveillance phase of the studies, the *Lm* surveillance period was reduced to 1 year instead of 3 years based on an agreement with the FDA in November 2020.

Biologic License Application (BLA). During clinical trials, companies usually also complete additional preclinical studies. Companies further develop additional information about the product candidate's physical characteristics and finalize the cGMP manufacturing process. The results of the clinical trials using biologics are submitted to the FDA as part of a BLA. Following the completion of Phase 3 studies, if the sponsor of a potential product in the United States believes it has sufficient information to support the safety and effectiveness of the investigational biologic, the sponsor submits a BLA to the FDA requesting marketing approval. The application is a comprehensive filing that includes the results of all preclinical and clinical studies, information about the product's composition, and the sponsor's plans for manufacturing, packaging, labeling and testing the investigational new product.

Subject to certain exceptions, the BLA must be accompanied by a substantial user fee at the time of the first submission. FDA has 60 days from its receipt of a BLA to determine whether the application is sufficiently complete for filing and for a substantive review. If the FDA determines that the NDA is incomplete, the FDA may refuse to file the application, in which case the applicant must address the FDA identified deficiencies before refiling. After the BLA is accepted for filing, the FDA reviews the application to determine whether the product meets FDA's approval standards. The FDA aims to complete its review within ten months of the 60-day filing date. For products that present significant improvements in the safety or effectiveness of the treatment, diagnosis, or prevention of serious conditions FDA aims to complete its review within 6 months of the 60-day filing date. The FDA, however, does not always meet its review goal. The review goal date may also be extended if FDA requests or the sponsor provides additional information regarding the application. As part of the approval process, FDA will typically inspect one or more clinical sites, as well as the facility or the facilities at which the product is manufactured to ensure GCP and cGMP compliance.

FDA may also refer an application for review by an independent advisory committee. Specifically, for a product candidate for which no active ingredient (including any ester or salt of active ingredients) has previously been approved by the FDA, the FDA must either refer that product candidate to an advisory committee or provide in an action letter, a summary of the reasons why the FDA did not refer the product candidate to an advisory committee. While FDA is not bound by the recommendation of an advisory committee, it does carefully consider the committee's recommendations.

After evaluating the application, FDA may issue an approval letter, authorizing product marketing, or a Complete Response Letter, or CRL, indicating that the application is not ready for approval. The CRL describes the application's deficiencies and conditions that must be met for product approval. If a CRL is issued, the applicant may resubmit the application, addressing the deficiencies, withdraw the application, or request a hearing. Even with submission of additional information, the FDA ultimately may decide that the application is not approvable.

If approval is granted, the FDA may limit the indications for use, including the indicated population, require contraindications, warnings or precautions be included in the product labeling, including black box warnings, or may not approve label statements necessary for successful commercialization. FDA may also require, or companies may conduct, additional clinical trials following approval, called Phase 4 studies, which can confirm or refute the effectiveness of a product candidate, and can provide important safety information. FDA may also require the implementation of a REMS which may include requirements for a medication guide or patient package insert, a communication plan on product risks, or other elements to assure safe use.

After approval, some types of changes to the approved product, such as adding new indications or label claims, which may themselves require further clinical testing, or changing the manufacturing process are subject to further FDA review and approval. FDA can also require the implementation REMS or the conduct of phase 4 studies after product approval.

Government Regulations

General

Government authorities in the United States and other countries extensively regulate, among other things, the preclinical and clinical testing, manufacturing, labeling, storage, record-keeping, advertising, promotion, import, export, marketing and distribution of biopharmaceutical and drug products. In the United States, the FDA subjects drugs to rigorous review under the Federal Food, Drug and Cosmetic Act, or FDCA, the Public Health Service Act, or PHSA, and implementing regulations.

Orphan Drug Designation

Under the ODA, the FDA may grant ODD, to a drug or biological product intended to treat a rare disease or condition, which means a disease or condition that affects fewer than 200,000 individuals in the United States, or more than 200,000 individuals in the United States, but for which there is no reasonable expectation that the cost of developing and making a drug or biological product available in the United States will be recovered from domestic sales of the product. Additionally, sponsors must present a plausible hypothesis for clinical superiority to obtain ODD if there is a product already approved by the FDA that that is considered by the FDA to be the same as the already approved product and is intended for the same indication. This hypothesis must be demonstrated to obtain orphan exclusivity.

The benefits of ODD can be substantial, including research and development tax credits, grants and exemption from user fees. The tax advantages, however, were limited in the 2017 Tax Cuts and Jobs Act. Moreover, if there is no other product that the FDA considers to be the same product that is approve for the orphan indication, the orphan designated product is eligible for 7 years of orphan market exclusivity once the product is approved. During that period, the FDA generally may not approve any other application for the same product for the same indication, although there are exceptions, most notably when the later product is shown to be clinically superior to the product with exclusivity. Other applicants, however, may receive approval of different products for the orphan indication or the same product for a different indication during the orphan exclusivity period. In order to qualify for these incentives, a company must apply for designation of its product as an "Orphan Drug" and obtain approval from the FDA. Orphan product designation does not convey any advantage in or shorten the duration of the regulatory review and approval process.

We currently have ODD with the FDA for AXAL for treatment of anal cancer (granted August 2013), HPV-associated head and neck cancer (granted November 2013); and treatment of Stage II-IV invasive cervical cancer (granted May 2014). We also have ODD with the FDA for ADXS-HER2 for the treatment of osteosarcoma (granted May 2014).

In Europe, the Committee for Orphan Medicinal Products, COMP, has issued a positive opinion on the application for ODD of AXAL for the treatment of anal cancer (December 2015) and on the application for ODD of ADXS-HER2 for osteosarcoma (November 2015).

Expedited Review and Approval Programs for Serious Conditions

Four core FDA programs are intended to facilitate and expedite development and review of new biologics to address unmet medical need in the treatment of serious or life-threatening conditions: Fast Track designation, breakthrough therapy designation, accelerated approval, and priority review. We intend to avail ourselves of any and all of these programs as applicable to our products.

FDA is required to facilitate the development, and expedite the review, of products that are intended for the treatment of a serious or life-threatening disease or condition, and which demonstrate the potential to address unmet medical needs for the condition. Under the Fast Track program, the sponsor of a new biologic product candidate may request that FDA designate the drug candidate for a specific indication as a Fast Track drug concurrent with, or after, the filing of the IND for the product candidate. FDA must determine if the product candidate qualifies for Fast Track designation within 60 days of receipt of the sponsor's request. If Fast Track designation is obtained, sponsors may be eligible for more frequent development meetings and correspondence with the FDA. FDA may also initiate review of sections of a Fast Track product's BLA before the application is complete. This rolling review is available if the applicant provides, and FDA approves, a schedule for the submission of the remaining information and the applicant pays applicable user fees. However, FDA's time period goal for reviewing an application does not begin until the last section of the BLA is submitted.

Under FDA's accelerated approval programs, FDA may approve a product for a serious or life-threatening illness that provides meaningful therapeutic benefit to patients over existing treatments based upon a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity or prevalence of the condition and the availability or lack of alternative treatments.

In clinical trials, a surrogate endpoint is a measurement of laboratory or clinical signs of a disease or condition that substitutes for a direct measurement of how a patient feels, functions or survives. Surrogate endpoints can often be measured more easily or more rapidly than clinical endpoints. A product candidate approved on this basis is subject to rigorous post-marketing compliance requirements, including the completion of Phase 4 or post-approval clinical trials to confirm the effect on the clinical endpoint. Failure to conduct required post-approval studies, or confirm a clinical benefit during post-marketing studies, will allow FDA to withdraw the product from the market on an expedited basis. All promotional materials for product candidates approved under accelerated regulations are subject to prior review by FDA.

Under the provisions of the FDA Safety and Innovation Act, or FDASIA, enacted in 2012, a sponsor can request designation of a product candidate as a "breakthrough therapy." A breakthrough therapy is defined as a product that is intended, 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. Products designated as breakthrough therapies are eligible for intensive guidance on an efficient development program beginning as early as Phase 1 trials, a commitment from the FDA to involve senior managers and experienced review staff in a proactive collaborative and cross-disciplinary review, rolling review, and the facilitation of cross-disciplinary review.

Another expedited pathway is the Regenerative Medicine Advanced Therapy, or RMAT, designation. Qualifying products must be a cell therapy, therapeutic tissue engineering product, human cell and tissue product, or a combination of such products, and not a product solely regulated as a human cell and tissue product. The product must be intended to treat, modify, reverse, or cure a serious or life-threatening disease or condition, and preliminary clinical evidence must indicate that the product has the potential to address an unmet need for such disease or condition. Advantages of the RMAT designation include all the benefits of the Fast Track and breakthrough therapy designation programs, including early interactions with the FDA. These early interactions may be used to discuss potential surrogate or intermediate endpoints to support accelerated approval.

Even if a product qualifies for one or more of these programs, the FDA may later decide that the product no longer meets the conditions for qualification or decide that the time period for FDA review or approval will not be shortened.

Disclosure of Clinical Trial Information

Sponsors of clinical trials of FDA regulated products, including biologics, are required to register and submit certain clinical trial information within specific timeframes to the National Institutes of Health, or NIH, for public dissemination on their clinicaltrials.gov website. Information related to the product, patient population, phase of investigation, Trial sites and investigators and other aspects of the clinical trial is then made public as part of the registration. Sponsors are also obligated to discuss the results of their clinical trials after completion. Disclosure of the results of these trials can be delayed in certain circumstances for up to two years, depending on the circumstances, after the date of completion of the trial. Competitors may use this publicly available information to gain knowledge regarding the progress of development programs.

Coverage, Pricing and Reimbursement

Successful commercialization of new drug products depends in part on the extent to which reimbursement for those drug products will be available from government health administration authorities, private health insurers and other organizations. Government authorities and third-party payors, such as private health insurers and health maintenance organizations, decide which drug products they will pay for and establish reimbursement levels. The availability and extent of reimbursement by governmental and private payors is essential for most patients to be able to afford a drug product. Sales of drug products depend substantially, both domestically and abroad, on the extent to which the costs of drugs products are paid for by health maintenance, managed care, pharmacy benefit and similar healthcare management organizations, or reimbursed by government health administration authorities, private health coverage insurers and other third-party payors.

A primary trend in the U.S. healthcare industry and elsewhere is cost containment. Government authorities and other third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular drug products. In many countries, the prices of drug products are subject to varying price control mechanisms as part of national health systems. In general, the prices of drug products under such systems are substantially lower than in the United States. Other countries allow companies to fix their own prices for drug products, but monitor and control company profits. Accordingly, in markets outside the United States, the reimbursement for drug products may be reduced compared with the United States. In the United States, the principal decisions about reimbursement for new drug products are typically made by CMS an agency within HHS. CMS decides whether and to what extent a new drug product will be covered and reimbursed under certain federal governmental healthcare programs, such as Medicare, and private payors tend to follow CMS to a substantial degree. However, no uniform policy of coverage and reimbursement for drug products exists among third-party payors and coverage and reimbursement levels for drug products can differ significantly from payor to payor. In the United States, the process for determining whether a third-party payor will provide coverage for a biological product typically is separate from the process for setting the price of such product or for establishing the reimbursement rate that the payor will pay for the product once coverage is approved. With respect to biologics, third-party payors may limit coverage to specific products on an approved list, also known as a formulary, which might not include all of the FDA-approved products for a particular indication, or place products at certain formulary levels that result in lower reimbursement levels and higher cost sharing obligation imposed on patients. A decision by a third-party payor not to cover our product candidates could reduce physician utilization of a product. Moreover, a third-party payor's decision to provide coverage for a product does not imply that an adequate reimbursement rate will be approved. Adequate third-party reimbursement may not be available to enable a manufacturer to maintain price levels sufficient to realize an appropriate return on its investment in product development. Additionally, coverage and reimbursement for products can differ significantly from payor to payor. One third-party payor's decision to cover a particular medical product does not ensure that other payors will also provide coverage for the medical product, or will provide coverage at an adequate reimbursement rate. As a result, the coverage determination process usually requires manufacturers to provide scientific and clinical support for the use of their products to each payor separately and is a time-consuming process.

Coverage policies and third-party reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which we receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future. Third-party payors are increasingly challenging the prices charged for medical products and services, examining the medical necessity and reviewing the cost-effectiveness of pharmaceutical products, in addition to questioning safety and efficacy. If third-party payors do not consider a product to be cost-effective compared to other available therapies, they may not cover that product after FDA approval or, if they do, the level of payment may not be sufficient to allow a manufacturer to sell its product at a profit.

In addition, in many foreign countries, the proposed pricing for a drug must be approved before it may be lawfully marketed. The requirements governing drug pricing and reimbursement vary widely from country to country. In the European Union, governments influence the price of products through their pricing and reimbursement rules and control of national healthcare systems that fund a large part of the cost of those products to consumers. Some jurisdictions operate positive and negative list systems under which products may only be marketed once a reimbursement price has been agreed to by the government. To obtain reimbursement or pricing approval, some of these countries may require the completion of clinical trials that compare the cost effectiveness of a particular product to currently available therapies. Other member states allow companies to fix their own prices for medicines, but monitor and control company profits. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any of our products. The downward pressure on healthcare costs in general, particularly prescription products, 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 a commercial pressure on pricing within a country (particularly in the EEA where it is illegal to impede such imports from elsewhere within the EEA).

Other Healthcare Laws

Manufacturing, sales, promotion and other activities following product approval are also subject to regulation by numerous regulatory authorities in the United States in addition to the FDA, including CMS, the HHS Office of Inspector General and HHS Office for Civil Rights, other divisions of the HHS and the Department of Justice.

Healthcare providers, physicians, and third-party payors will play a primary role in the recommendation and prescription of any products for which we obtain marketing approval. Our current and future arrangements with third-party payors, healthcare providers and physicians may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we market, sell and distribute any drugs for which we obtain marketing approval. In the United States, these laws include, without limitation, state and federal anti-kickback, false claims, physician transparency, and patient data privacy and security laws and regulations, including but not limited to those described below.

The AKS prohibits, among other things, any person or entity from knowingly and willfully offering, paying, soliciting, receiving or providing any remuneration, directly or indirectly, overtly or covertly, to induce or in return for purchasing, leasing, ordering or arranging for or recommending the purchase, lease or order of any good, facility, item or service reimbursable, in whole or in part, under Medicare, Medicaid or other federal healthcare programs. The term "remuneration" has been broadly interpreted to include anything of value. The AKS has been interpreted to apply to arrangements between pharmaceutical and medical device manufacturers on the one hand and prescribers, purchasers, formulary managers and beneficiaries on the other hand. Although there are a number of statutory exceptions and regulatory safe harbors protecting some common activities from prosecution, the exceptions and safe harbors are drawn narrowly. Failure to meet all of the requirements of a particular applicable statutory exception or regulatory safe harbor does not make the conduct per se illegal under the AKS. Instead, the legality of the arrangement will be evaluated on a case-by-case basis based on a cumulative review of all its facts and circumstances. Several courts have interpreted the statute's intent requirement to mean that if any one purpose of an arrangement involving remuneration is to induce referrals of federal healthcare covered business, the statute has been violated. In addition, 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. Moreover, a claim including items or services resulting from a violation of the AKS constitutes a false or fraudulent claim for purposes of the FCA.

Although we would not submit claims directly to payors, drug manufacturers can be held liable under the FCA, which imposes civil penalties, including through civil whistleblower or qui tam actions, against individuals or entities (including manufacturers) for, among other things, knowingly presenting, or causing to be presented to federal programs (including Medicare and Medicaid) claims for items or services, including drugs, that are false or fraudulent, claims for items or services not provided as claimed, or claims for medically unnecessary items or services. The government may deem manufacturers to have "caused" the submission of false or fraudulent claims by, for example, providing inaccurate billing or coding information to customers or promoting a product off-label. Several biopharmaceutical, medical device and other healthcare companies have been prosecuted under the FCA and civil monetary penalty laws for, among other things, allegedly providing free product to customers with the expectation that the customers would bill federal programs for the product. Other companies have been prosecuted for causing false claims to be submitted because of the companies' marketing of products for unapproved (e.g., or off-label), and thus non-covered, uses. In addition, the civil monetary penalties statute imposes penalties against any person who is determined to have presented or caused to be presented a claim to a federal health program that the person knows or should know is for an item or service that was not provided as claimed or is false or fraudulent. Claims which include items or services resulting from a violation of the federal AKS are false or fraudulent claims for purposes of the FCA.

Our future marketing and activities relating to the reporting of wholesaler or estimated retail prices for our products, if approved, the reporting of prices used to calculate Medicaid rebate information and other information affecting federal, state and third-party reimbursement for our products, and the sale and marketing of our product candidates, are subject to scrutiny under these laws.

HIPAA, created additional federal criminal statutes that prohibit, among other actions, knowingly and willfully executing, or attempting to execute, a scheme to defraud or to obtain, by means of false or fraudulent pretenses, representations or promises, any money or property owned by, or under the control or custody of, any healthcare benefit program, including private third-party payors, knowingly and willfully embezzling or stealing from a healthcare benefit program, willfully obstructing a criminal investigation of a healthcare offense and knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for healthcare benefits, items or services. Similar to the AKS, 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, there has been a recent trend of increased federal and state regulation of payments made to physicians and certain other healthcare providers. The Affordable Care Act, or the ACA, imposed, among other things, new annual reporting requirements through the Physician Payments Sunshine Act for covered manufacturers for certain payments and "transfers of value" provided to physicians and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members. Failure to submit timely, accurately and completely the required information for all payments, transfers of value and ownership or investment interests may result in civil monetary penalties. Covered manufacturers must submit reports by the 90th day of each subsequent calendar year and the reported information is publicly made available on a searchable website.

We may also be subject to data privacy and security regulation by both the federal government and the states in which we conduct our business. HIPAA, as amended by HITECH and their respective implementing regulations, including the Final HIPAA Omnibus Rule published on January 25, 2013, impose specified requirements relating to the privacy, security and transmission of individually identifiable health information held by covered entities and their business associates. Among other things, HITECH made HIPAA's security standards directly applicable to "business associates," defined as independent contractors or agents of covered entities that create, receive, maintain or transmit protected health information in connection with providing a service for or on behalf of a covered entity, although it is unclear that we would be considered a "business associate" in the normal course of our business. HITECH also increased the civil and criminal penalties that may be imposed against covered entities, business associates and possibly other persons, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorney's fees and costs associated with pursuing federal civil actions. In addition, state laws govern 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 requirements, thus complicating compliance efforts.

Similar state and foreign fraud and abuse 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. Such laws are generally broad and are enforced by various state agencies and private actions. Also, many states have similar fraud and abuse statutes or regulations that may be broader in scope and may apply regardless of payor, in addition to items and services reimbursed under Medicaid and other state programs. Some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant federal government compliance guidance, and require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers, marketing expenditures or drug pricing.

In order to distribute products commercially, we must comply with state laws that require the registration of manufacturers and wholesale distributors of drug and biological products in a state, including, in certain states, manufacturers and distributors who ship products into the state even if such manufacturers or distributors have no place of business within the state. Some states also impose requirements on manufacturers and distributors to establish the pedigree of product in the chain of distribution, including some states that require manufacturers and others to adopt new technology capable of tracking and tracing product as it moves through the distribution chain. Several states have enacted legislation requiring pharmaceutical and biotechnology companies to establish marketing compliance programs, file periodic reports with the state, make periodic public disclosures on sales, marketing, pricing, clinical trials and other activities, and/or register their sales representatives, as well as to prohibit pharmacies and other healthcare entities from providing certain physician prescribing data to pharmaceutical and biotechnology companies for use in sales and marketing, and to prohibit certain other sales and marketing practices. All of our activities are potentially subject to federal and state consumer protection and unfair competition laws.

The scope and enforcement of each of these laws is uncertain and subject to rapid change in the current environment of healthcare reform, especially in light of the lack of applicable precedent and regulations. Federal and state enforcement bodies have recently increased their scrutiny of interactions between healthcare companies and healthcare providers, which has led to a number of investigations, prosecutions, convictions and settlements in the healthcare industry. 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, disgorgement, contractual damages, reputational harm, diminished profits and future earnings, imprisonment, exclusion of drugs from government funded healthcare programs, such as Medicare and Medicaid, and the curtailment or restructuring of our operations, as well as additional reporting obligations and oversight if we become subject to a corporate integrity agreement or other agreement to resolve allegations of non-compliance with these laws, any of which could adversely affect our ability to operate our business and our financial results. If any of the physicians or other healthcare providers or entities with whom we expect to do business is found to be not in compliance with applicable laws, they may be subject to significant criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs. Ensuring business arrangements comply with applicable healthcare laws, as well as responding to possible investigations by government authorities, can be time- and resource-consuming and can divert a company's attention from the business.

Current and Future Legislation

In the United States and 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 of our product candidates, restrict or regulate post-approval activities and affect our ability to profitably sell any product candidates for which we obtain marketing approval. We expect that current laws, as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and additional downward pressure on the price that we, or any collaborators, may receive for any approved products.

The ACA, for example, contains provisions that subject biological products to potential competition by lower-cost biosimilars and may reduce the profitability of drug products through increased rebates for drugs reimbursed by Medicaid programs, extend Medicaid rebates to Medicaid managed care plans, provide for mandatory discounts for certain Medicare Part D beneficiaries and annual fees based on pharmaceutical companies' share of sales to federal healthcare programs. With the current Congress, there will likely be additional administrative or legislative changes, including modification, repeal or replacement of all, or certain provisions of the ACA, which may impact reimbursement for drugs and biologics. On January 20, 2017, former President Trump signed an Executive Order directing federal agencies with authorities and responsibilities under the ACA to waive, defer, grant exemptions from, or delay the implementation of any provision of the ACA that would impose a fiscal or regulatory burden on states, individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. On October 13, 2017, former President Trump signed an Executive Order terminating the cost-sharing subsidies that reimburse insurers under the ACA. Several state Attorneys General filed suit to stop the administration from terminating the subsidies, but their lawsuit was dismissed by a federal judge in California on July 18, 2018. In addition, CMS has recently finalized regulations that would give states greater flexibility in setting benchmarks for insurers in the individual and small group marketplaces, which may have the effect of relaxing the essential health benefits required under the ACA for plans sold through such marketplaces. Further, each chamber of Congress has put forth multiple bills, and may do so again in the future, designed to repeal or repeal and replace portions of the ACA.

While Congress has not passed repeal legislation, the Tax Reform Act includes a provision that repealed, effective January 1, 2019, the tax-based shared responsibility payment imposed by the ACA on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the "individual mandate." Further, the Bipartisan Budget Act of 2018, or the BBA, among other things, amended the ACA, effective January 1, 2019, to increase from 50 percent to 70 percent the point-of-sale discount that is owed by pharmaceutical manufacturers who participate in Medicare Part D and to close the coverage gap in most Medicare drug plans, commonly referred to as the "donut hole." Congress may consider other legislation to repeal and replace elements of the ACA. On December 14, 2018, a U.S. District Court judge in the Northern District of Texas ruled that the individual mandate portion of the ACA is an essential and inseverable feature of the ACA, and therefore because the mandate was repealed as part of the Tax Cuts and Jobs Act, the remaining provisions of the ACA are invalid as well. The Trump administration and CMS have both stated that the ruling will have no immediate effect, and on December 30, 2018 the same judge issued an order staying the judgment pending appeal. A Fifth Circuit U.S. Court of Appeals hearing to determine whether certain states and the House of Representatives have standing to appeal the lower court decision was held on July 9, 2019, but it is unclear when a Court will render its decision on this hearing, and what effect it will have on the status of the ACA. Litigation and legislation over the ACA are likely to continue, with unpredictable and uncertain results.

Additionally, other federal health reform measures have been proposed and adopted in the United States since the ACA was enacted:

- The Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. These changes included aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, which went into effect in April 2013 and, due to subsequent legislative amendments to the statute, including the BBA, will remain in effect through 2027, unless additional Congressional action is taken.

- The American Taxpayer Relief Act of 2012, 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.

- The Middle Class Tax Relief and Job Creation Act of 2012 required that CMS reduce the Medicare clinical laboratory fee schedule by 2% in 2013, which served as a base for 2014 and subsequent years. In addition, effective January 1, 2014, CMS also began bundling the Medicare payments for certain laboratory tests ordered while a patient received services in a hospital outpatient setting.

Further, there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which have resulted in several recent Congressional inquiries and proposed and enacted bills designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for products. In addition, the U.S. 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 for branded prescription drugs to limit the growth of government paid healthcare costs. For example, the U.S. government has passed legislation requiring pharmaceutical manufacturers to provide rebates and discounts to certain entities and governmental payors to participate in federal healthcare programs. Further, Congress and the current administration have each indicated that it will continue to seek new legislative and/or administrative measures to control drug costs, and the current administration recently released a "Blueprint", or plan, to reduce the cost of drugs. The Blueprint contains certain measures that HHS is already working to implement. For example, in May 2019, CMS issued a final rule to allow Medicare Advantage Plans the option of using step therapy for Part B drugs beginning January 1, 2020. This final rule codified CMS's policy change that was effective January 1, 2019. Congress has indicated that it will continue to seek new legislative and/or administrative measures to control drug costs. Individual states in the United States have also been increasingly passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing.

Non-U.S. Regulation

Before our products can be marketed outside the United States, they are subject to regulatory approval of the respective authorities in the country in which the product should be marketed. The requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement vary widely from country to country. No action can be taken to market any product in a country until an appropriate application has been approved by the regulatory authorities in that country. The time spent in gaining approval varies from that required for FDA approval, and in certain countries, the sales price of a product must also be approved. The pricing review period often begins after market approval is granted. Even if a product is approved by a regulatory authority, satisfactory prices might not be approved for such product.

Collaborations, Partnerships and Agreements

Collaborations, partnerships and agreements are a key component of New Ayala's corporate strategy. As a clinical stage biotechnology company without sales revenue, partnerships are an essential part of the ongoing strategy. Additionally, the evolution of the field of immunotherapy has resulted in combination treatments becoming ubiquitous; ongoing clinical studies and agreements with many of the leading, large oncology pharmaceutical companies helps validate that *Lm* Technology may play a key role in the cancer treatment protocols of the future.

Our collaborators and partners include Merck, OS Therapies, Biocon, Global BioPharma, Knight, and others. For more information, see Note 12, "*Licensing Agreements*" of the "*Notes to the Consolidated Financial Statements*" included in Item 8.

We entered into an exclusive worldwide license agreement with Penn, on July 1, 2002 with respect to the innovative work of Yvonne Paterson, Ph.D., Associate Dean for Research at the School of Nursing at Penn, and former Professor of Microbiology at Penn, in the area of innate immunity, or the immune response attributed to immune cells, including dendritic cells, macrophages and natural killer cells, that respond to pathogens non-specifically (subject to certain U.S. government rights). This agreement was amended and restated as of February 13, 2007, and, thereafter, has been amended from time to time.

This license, unless sooner terminated in accordance with its terms, terminates upon the latter of (a) the expiration of the last to expire of the Penn patent rights; or (b) twenty years after the effective date of the license. Penn may terminate the license agreement early upon the occurrence of certain defaults by us, including, but not limited to, a material breach by us of the Penn license agreement that is not cured within 60 days after notice of the breach is provided to us.

The license provides us with the exclusive commercial rights to the patent portfolio developed by Penn as of the effective date of the license, in connection with Dr. Paterson and requires us to pay various milestone, legal, filing and licensing payments to commercialize the technology. In exchange for the license, Penn received shares of our Common Stock. In addition, Penn is entitled to receive a non-refundable initial license fee, royalty payments and milestone payments based on net sales and percentages of sublicense fees and certain commercial milestones. Under the amended licensing agreement, Penn is entitled to receive 2.5% of net sales in the territory. Should annual net sales exceed $250 million, the royalty rate will increase to 2.75%, but only with respect to those annual net sales in excess of $250 million. Additionally, Penn will receive tiered sales milestone payments upon the achievement of cumulative global sales ranging between $250 million and $2 billion, with the maximum aggregate amounts payable to Penn in the event that maximum sales milestones are achieved is $40 million. Notwithstanding these royalty rates, upon first in-human commercial sale (U.S. & E.U.), we have agreed to pay Penn a total of $775,000 over a four-year period as an advance minimum royalty, which shall serve as an advance royalty in conjunction with the above terms. In addition, under the license, we are obligated to pay an annual maintenance fee of $100,000 commencing on December 31, 2010, and each December 31st thereafter for the remainder of the term of the agreement until the first commercial sale of a Penn licensed product. We are responsible for filing new patents and maintaining and defending the existing patents licensed to us and we are obligated to reimburse Penn for all attorney's fees, expenses, official fees and other charges incurred in the preparation, prosecution and maintenance of the patents licensed from Penn.

Upon first regulatory approval in humans (US or EU), Penn will be entitled to a milestone payment of $600,000. Furthermore, upon the achievement of the first sale of a product in certain fields, Penn will be entitled to certain milestone payments, as follows: $2.5 million will be due upon the first in-human commercial sale (US or EU) of the first product in the cancer field and $1.0 million will be due upon the date of first in-human commercial sale (US or EU) of a product in each of the secondary strategic fields sold.

Manufacturing

cGMPs, are the standards identified to conform to requirements by governmental agencies that control authorization and licensure for manufacture and distribution of biologic products for either clinical investigations or commercial sale. GMPs identify the requirements for procurement, manufacturing, testing, storage, distribution and the supporting quality systems to ensure that a drug product is safe for its intended application. cGMPs are enforced in the United States by the FDA, under the authorities of the Federal Food, Drug and Cosmetic Act and its implementing regulations and use the phrase "current good manufacturing practices" to describe these standards.

Each of New Ayala's wholly owned product candidates is manufactured using a platform process, with uniform methods and testing procedures. This allows for an expedited pathway from construct discovery to clinical product delivery, while helping to keep cost of goods low.

New Ayala has entered into agreements with multiple third-party organizations, or CMOs, to handle the manufacturing, testing, and distribution of product candidates. These organizations have extensive experience within the biologics space and with the production of clinical and commercial GMP supplies.

Competition

The biotechnology and biopharmaceutical industries are characterized by rapid technological developments and a high degree of competition. As a result, our actual or proposed immunotherapies could become obsolete before we recoup any portion of our related research and development expenses. While we believe that our product candidates, technology, knowledge and experience provide us with competitive advantages, we face competition from established and emerging pharmaceutical and biotechnology companies, among others. The biotechnology and biopharmaceutical industries are highly competitive, and this competition comes from both biotechnology firms and from major pharmaceutical companies, including: BioNtech, Moderna, Gritstone, BMS, AstraZeneca, Merck, Neon Therapeutics, et al., each of which is pursuing cancer vaccines and/or immunotherapies.

Many of these companies have substantially greater financial, marketing, and human resources than we do (including, in some cases, substantially greater experience in clinical testing, manufacturing, and marketing of pharmaceutical products). We also experience competition in the development of our immunotherapies from universities and other research institutions and compete with others in acquiring technology from such universities and institutions. In addition, certain of our immunotherapies may be subject to competition from investigational new drugs and/or products developed using other technologies, some of which have completed numerous clinical trials.

Our competition will be determined in part by the potential indications for which drugs are developed and ultimately approved by regulatory authorities. Additionally, the timing of market introduction of some of our potential immunotherapies or of competitors' products may be an important competitive factor. Accordingly, the speed with which we can develop immunotherapies, complete preclinical testing, clinical trials and approval processes and supply commercial quantities to market are expected to be important competitive factors. We expect that competition among products approved for sale will be based on various factors, including product efficacy, safety, administration, reliability, acceptance, availability, price and patent position.

Experience and Expertise

Our management team has extensive experience in oncology development, including contract research, development, manufacturing and commercialization across a board range of science, technologies, and process operations. We have built internal capabilities supporting research, clinical, medical, manufacturing and compliance operations and have extended our expertise with collaborations.

Employees

As of October 31, 2022, we had 15 employees, 14 of which were full time employees. Of our full-time employees, 1 holds a Ph.D. degree. None of our employees are represented by a labor union, and we consider our relationship with our employees to be good.

Properties

New Ayala's principal office is located at 9 Deer Park Drive, Suite K-1, Monmouth Junction, New Jersey 08852. We will continue to rent necessary offices and laboratories to support our business. New Ayala believes that its facilities are sufficient to meet its current needs and that suitable additional space will be available as and when needed.

Legal Proceedings

The Company is from time to time involved in legal proceedings in the ordinary course of our business. The Company does not believe that any of these claims or proceedings against us is likely to have, individually or in the aggregate, a material adverse effect on the financial condition or results of operations. For more information regarding legal proceedings involving the Company, please see Note 8 – Commitments and Contingencies to our consolidated financial statements.

Item 1B. Unresolved Staff Comments.

None.

Item 2. Properties.

Our principal office is located at Oppenheimer 4, Rehovot 7670104, Israel, where we lease office and laboratory space under a lease agreement that terminates in 2029.

We believe that our facilities are sufficient to meet our current needs and that suitable additional space will be available as and when needed.

Item 3. Legal Proceedings.

We are not subject to any material legal proceedings.

Item 4. Mine Safety Disclosures.

Not applicable.

INFORMATION ABOUT OUR EXECUTIVE OFFICERS AND DIRECTORS

The following table sets forth information regarding our executive officers and directors as of the date of this Annual Report on Form 10-K.

Name	Age	Position
Executive Officers		
Kenneth A. Berlin	58	President and Chief Executive Officer, Director
Igor Gitelman	52	Interim Chief Financial Officer, VP of Finance
Andres Gutierrez, M.D., Ph.D.	62	Chief Medical Officer and Executive Vice President

Executive Officers

Kenneth Berlin has served as our President and Chief Executive Officer and is the sole Director of the Board since January 2023. Mr. Berlin served as New Ayala's Interim Chief Financial Officer from September 2020 to May 2022. Prior to joining New Ayala, Mr. Berlin served as President and Chief Executive Officer of Rosetta Genomics from November 2009 until April 2018. Prior to Rosetta Genomics, Mr. Berlin was Worldwide General Manager at cellular and molecular cancer diagnostics developer Veridex, LLC, a Johnson & Johnson company. At Veridex he grew the organization to over 100 employees, launched three cancer diagnostic products, led the acquisition of its cellular diagnostics partner, and delivered significant growth in sales as Veridex transitioned from an R&D entity to a commercial provider of oncology diagnostic products and services. Mr. Berlin joined Johnson & Johnson in 1994 and served as corporate counsel for six years. From 2001 until 2004 he served as Vice President, Licensing and New Business Development in the pharmaceuticals group, and from 2004 until 2007 served as Worldwide Vice President, Franchise Development, Ortho-Clinical Diagnostics. Mr. Berlin holds an A.B. degree from Princeton University and a J.D. from the University of California Los Angeles School of Law. Mr. Berlin's experience in life science companies, as well as his business experience in general, qualify him to service as our director.

Igor Gitelman has served as our Interim Chief Financial Officer since January 2023. Mr. Gitelman served as New Ayala's VP of Finance since November 2020 and Chief Accounting Officer since February 2021. Prior to joining New Ayala, Mr. Gitelman served as CFO Executive Financial Consultant for Accu Reference Medical Labs, a clinical diagnostic laboratory. Before that, from February 2017 through November 2018, Mr. Gitelman served as a chief accounting officer of Cancer Genetics, Inc., a drug discovery, preclinical oncology, and immuno-oncology services company. Prior to that, Mr. Gitelman served as an Assistant to Vice President (AVP) of Finance and Tax at clinical diagnostic laboratory, BioReference Laboratories, Inc., from October 2005 to October 2016. During this time at BioReference Laboratories, Inc., Mr. Gitelman held various positions of increasing responsibility managing the company's internal audit function, SEC financial reporting, tax, and corporate finance functions.

Andres Gutierrez, M.D., Ph.D. has served as our Executive Vice President and Chief Medical Officer since January 2023. Prior to joining New Ayala, Dr. Gutierrez served as Chief Medical Officer for Oncolytics Biotech, Inc. from November 2016 to April 2018. Prior to Oncolytics, Dr. Gutierrez was Chief Medical Officer at SELLAS Life Sciences Group from November 2015 to September 2016 and was Medical Director, Early Development Immuno-Oncology at BMS from October 2012 to November 2015, where he oversaw the development of translational and clinical development of immuno-oncology programs in solid tumors and hematological malignancies. Earlier, Dr. Gutierrez was Medical Director for several biotechnology companies, including Sunesis Pharmaceuticals, BioMarin Pharmaceutical, Proteolix and Oculus Innovative Sciences, leading key programs with talazoparib and carfilzomib, among others. Prior to Oculus, he served as Director of the Gene & Cell Therapy Unit at the National Institutes of Health in Mexico City and as a consultant physician at the Hospital Angeles del Pedregal

PART II

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

Market Information and Holders

Our common stock is traded on The Nasdaq Global Market under the symbol "AYLA." On March 1, 2022, there were 22 holders of record of our common stock.

Dividends

We have never declared or paid any cash dividends on our capital stock. We currently intend to retain all available funds and future earnings, if any, for the operation and expansion of our business and do not anticipate declaring or paying any dividends in the foreseeable future. The payment of dividends, if any, will be at the discretion of our board of directors and will depend on our results of operations, capital requirements, financial condition, prospects, contractual arrangements, any limitations on payment of dividends present in our future debt agreements, and other factors that our board of directors may deem relevant.

Purchases of Equity Securities by the Issuer or Affiliated Purchasers

None.

Recent Sales of Unregistered Securities

None.

Use of Proceeds

On May 12, 2020, we completed our IPO and issued and sold 3,666,667 shares of our common stock at a price to the public of $15.00 per share. On June 9, 2020, in connection with the partial exercise of the underwriters' option to purchase additional shares, we issued and sold 274,022 additional shares of common stock at a price of $15.00 per share. The offer and sale of all of the shares in the offering was registered under the Securities Act pursuant to a Registration Statement on Form S-1 (File No. 333-236942), as amended, filed in connection with our IPO, or the Registration Statement, which was declared effective by the SEC on May 7, 2020. The offering terminated after the sale of all securities registered pursuant to the Registration Statement. The net proceeds have been invested in short- and intermediate-term investments in accordance with our investment policy. These investments may include money market funds and investment securities consisting of U.S. Treasury notes, and high quality, marketable debt instruments of corporations and government sponsored enterprises. There has been no material change in the expected use of the net proceeds from our IPO as described in the final prospectus (File No. 333-236942) filed with the SEC pursuant to Rule 424(b)(4) under the Securities Act on May 11, 2020 in connection with our IPO, or the Final Prospectus.

Item 6. [Reserved].

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

You should read the following discussion and analysis of our financial condition and results of operations together with our consolidated financial statements and the related notes included elsewhere in this Annual Report on Form 10-K. Some of the information contained in this discussion and analysis or set forth elsewhere in this Annual Report on Form 10-K, including information with respect to our plans and strategy for our business and related financing, includes forward-looking statements that involve risks and uncertainties. As a result of many factors, , our actual results could differ materially from the results described in or implied by the forward-looking statements contained in the following discussion and analysis.

A discussion of the year ended December 31, 2021 compared to the year ended December 31, 2020 has been reported previously in our Annual Report on Form 10-K for the year ended December 31, 2021, filed with the SEC on March 28, 2022, under the heading "Management's Discussion and Analysis of Financial Condition and Results of Operations."

Overview

We are a clinical-stage oncology company focused on developing and commercializing small molecule therapeutics for patients suffering from rare and aggressive cancers, primarily in genetically defined patient populations. Our differentiated development approach is predicated on identifying and addressing tumorigenic drivers of cancer, through a combination of our bioinformatics platform and next-generation sequencing to deliver targeted therapies to underserved patient populations. Our current portfolio of product candidates, AL101 and AL102, targets the aberrant activation of the Notch pathway using gamma secretase inhibitors. Gamma secretase is the enzyme responsible for Notch activation and, when inhibited, turns off the Notch pathway activation. Aberrant activation of the Notch pathway has long been implicated in multiple solid tumor and hematological cancers and has often been associated with more aggressive cancers. In cancers, Notch is known to serve as a critical facilitator in processes such as cellular proliferation, survival, migration, invasion, drug resistance and metastatic spread, all of which contribute to a poorer patient prognosis. AL101 and AL102 are designed to address the underlying key drivers of tumor growth, and our initial Phase 2 clinical data of AL101 suggest that our approach may address shortcomings of existing treatment options. We believe that our novel product candidates, if approved, have the potential to transform treatment outcomes for patients suffering from rare and aggressive cancers.

Our product candidates, AL101 and AL102, are being developed as potent, selective, small molecule gamma secretase inhibitors, or GSIs. We obtained an exclusive, worldwide license to develop and commercialize AL101 and AL102 from Bristol-Myers Squibb Company, or BMS, in November 2017. BMS evaluated AL101 in three Phase 1 studies involving more than 200 total subjects and AL102 in a single Phase 1 study involving 36 subjects with various cancers who had not been prospectively characterized for Notch activation, and to whom we refer to as unselected subjects. While these Phase 1 studies did not report statistically significant overall results, clinical activity was observed across these studies in cancers in which Notch has been implicated as a tumorigenic driver.

We are currently evaluating AL102, our oral GSI for the treatment of desmoid tumors, in a Phase 2/3 pivotal study. Initial interim data read-out from Part A and dose selection is expected around mid-2022 with Part B of the study to commence immediately thereafter. Part B of the study will be a double-blind placebo-controlled study enrolling up to 156 patients with progressive disease, randomized between AL102 or placebo. The study's primary endpoint will be progression free survival, or PFS with secondary endpoints including ORR, duration of response, or DOR and patient reported QOL measures.

In addition, we had a collaboration with Novartis International Pharmaceutical Limited, or Novartis, to develop AL102 for the treatment of multiple myeloma, or MM, in combination with Novartis' B-cell maturation antigen, or BCMA, targeting therapies. The first patient was dosed with AL102 in combination with Novartis' BCMA targeting agent in April 2021.

We are currently evaluating AL101 as a monotherapy in an open-label Phase 2 clinical trial for the treatment of recurrent/metastatic adenoid cystic carcinoma, or R/M ACC, for patients bearing Notch-activating mutations. We refer to this trial as the ACCURACY trial. We use next-generation sequencing, or NGS, to identify patients with Notch-activating mutations, an approach that we believe will enable us to target the patient population with cancers that we believe are most likely to respond to and benefit from AL101 treatment. We chose to initially target R/M ACC based on our differentiated approach, which is comprised of: data generated in a Phase 1 study of AL101 in unselected, heavily pretreated subjects conducted by BMS, our own data generated in patient-derived xenograft models, our bioinformatics platform and our expertise in the Notch pathway.

We are currently conducting our ongoing Phase 2 ACCURACY trial for the treatment of recurrent/metastatic adenoid cystic carcinoma, or R/M ACC, in subjects with progressive disease and Notch-activating mutations. If approved, we believe that AL101 has the potential to be the first therapy approved by the FDA for patients with R/M ACC and address the unmet medical need of these patients. AL101 was granted Orphan Drug Designation in May 2019 for the treatment of adenoid cystic carcinoma, or ACC, and fast track designation in February 2020 for the treatment of R/M ACC. In the second quarter of 2020, we commenced dosing of patients in our ACCURACY trial for the treatment of R/M ACC with Notch-activating mutations at the higher dose of 6mg. We reported initial data from this trial in 2021 and plan to report additional data in 2022.

We are also developing AL102 for the treatment of T-ALL, an aggressive, rare form of T-cell specific leukemia. Based on findings from our Phase 1 study of AL101 and supporting data from our preclinical studies.

As part of our efforts to focus our resources on the more advanced programs and studies including the RINGSIDE study in desmoid tumors and the ACCURACY study for ACC, we elected to discontinue the TENACITY trial, which was evaluating AL101 as a monotherapy in an open-label Phase 2 clinical trial for the treatment of patients with Notch-activated R/M TNBC.

We were incorporated as a Delaware corporation on November 14, 2017, and our headquarters is located in Rehovot, Israel. Our operations to date have been limited to organizing and staffing our company, business planning, raising capital and conducting research and development activities for our product candidates. To date, we have funded our operations primarily through the sales of common stock and convertible preferred stock.

We have incurred significant net operating losses in every year since our inception and expect to continue to incur significant expenses and increasing operating losses for the foreseeable future. Our net losses may fluctuate significantly from quarter to quarter and year to year and could be substantial. Our net losses were $38.0 million and $40.3 million for the years ended December 31, 2022 and 2021, respectively. As of December 31, 2022, we had an accumulated deficit of $149.2 million. We anticipate that our expenses will increase significantly as we:

- advance our development of AL101 for the treatment of R/M ACC;
- advance our Phase 2/3 RINGSIDE pivotal trial of AL102 for the treatment of desmoid tumors, or obtain and conduct clinical trials for any other product candidates;
- assuming successful completion of our Phase 2 ACCURACY trial of AL101 for the treatment of R/M ACC, may be required by the FDA to complete Phase 3 clinical trials to support submission of a New Drug Application, or NDA, of AL101 for the treatment of R/M ACC;
- establish a sales, marketing and distribution infrastructure to commercialize AL101 and/or AL102, if approved, and for any other product candidates for which we may obtain marketing approval;
- collaborate with leading diagnostic companies to develop diagnostic tests for identifying patients with Notch-activating mutations;
- maintain, expand, protect and enforce our intellectual property portfolio;
- hire additional staff, including clinical, scientific, technical, regulatory operational, financial, commercial and other personnel, to execute our business plan; and
- add clinical, scientific, operational, financial and management information systems and personnel to support our product development and potential future commercialization efforts, and to enable us to operate as a public company.

We do not expect to generate revenue from product sales unless and until we successfully complete clinical development and obtain regulatory approval for a product candidate. Additionally, we currently use contract research organizations, or CROs, to carry out our clinical development activities. Furthermore, we incur additional costs associated with operating as a public company. As a result, we will need substantial additional funding to support our continuing operations, pursue our growth strategy and continue as a going concern. Until such time as we can generate significant revenue from product sales, if ever, we expect to fund our operations through public or equity offerings or debt financings, marketing and distribution arrangements and other collaborations, strategic alliances and licensing arrangements or other sources. We may, however, be unable to raise additional funds or enter into such other arrangements when needed on favorable terms or at all. Our failure to raise capital or enter into such other arrangements as and when needed would have a negative impact on our financial condition and our ability to develop our current or any future product candidates.

Because of the numerous risks and uncertainties associated with therapeutics product development, we are unable to predict accurately the timing or amount of increased expenses or when or if we will be able to achieve or maintain profitability. Even if we are able to generate revenue from product sales, we may not become profitable. If we fail to become profitable or are unable to sustain profitability on a continuing basis, then we may be unable to continue our operations at planned levels and be forced to reduce or terminate our operations.

As of December 31, 2022, we had cash and cash equivalents totalling $2.4 million. Due to the uncertainty in securing additional funding, and the insufficient amount of cash and cash equivalent resources at December 31, 2022, we have concluded that substantial doubt exists with respect to our ability to continue as a going concern within one year after the date of the filing of this Annual Report on Form 10-K. See "—Liquidity and Capital Resources." Substantial doubt about our ability to continue as a going concern may materially and adversely affect the price per share of our common stock, and it may be more difficult for us to obtain financing. If potential collaborators decline to do business with us or potential investors decline to participate in any future financings due to such concerns, our ability to increase our cash position may be limited. We will need to generate significant revenues to achieve profitability, and we may never do so. Because of the numerous risks and uncertainties associated with the development of our current and any future product candidates, the development of our platform and technology and because the extent to which we may enter into collaborations with third parties for development of any of our product candidates is unknown, we are unable to estimate the amounts of increased capital outlays and operating expenses required for completing the research and development of our product candidates.

If we raise additional funds through marketing and distribution arrangements and other collaborations, strategic alliances and licensing arrangements with third parties, we may be required to relinquish valuable rights to our technologies, intellectual property, future revenue streams or product candidates or grant licenses on terms that may not be favourable to us. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce or terminate product candidate development programs or future commercialization efforts, grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves or discontinue operations.

License Agreements

Bristol-Myers Squibb

In November 2017, we entered into an exclusive worldwide license agreement with Bristol-Myers Squibb Company, or BMS, for AL101 and AL102, each a small molecule gamma secretase inhibitor in development for the treatment of cancers. Under the terms of the license agreement, we have licensed the exclusive worldwide development and commercialization rights for AL101 (previously known as BMS-906024) and AL102 (previously known as BMS-986115).

We are responsible for all future development and commercialization of AL101 and AL102. In consideration for the rights granted under the agreement, we paid BMS a payment of $6 million and issued to BMS 1,125,929 shares of Series A preferred stock valued at approximately $7.3 million. We are obligated to pay BMS up to approximately $142 million in the aggregate upon the achievement of certain clinical development or regulatory milestones and up to $50 million in the aggregate upon the achievement of certain commercial milestones by each product containing the licensed BMS compounds. In addition, we are obligated to pay BMS tiered royalties ranging from a high single-digit to a low teen percentage on worldwide net sales of all products containing the licensed BMS compounds.

BMS has the right to terminate the BMS License Agreement in its entirety upon written notice to us (a) for insolvency-related events involving us, (b) for our material breach of the BMS License Agreement if such breach remains uncured for a defined period of time, (c) for our failure to fulfill our obligations to develop or commercialize the BMS Licensed Compounds and/or BMS Licensed Products not remedied within a defined period of time following written notice by BMS, or (d) if we or our affiliates commence any action challenging the validity, scope, enforceability or patentability of any of the licensed patent rights. We have the right to terminate the BMS License Agreement (a) for convenience upon prior written notice to BMS, the length of notice dependent on whether a BMS Licensed Product has received regulatory approval, (b) upon immediate written notice to BMS for insolvency-related events involving BMS, (c) for BMS's material breach of the BMS License Agreement if such breach remains uncured for a defined period of time, or (d) on a BMS Licensed Compound-by-BMS Licensed Compound and/or BMS Licensed Product-by-BMS Licensed Product basis upon immediate written notice to BMS if we reasonably determine that there are unexpected safety and public health issues relating to the applicable BMS Licensed Compounds and/or BMS Licensed Products. Upon termination of the BMS License Agreement in its entirety by us for convenience or by BMS, we grant an exclusive, non-transferable, sublicensable, worldwide license to BMS under certain of our patent rights that are necessary to develop, manufacture or commercialize BMS Licensed Compounds or BMS Licensed Products. In exchange for such license, BMS must pay us a low single-digit percentage royalty on net sales of the BMS Licensed Compounds and/or BMS Licensed Products by it or its affiliates, licensees or sublicensees, provided that the termination occurred after a specified developmental milestone for such BMS Licensed Compounds and/or BMS Licensed Products. For more information regarding this agreement, please see "Business—License Agreements."

Novartis

In December 2018, we entered into an evaluation, option and license agreement, or the Novartis Agreement, with Novartis International Pharmaceutical Limited, or Novartis, pursuant to which we granted Novartis an exclusive option to obtain an exclusive license to research, develop, commercialize and manufacture AL102 for the treatment of multiple myeloma.

We will continue to supply Novartis quantities of AL102, products containing AL102 and certain other materials for purposes of conducting evaluation studies not comprising human clinical trials during the option period, together with our know-how as may reasonably be necessary in order for Novartis to conduct such evaluation studies. Novartis has agreed to reimburse us for all such expenses.

At any time during the option term, Novartis may exercise its option by payment of a low eight figure option exercise fee. If Novartis exercises its option, it will be obligated to pay us up to an additional $245 million upon the achievement of certain clinical development and commercial milestones. In addition, Novartis is obligated to pay us tiered royalties at percentages ranging from a mid-single digit to a low double-digit percentage on worldwide net sales of products licensed under the agreement.

The option we granted to Novartis will remain in effect until the earlier of (a) 60 days following the last visit of the last subject in the evaluation studies, (b) the termination of the Novartis Agreement, or (c) 36 months following the delivery by us to Novartis of sufficient amounts of clinical evaluation materials to conduct the anticipated clinical studies. The Novartis Agreement remains in effect until such time as no Novartis Licensed Product is being developed or commercialized by Novartis, its affiliates, or sublicensees (including distributors or commercial partners), unless terminated earlier. We have the right to terminate the Novartis Agreement (a) for Novartis's material breach if such breach remains uncured for 60 days (such cure period shall be extended for an additional period during which Novartis is making good faith efforts to cure such breach) or (b) for Novartis's failure to use commercially reasonable efforts to develop or commercialize AL102 and/or the Novartis Licensed Product not remedied within four months following written notice to Novartis. Novartis has the right to terminate the Novartis Agreement (a) in its entirety or on a country-by-country basis for convenience, upon 60 days' written notice to us, (b) for our material breach if such breach remains uncured for 60 days (such cure period shall be extended for an additional period during which we are making good faith efforts to cure such breach) or (c) upon immediate written notice to us for insolvency-related events involving us. For more information regarding this agreement, please see "Business—License Agreements."

On June 2, 2022, Novartis informed the Company that Novartis does not intend to exercise its option to obtain an exclusive license for AL102, thereby terminating the agreement.

Components of Results of Operations

Revenue Recognition

We recognize revenue in accordance with ASC Topic 606, Revenue from Contracts with Customers, which applies to all contracts with customers. Under Topic 606, an entity recognizes revenue when its customer obtains control of promised goods or services, in an amount that reflects the consideration that the entity expects to receive in exchange for those goods or services. To determine revenue recognition for arrangements that an entity determines are within the scope of Topic 606, the entity performs the following five steps:

(i) identify the contract(s) with a customer;

(ii) identify the performance obligations in the contract;

(iii) determine the transaction price;

(iv) allocate the transaction price to the performance obligations in the contract; and

(v) recognize revenue when (or as) the entity satisfies a performance obligation.

At contract inception, once the contract is determined to be within the scope of Topic 606, we assess the goods or services promised within the contract and determine those that are performance obligations and assess whether each promised good or service is distinct.

Customer option to acquire additional goods or services gives rise to a performance obligation in the contract only if the option provides a material right to the customer that it would not receive without entering into that contract.

In a contract with multiple performance obligations, we must develop estimates and assumptions that require judgment to determine the underlying stand-alone selling price for each performance obligation, which determines how the transaction price is allocated among the performance obligations.

We evaluate each performance obligation to determine if it can be satisfied at a point in time or over time.

Revenue is recognized when control of the promised goods or services is transferred to the customers, in an amount that reflects the consideration we expect to be entitled to receive in exchange for those goods or services.

In December 2018, we entered into the Novartis Agreement for which we paid for its research and development costs. For additional details regarding the Novartis Agreement, refer to Note 5 of our consolidated financial statements included elsewhere in this Annual Report on Form 10-K.

We concluded that there is one distinct performance obligation under the Novartis Agreement: Research and development services, an obligation which is satisfied over time.

Revenue associated with the research and development services in the amount of $0.7 million was recognized in the year ended December 31, 2022, compared to $3.5 million in fiscal year 2021.

We concluded that progress towards completion of the research and development performance obligation related to the Novartis Agreement is best measured in an amount proportional to the expenses incurred from the total estimated expenses. We periodically review and update our estimates, when appropriate, which may adjust revenue recognized for the period. The transaction price to be recognized as revenue under the Novartis Agreement consists of the reimbursable research and development costs.

Operating Expenses

Our operating expenses since inception have consisted solely of research and development expenses and general and administrative expenses.

Research and Development Expenses

Research and development expenses consist primarily of costs incurred for our research activities, including the development of and pursuit of regulatory approval of our lead product candidates, AL101 and AL102, which include:

- employee-related expenses, including salaries, benefits and stock-based compensation expense for personnel engaged in research and development functions;
- expenses incurred in connection with the preclinical and clinical development of our product candidates, including under agreements with CROs, investigative sites and consultants;
- costs of manufacturing our product candidates for use in our preclinical studies and clinical trials, as well as manufacturers that provide components of our product candidates for use in our preclinical and current and potential future clinical trials;
- costs associated with our bioinformatics platform;
- consulting and professional fees related to research and development activities;
- costs related to compliance with clinical regulatory requirements; and
- facility costs and other allocated expenses, which include expenses for rent and maintenance of our facility, utilities, depreciation and other supplies.

We expense research and development costs as incurred. Our external research and development expenses consist primarily of costs such as fees paid to consultants, contractors and CROs in connection with our preclinical and clinical development activities. We typically use our employee and infrastructure resources across our development programs and we do not allocate personnel costs and other internal costs to specific product candidates or development programs with the exception of the costs to manufacture our product candidates.

The following table summarizes our research and development expenses by product candidate or development program for the years ended December 31, 2022 and 2021:

	Years Ended December 31,	
	2022	**2021**
Program-specific costs:		
AL101		
ACC	$ 3,601	$ 15,363
TNBC	3,747	8,051
General Expenses	2,533	1,484
AL102		
General Expenses	295	42
Desmoid	17,675	5,001
Total research and development expenses	$ 27,851	$ 29,941

Research and development activities are central to our business model. Product candidates in later stages of clinical development generally have higher development costs than those in earlier stages of clinical development, primarily due to the increased size and duration of later-stage clinical trials. We expect that our research and development expenses will continue to be significant for the foreseeable future as we continue to advance our pivotal Phase 2/3 RINGSIDE study of AL102 for the treatment of desmoid tumors and initiate additional clinical trials, including AL102 for the treatment of R/R T-ALL, scale our manufacturing processes, continue to develop additional product candidates and hire additional clinical and scientific personnel.

The successful development of AL101, AL102 and any future product candidate is highly uncertain. Accordingly, at this time, we cannot reasonably estimate or know the nature, timing and costs of the efforts that will be necessary to complete the development of these product candidates. We are also unable to predict when, if ever, we will generate revenue and material net cash inflows from the commercialization and sale of any of our product candidates for which we may obtain marketing approval. We may never succeed in achieving regulatory approval for any of our product candidates. The duration, costs and timing of preclinical studies, clinical trials and development of our product candidates will depend on a variety of factors, including:

- successful completion of clinical trials with adequate safety, tolerability and efficacy profiles for AL101, AL102 and any potential future product candidates that are satisfactory to the FDA or any comparable foreign regulatory authority;
- approval of INDs for AL101 and AL102 and any potential future product candidate to commence planned or future clinical trials in the United States or foreign countries;
- significant and changing government regulation and regulatory guidance;
- timing and receipt of marketing approvals from applicable regulatory authorities;
- establishing arrangements with contract manufacturing organizations, or CMOs, for third-party clinical and commercial manufacturing to obtain sufficient supply of our product candidates;
- obtaining, maintaining, protecting and enforcing patent and other intellectual property rights and regulatory exclusivity for our product candidates;
- commercializing the product candidates, if and when approved, whether alone or in collaboration with other organizations;
- acceptance of the product, if and when approved, by patients, the medical community and third-party payors;
- competition with other therapies; and
- maintenance of a continued acceptable safety profile of the products following approval.

A change in the outcome of any of these variables with respect to the development, manufacture or commercialization enabling activities of any of our product candidates would significantly change the costs, timing and viability associated with the development of that product candidate. For example, if the FDA or another regulatory authority were to require us to conduct clinical trials beyond those that we anticipate will be required for the completion of clinical development of a product candidate, or if we experience significant delays in our clinical trials due to patient enrollment or other reasons, we would be required to expend significant additional financial resources and time on the completion of clinical development.

General and Administrative Expenses

General and administrative expenses consist primarily of salaries and other related costs, including stock-based compensation, for personnel in executive, finance and administrative functions. General and administrative expenses also include direct and allocated facility-related costs as well as professional fees for legal, patent, consulting, investor and public relations, accounting, auditing, tax services and insurance costs.

We expect that our general and administrative expenses will increase in the future to support continued research and development activities and potential commercialization of our product candidates. These increases will likely include increased costs related to the hiring of additional personnel and fees to outside consultants, attorneys and accountants, among other expenses. Additionally, we expect to incur increased expenses associated with being a public company, including the costs of additional personnel, accounting, audit, legal, regulatory and tax-related services associated with maintaining compliance with exchange listing and Securities and Exchange Commission, or SEC, requirements, director and officer insurance costs, and investor and public relations costs.

Financial Income, Net

Financial income, net primarily consists of interest income earned on our cash and cash equivalents and restricted bank deposits.

Critical Accounting Policies and Use of Estimates

Our management's discussion and analysis of financial condition and results of operations is based on our consolidated financial statements, which have been prepared in accordance with accounting principles generally accepted in the United States, or GAAP. The preparation of these financial statements requires us to make estimates and judgments that affect the reported amounts of assets, liabilities and expenses and the disclosure of contingent assets and liabilities in our consolidated financial statements during the reporting periods. These items are monitored and analyzed by us for changes in facts and circumstances, and material changes in these estimates could occur in the future. We base our estimates on historical experience, known trends and events, and on various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. Changes in estimates are reflected in reported results for the period in which they become known. Actual results may differ materially from these estimates under different assumptions or conditions.

While our significant accounting policies are described in more detail in the notes to our consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K, we believe the following accounting policies used in the preparation of our consolidated financial statements require the most significant judgments and estimates.

Accrued Research and Development Expenses

As part of the process of preparing our consolidated financial statements, we are required to estimate our accrued research and development expenses. This process involves reviewing purchase orders and open contracts, communicating with our personnel to identify services that have been performed on our behalf and calculating the level of service performed and the associated cost incurred for the services when we have not yet been invoiced or otherwise notified of the actual cost. The majority of our service providers invoice us monthly in arrears for services performed, on a pre-determined schedule or when contractual milestones are met; however, some require advance payments. We make calculations of our accrued expenses as of each balance sheet date in our consolidated financial statements based on facts and circumstances known to us at that time. We periodically confirm the accuracy of our calculations with the service providers and make adjustments if necessary. The significant calculation in our accrued research and development expenses include the following costs incurred for services in connection with research and development activities for which we have not yet been invoiced:

- vendors in connection with clinical development activities;
- vendors in connection with the testing of clinical trial materials;
- CROs in connection with clinical trials; and
- investigative sites in connection with clinical trials.

We contract with CROs to conduct clinical and other research and development services on our behalf. We base our expenses related to CROs on our calculations of the services received and efforts expended pursuant to quotes and contracts with them. The financial terms of these agreements are subject to negotiation, vary from contract to contract and may result in uneven payment flows. There may be instances in which payments made to our CROs will exceed the level of services provided and result in a prepayment of the research and development expense. In accruing service fees, we estimate the time 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 our estimate, we adjust the accrual or amount of prepaid expense accordingly. Non-refundable advance payments for goods and services that will be used in future research and development activities are expensed when the activity has been performed or when the goods have been received rather than when the payment is made.

Although we do not expect our calculations to be materially different from amounts actually incurred, our understanding of the status and timing of services performed relative to the actual status and timing of services performed may vary and may result in reporting amounts that are too high or too low in any particular period. To date, there have not been any material adjustments to our prior calculations of accrued research and development expenses.

Stock-Based Compensation

We measure stock options and other stock-based awards granted to employees, directors, consultants or advisors of the company or its affiliates based on their fair value on the date of the grant and recognize compensation expense of those awards, over the requisite service period, which is generally the vesting period of the respective award. We apply the accelerated method of expense recognition to all awards with only service-based vesting conditions.

For stock-based awards granted to non-employees, compensation expense is recognized over the period during which services are rendered by such non-employees until completed.

We estimate the fair value of each stock option grant on the date of grant using the Black-Scholes option-pricing model, which uses as inputs the fair value of our common stock and assumptions we make for the volatility of our common stock, the expected term of our stock options, the risk-free interest rate for a period that approximates the expected term of our stock options and our expected dividend yield.

Previously, as a private company with no active public market for our common stock, our board of directors historically determined the fair value of our common stock on each date of grant, with input from management. Our board of directors periodically determined the estimated per share fair value of our common stock at various dates using valuations performed by third parties. All options to purchase shares of our common stock were intended to be granted with an exercise price per share no less than the fair value per share of our common stock underlying those options on the date of grant, based on the information known to us on the date of grant. Our determinations of the fair value of our common stock were made using methodologies, approaches and assumptions consistent with the American Institute of Certified Public Accountants Audit and Accounting Practice Aid Series: *Valuation of Privately Held Company Equity Securities Issued as Compensation*, or the Practice Guide.

Our board of directors considered various objective and subjective factors, along with input from management, to determine the fair value of our common stock, including:

- the lack of an active public market for our common stock and convertible preferred stock;
- the prices at which we sold shares of our convertible preferred stock in arm's-length transactions and the superior rights, preferences and privileges of the convertible preferred stock relative to our common stock, including the liquidation preferences of our preferred stock;
- our results of operations and financial condition, including cash on hand;
- the material risks related to our business;
- our stage of development and business strategy;
- the composition of, and changes to, our management team and board of directors;
- the market performance of publicly traded companies in the life sciences and biotechnology sectors, as well as recently completed initial public offerings, or IPOs, of companies in the life sciences and biotechnology sectors; and
- the likelihood of achieving a liquidity event such as an IPO given prevailing market conditions.

There are significant judgments and estimates inherent in the determination of the fair value of our common stock. These judgments and estimates are management's best estimates and include assumptions regarding our future operating performance, the time to completing an initial public offering or other liquidity event, the related company valuations associated with such events and the determinations of the appropriate valuation methods. If we had made different assumptions, our stock-based compensation expense, net loss and net loss per common share could have been different.

Results of Operations

Comparison of the year ended December 31, 2022 and 2021

The following table summarizes our results of operations for the year ended December 31, 2022 and 2021 (in thousands):

	Years Ended December 31,		
	2022	2021	% Change
Revenue from license agreement	$ 692	$ 3,506	(80)%
Cost of revenue	(602)	(3,506)	(83)
Gross profit	90	—	-
Operating expenses:			-
Research and development	27,851	29,941	(7)
General and administrative	9,742	9,277	5
Operating loss	(37,503)	(39,218)	(4)
Financial income (expense), net	74	(260)	(128)
Loss before income tax	(37,429)	(39,478)	(5)
Taxes on income	(584)	(776)	(25)
Net loss	$ (38,013)	$ (40,254)	(6)%

Revenue

Revenue associated with the research and development services mainly under the Novartis Agreement in the amount of $0.7 million was recognized in the year ended December 31, 2022, compared to $3.5 million recognized in fiscal year 2021. For additional details regarding the Novartis Agreement, refer to Note 5 of our consolidated financial statements included elsewhere in this Annual Report on Form 10-K.

Research and Development Expenses

Research and development expenses were $27.9 million for the year ended December 31, 2022 compared to $29.9 million for the year ended December 31, 2021, an decrease of $2.0 million. This decrease was primarily driven by additional costs in connection with the initiation and advancement of the Phase 2/3 RINGSIDE pivotal study for desmoids tumors.

General and Administrative Expenses

General and administrative expenses were $9.7 million for the year ended December 31, 2022 compared to $9.3 million for the year ended December 31, 2021, an increase of $0.4 million. This increase was primarily due to lower expenses in connection with our operations as a public company, including officer and director insurance, increased headcount and stock-based compensation.

Financial Income (expense), net

Financial Income, net was $74 thousand for the year ended December 31, 2022 compared to financial expenses, net of $260 thousand for the year ended December 31, 2021.

Liquidity and Capital Resources

Sources of Liquidity

Since our inception, we have not generated any revenue from product sales and have incurred significant operating losses and negative cash flows from our operations. Our net losses were $38.0 million and $40.3 million for the year ended December 31, 2022 and 2021, respectively. As of December 31, 2022, we had an accumulated deficit of $149.2 million.

On May 12, 2020, we completed the sale of shares of our common stock in our IPO. In connection with the IPO, we issued and sold 3,940,689 shares of common stock, including 274,022 shares associated with the partial exercise on June 4, 2020 of the underwriters' option to purchase additional shares, at a price to the public of $15.00 per share, resulting in net proceeds to us of approximately $52.2 million after deducting underwriting discounts and commissions and estimated offering expenses payable by us. All shares issued and sold were registered pursuant to the Registration Statement.

On February 19, 2021, we entered into a Securities Purchase Agreement (the "2021 Purchase Agreement") with the purchasers named therein (the "Investors"). Pursuant to the 2021 Purchase Agreement, we agreed to sell (i) an aggregate of 333,333 shares of our common stock (the "Private Placement Shares"), par value $0.01 per share, together with warrants to purchase an aggregate of 116,666 shares of our common stock with an exercise price of $18.10 per share (the "Common Warrants"), for an aggregate purchase price of $4,999,995.00 and (ii) pre-funded warrants to purchase an aggregate of 1,333,333 shares of our common stock with an exercise price of $0.01 per share (the "Pre-Funded Warrants" and collectively with the Common Warrants, the "Private Placement Warrants"), together with an aggregate of 466,666 Common Warrants, for an aggregate purchase price of $19,986,661.67 (collectively, the "Private Placement"). The Private Placement closed on February 23, 2021.

In June 2021, we entered into an Open Market Sales Agreement, or the Sales Agreement, with Jefferies LLC, or Jefferies, as sales agent, pursuant to which we may, from time to time, issue and sell common stock with an aggregate value of up to $200.0 million in "at-the-market" offerings, under our Registration Statement on Form S-3 (File No. 333-256792) filed with the SEC on June 4, 2021 (the "ATM"). Sales of common stock, if any, pursuant to the Sales Agreement, may be made in sales deemed to be an "at the market offering" as defined in Rule 415(a) of the Securities Act, including sales made directly through The Nasdaq Global Market or on any other existing trading market for our common stock. Pursuant to the Sales Agreement, during the year ended December 31, 2021, we sold a total of 827,094 shares of common stock for total gross proceeds of approximately $10.4 million. December 31, 2022, we sold a total of 310,417 shares of common stock for total gross proceeds of approximately $0.6 million.

The exercise price and the number of shares of common stock issuable upon exercise of each Private Placement Warrant are subject to adjustment in the event of certain stock dividends and distributions, stock splits, stock combinations, reclassifications or similar events affecting the common stock. In addition, in certain circumstances, upon a fundamental transaction, a holder of Common Warrants will be entitled to receive, upon exercise of the Common Warrants, the kind and amount of securities, cash or other property that such holder would have received had they exercised the Private Placement Warrants immediately prior to the fundamental transaction. The Pre-Funded Warrants will be automatically exercised on cashless basis upon the occurrence of a fundamental transaction. Each Common Warrant is exercisable from the date of issuance and has a term of three years and each Pre-Funded Warrant is exercisable from the date of issuance and has a term of ten years. Pursuant to the 2021 Purchase Agreement, we registered the Private Placement Shares and Private Placement Warrants for resale by the Investors on a registration statement on Form S-3.

On October 18, 2022, we entered into an Agreement and Plan of Merger, or the Merger Agreement, with Advaxis, Inc., a Delaware corporation, or Advaxis, and Doe Merger Sub, Inc., a Delaware corporation and a wholly-owned subsidiary of Advaxis, or Merger Sub, pursuant to which Merger Sub will merge with and into us, with us as the surviving corporation and a wholly-owned subsidiary of Advaxis, or the Merger, and, collectively with the other transactions contemplated by the Merger Agreement, the Transactions. As a result of the Merger, Advaxis was renamed "Ayala Pharmaceuticals, Inc." Closing of the Merger occured during the first quarter of 2023. The representations, warranties, agreements and covenants of the parties set forth in the Merger Agreement will terminate at the Closing.

The Private Placement was exempt from registration pursuant to Section 4(a)(2) of the Securities Act and Regulation D promulgated thereunder, as a transaction by an issuer not involving a public offering.

The following table provides information regarding our total cash and cash equivalents and restricted bank cash at December 31, 2022 and 2021 (in thousands):

	As of December 31,	
	2022	2021
Cash and cash equivalents and restricted cash	$ 2,724	$ 37,339

Cash Flows

The following table provides information regarding our cash flows for the years ended December 31, 2022 and 2021 (in thousands):

	Years Ended December 31,	
	2022	2021
Net cash used in operating activities	$ (34,510)	$ (38,356)
Net cash (used in) provided by investing activities	(2)	(5)
Net cash provided by financing activities	(103)	33,330
Net increase (decrease) in cash and cash equivalents and restricted cash	$ (34,615)	$ (5,031)

Net Cash Used in Operating Activities

The cash used in operating activities resulted primarily from expenses associated with our clinical development programs and early-stage research and general and administrative expenses.

Net cash used in operating activities during the year ended December 31, 2022 of $34.5 million was primarily attributable to our net loss of $38.0 million, adjusted for non-cash expenses of $2.7 million, which includes stock-based compensation of $2.2 million and a net increase in working capital of $0.8 million.

Net cash used in operating activities during the year ended December 31, 2021 of $38.4 million was primarily attributable to our net loss of $40.3 million, adjusted for stock-based compensation of $2.7 million.

Net Cash Used in Investing Activities

Net cash used by investing activities during the year ended December 31, 2022, of $2 thousand attributable to purchases of property and equipment.

Net cash used in investing activities during the year ended December 31, 2021, of $5 thousand was attributable to purchases of property and equipment.

Net Cash Provided by Financing Activities

Net cash provided by financing activities during the year ended December 31, 2022 of $0.1 million was primarily attributable to our issuance of shares at market, net of issuance costs.

Net cash provided by financing activities during the year ended December 31, 2021 of $33.3 million was primarily attributable to our issuance of shares and warrants, net of issuance costs.

Funding Requirements and Going Concern

We expect our expenses to continue to be significant in connection with our ongoing activities, particularly as we continue the research and development for, initiate later-stage clinical trials for, and seek marketing approval for, our product candidates. In addition, if we obtain marketing approval for any of our product candidates, we expect to incur significant commercialization expenses related to product sales, marketing, manufacturing and distribution. Furthermore, we incur additional costs associated with operating as a public company. Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations. If we are unable to raise capital when needed or on attractive terms, we would be forced to delay, reduce or eliminate our research and development programs or future commercialization efforts.

As of December 31, 2022, we had cash and cash equivalents and restricted cash of $2.7 million. We evaluated whether there are conditions and events, considered in the aggregate, that raise substantial doubt about our ability to continue as a going concern within one year after the date that the audited consolidated financial statements are issued. Due to the uncertainty in securing additional funding, and the insufficient amount of cash and cash equivalent resources at December 31, 2022, we have concluded that substantial doubt exists with respect to our ability to continue as a going concern within one year after the date of the filing of this Annual Report on Form 10-K.

Our future capital requirements will depend on many factors, including:

- the costs of conducting future clinical trials of AL101 and AL102;
- the costs of manufacturing additional material for future clinical trials of AL101 and AL102;
- the scope, progress, results and costs of discovery, preclinical development, laboratory testing and clinical trials for other potential product candidates we may develop, if any;
- the costs, timing and outcome of regulatory review of our product candidates;
- the achievement of milestones or occurrence of other developments that trigger payments under any current or future license, collaboration, or other agreements;
- the costs and timing of future commercialization activities, including product sales, marketing, manufacturing and distribution, for any of our product candidates for which we receive marketing approval;
- the amount of revenue, if any, received from commercial sales of our product candidates, should any of our product candidates receive marketing approval;
- the costs of preparing, filing and prosecuting patent applications, obtaining, maintaining, protecting and enforcing our intellectual property rights and defending intellectual property-related claims;
- the severity, duration and impact of the COVID-19 pandemic, which may adversely impact our business and clinical trials;
- our headcount growth and associated costs as we expand our business operations and our research and development activities; and
- the costs of operating as a public company.

Conducting preclinical testing and clinical trials is a time-consuming, expensive and uncertain process that takes years to complete, and we may never generate the necessary data or results required to obtain marketing approval and achieve product sales. In addition, our product candidates, if approved, may not achieve commercial success. Our commercial revenues, if any, will be derived from sales of products that we do not expect to be commercially available for many years, if at all. Accordingly, we will need to continue to rely on additional financing to achieve our business objectives. Adequate additional financing may not be available to us on acceptable terms, or at all.

Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs through a combination of equity offerings, debt financings, collaborations, strategic alliances and licensing arrangements. We do not have any committed external source of funds. To the extent that we raise additional capital through the sale of equity or convertible debt securities, your ownership interests may be diluted, and the terms of these securities may include liquidation or other preferences that could adversely affect your rights as a common stockholder. Any debt financing, if available, may involve agreements that include restrictive covenants that limit our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends, that could adversely impact our ability to conduct our business.

If we raise funds through collaborations, strategic alliances or licensing arrangements with third parties, such as the Novartis Agreement, we may have to relinquish valuable rights to our technologies, intellectual property, future revenue streams, research programs or product candidates or to grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts, grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves or discontinue operations.

Emerging Growth Company Status

The Jumpstart Our Business Startups Act of 2012, or the JOBS Act, permits an "emerging growth company" such as us to take advantage of an extended transition period to comply with new or revised accounting standards applicable to public companies. We have elected to use this extended transition period under the JOBS Act. As a result, our financial statements may not be comparable to the financial statements of issuers who are required to comply with the effective dates for new or revised accounting standards that are applicable to public companies, which may make comparison of our financials to those of other public companies more difficult.

We will remain an emerging growth company until the earliest to occur of: (1) the last day of the fiscal year (a) following the fifth anniversary of the completion of our IPO, or December 31, 2025, (b) in which we have total annual gross revenues of $1.07 billion or more, or (c) in which we are deemed to be a large accelerated filer under the rules of the SEC, which means the market value of our outstanding common stock held by non-affiliates exceeds $700 million as of last business day of our most recently completed second fiscal quarter, and (2) the date on which we have issued more than $1.0 billion in nonconvertible debt during the previous three years.

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

We are exposed to market risk related to changes in interest rates. As of December 31, 2022, and 2022, our cash equivalents consisted of interest-bearing checking accounts. Our primary exposure to market risk is interest rate sensitivity, which is affected by changes in the general level of U.S. interest rates. Due to the short-term nature and the low-risk profile of our interest-bearing accounts, an immediate 10% change in interest rates would not have a material effect on the fair market value of our cash and cash equivalents and short-term restricted bank deposits or on our financial position or results of operations. We are not currently exposed to significant market risk related to changes in foreign currency exchange rates; however, we have contracted with and may continue to contract with foreign vendors located in Europe and Israel. Our operations may be subject to fluctuations in foreign currency exchange rates in the future. Inflation generally affects us by increasing our clinical trial costs. We do not believe that inflation had a material effect on our business, financial condition or results of operations during the years ended December 31, 2022 or 2021.

Item 8. Financial Statements and Supplementary Data.

AYALA PHARMACEUTICALS, INC.

INDEX TO FINANCIAL STATEMENTS

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Report of Independent Registered Public Accounting Firm
To the Shareholders and the Board of Directors of

AYALA PHARMACEUTICALS, INC.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Ayala Pharmaceuticals, Inc. (the Company) as of December 31, 2022 and 2021, the related consolidated statements of operations, changes in stockholders' equity and cash flows for each of the two years in the period ended December 31, 2022, and the related notes (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company at December 31, 2022 and 2021, and the results of its operations and its cash flows for each of the two years in the period ended December 31, 2022, in conformity with U.S. generally accepted accounting principles.

The Company's Ability to Continue as a Going Concern

The accompanying consolidated financial statements have been prepared assuming that the Company will continue as a going concern. As discussed in Note 1 to the financial statements, the Company has suffered recurring losses from operations, has a negative cash flows from operating activities, and has stated that substantial doubt exists about the Company's ability to continue as a going concern. Management's evaluation of the events and conditions and management's plans regarding these matters are also described in Note 1. The consolidated financial statements do not include any adjustments that might result from the outcome of this uncertainty.

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 misstatements, 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.

/s/ KOST FORER GABBAY & KASIERER
KOST FORER GABBAY & KASIERER

A Member of Ernst & Young Global

We have served as the Company's auditor since 2017.

Tel-Aviv, Israel

March 31, 2023

AYALA PHARMACEUTICALS, INC.
CONSOLIDATED BALANCE SHEETS
U.S. dollars in thousands (except share and per share data)

	December 31, 2022	December 31, 2021
Assets		
Current Assets:		
Cash and Cash Equivalents	$ 2,408	$ 36,982
Short-Term Restricted Bank Deposits	110	122
Trade Receivables	234	-
Prepaid Expenses and Other Current Assets	436	2,636
Total Current Assets	3,188	39,740
Long-Term Assets:		
Deferred issuance costs	1,953	-
Other Assets	206	267
Operating lease right of use asset	1,462	-
Property and Equipment, Net	960	1,120
Total Long-Term Assets	4,581	1,387
Total Assets	$ 7,769	$ 41,127
Liabilities and Stockholders' Equity:		
Current Liabilities:		
Trade Payables	$ 4,080	$ 3,214
Operating lease liabilities	419	-
Other Accounts Payables	3,037	3,258
Total Current Liabilities	7,536	6,472
Long-Term Liabilities:		
Long-term operating lease liabilities	1,332	-
Long-Term Rent Liability		497
Total Long-Term Liabilities	$ 1,332	$ 497
Stockholders' Equity:		
Common Stock of $0.01 par value per share; 200,000,000 shares authorized at December 31, 2022 and 2021; 14,381,361 and 14,812,737 shares issued at December 31, 2022 and 2021, respectively; 14,080,383 and 13,956,035 shares outstanding at December 31, 2022 and 2021, Respectively.	$ 139	$ 139
Additional Paid-in Capital	147,916	145,160
Accumulated Deficit	(149,154)	(111,141)
Total Stockholders' Equity	(1,099)	34,158
Total Liabilities and Stockholders' Equity	$ 7,769	$ 41,127

The accompanying notes are an integral part of the consolidated financial statements.

AYALA PHARMACEUTICALS, INC.
CONSOLIDATED STATEMENTS OF OPERATIONS
U.S. dollars in thousands (except shares and per shares data)

	Year ended December 31, 2022	Year ended December 31, 2021
Revenue from License Agreement	$ 692	$ 3,506
Cost of Revenue	(602)	(3,506)
Gross Profit	90	—
Research and Development	$ 27,851	$ 29,941
General and Administrative	9,742	9,277
Operating Loss	(37,503)	(39,218)
Financial income (expenses), net	74	(260)
Loss before taxes on income	(37,429)	(39,478)
Taxes on Income	(584)	(776)
Net Loss	$ (38,013)	$ (40,254)
Net Loss per Share attributable to Common Stockholders, Basic and Diluted	$ (2.46)	$ (2.80)
Weighted Average Shares Used to Compute Net Loss per Share, Basic and Diluted	15,448,931	14,398,905

The accompanying notes are an integral part of the consolidated financial statements.

AYALA PHARMACEUTICALS, INC.
STATEMENT OF CHANGES IN STOCKHOLDERS' EQUITY
U.S. dollars in thousands (except share amounts)

	Common Stock		Additional paid-in	Accumulated	Total Stockholders' (Deficit)
	Number	Amount	capital	Deficit	Equity
Balance as of December 31, 2020	12,728,446	$ 128	$ 109,157	$ (70,887)	$ 38,398
Proceeds from Issuance of common stock and warrants, net of issuance cost of $1,724	333,333	3	23,259	—	23,262
Proceeds from Issuance of common stock, net of issuance cost of $438	827,094	8	9,959	—	9,967
Exercise of Stock Option	18,328	*	101	—	101
Stock Based Compensation	48,834	*	2,684	—	2,684
Net Loss	—	—	—	(40,254)	(40,254)
Balance as of December 31, 2021	13,956,035	$ 139	$ 145,160	$ (111,141)	$ 34,158
Share based compensation	114,909	*	2,244	—	2,244
Proceeds from issuance of common stock, net of issuance costs of $14	310,417	*	512	—	512
Net Loss	—	—	—	(38,013)	(38,013)
Balance as of December 31, 2022	14,381,361	$ 139	$ 147,916	$ (149,154)	$ (1,099)

* Represents an amount lower than $1.

The accompanying notes are an integral part of the consolidated financial statements.

AYALA PHARMACEUTICALS, INC.
STATEMENTS OF CONSOLIDATED CASH FLOWS
U.S. dollars in thousands

	Year Ended December 31, 2022	Year Ended December 31, 2021
Cash Flows from Operating Activities:		
Net Loss	$ (38,013)	$ (40,254)
Adjustments to reconcile Net Loss to Net Cash used in Operating Activities:		
Shared Based Compensation	2,244	2,684
Depreciation	162	168
(Increase) Decrease in Prepaid Expenses and other Assets	2,232	(1,174)
Decrease (Increase) in trade receivables	(234)	681
Increase (Decrease) in Trade Payables	(472)	(512)
Decrease in operating lease right-of-use assets	288	-
Decrease in operating lease liabilities	(536)	-
Increase (Decrease) in other Accounts Payable	(181)	51
Net Cash used in Operating Activities	(34,510)	(38,356)
Cash Flows from Investing Activities:		
Purchase of Property and Equipment	(2)	(5)
Net Cash used in Investing Activities	(2)	(5)
Cash Flows from Financing Activities:		
Exercise of Stock Options	-	101
Issuance of common stock and warrants, net	-	23,262
Proceeds from issuance of common stock, net	512	9,967
Prepaid Transaction expenses	(615)	-
Net Cash used in Financing Activities	(103)	33,330
Decrease in Cash and Cash Equivalents and Restricted Cash	(34,615)	(5,031)
Cash and Cash Equivalents and Restricted Cash at Beginning of the Year	37,339	42,370
Cash and Cash Equivalents and Restricted Cash at End of the Year	$ 2,724	$ 37,339
Supplemental Disclosure of Non-Cash Activities		
Lease liabilities arising from new right-of-use assets	$ 537	$ -
Non-cash deferred issuance costs	$ 1,338	$ -
Supplemental Disclosures of Cash Flow Information:		
Cash Paid for Income Taxes	$ 244	$ 209

	Year Ended December 31, 2022	Year Ended December 31, 2021
Cash and Cash Equivalents	$ 2,408	$ 36,982
Restricted Cash	110	122
Restricted Cash in Other Assets	206	235
Cash and Cash Equivalents and Restricted Cash at End of the Year	$ 2,724	$ 37,339

The accompanying notes are an integral part of the consolidated financial statements.

1. General

a) Ayala Pharmaceuticals, Inc. (the "Company") was incorporated in November 2017. The Company is a clinical stage oncology company dedicated to developing and commercializing small molecule therapeutics for patients suffering from rare and aggressive cancers, primarily in genetically defined patient populations. The Company's current portfolio of product candidates, AL101 and AL102, target the aberrant activation of the Notch pathway with gamma secretase inhibitors.

b) In 2017, the Company entered into an exclusive worldwide license agreement with respect to AL101 and AL102. See note 6.

c) The Company's lead product candidates, AL101 and AL102, have completed preclinical and Phase 1 studies. AL102 is currently being evaluated in a pivotal Phase 2/3 trial (RINGSIDE) in patients with Desmoids tumors and is being evaluated in a Phase 1 clinical trial in combination with Novartis' BMCA targeting agent, WVT078, in Patients with relapsed/refractory Multiple Myeloma. AL101 is currently being evaluated in a Phase 2 trial (ACCURACY) in patients with recurrent/metastatic adenoid cystic carcinoma ("R/M ACC") bearing Notch-activating mutations is ongoing.

d) The Company has a wholly-owned Israeli subsidiary, Ayala-Oncology Israel Ltd. (the "Subsidiary"), which was incorporated in November 2017.

Going Concern

The Company has incurred recurring losses since inception as a research and development organization and has an accumulated deficit of $149.2 million as of December 31, 2022. For the year ended December 31, 2022, the Company used $34.5 million of cash in operations. The Company has relied on its ability to fund its operations through public and private equity financings. The Company expects operating losses and negative cash flows to continue at significant levels in the future as it continues its clinical trials. As of December 31, 2022, the Company had approximately $2.4 million in cash and cash equivalents, which, without additional funding, the Company believes will not be sufficient to meet its obligations within the next twelve months from the date of issuance of these consolidated financial statements. The Company plans to continue to fund its operations through public or private debt and equity financings, but there can be no assurances that such financing will continue to be available to the Company on satisfactory terms, or at all. If the Company is unable to obtain funding, the Company would be forced to delay, reduce or eliminate its research and development programs, which could adversely affect its business prospects, or the Company may be unable to continue operations. As such, those factors raise substantial doubt about the Company's ability to continue as a going concern.

The consolidated financial statements have been prepared assuming that the Company will continue as a going concern. Therefore, the consolidated financial statements for the year ended December 31, 2022 do not include any adjustments to reflect the possible future effects on the recoverability and classification of assets or the amounts and classification of liabilities that may result from uncertainty related to the Company's ability to continue as a going concern.

2. Significant Accounting Policies

Basis of Presentation

The consolidated financial statements have been prepared in accordance with U.S. generally accepted accounting principles ("U.S. GAAP"). The significant accounting policies followed in the preparation of the consolidated financial statements, are as follows:

Use of Estimates:

The preparation of financial statements in conformity with U.S. GAAP requires management to make estimates, judgments and assumptions that affect the amounts reported in the consolidated financial statements and accompanying notes. The Company's management believes that the estimates, judgment and assumptions used are reasonable based upon information available at the time they are made. These estimates, judgments and assumptions can affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities at the dates of the consolidated financial statements. Actual results could differ from those estimates.

Consolidated Financial Statements in U.S. Dollars

A substantial portion of the Company's financing activities, including equity transactions and cash investments, are incurred in U.S. dollars. The Company's management believes that the U.S. dollar is the currency of the primary economic environment in which the Company operates. Thus, the functional and reporting currency of the Company is the U.S. dollar.

A subsidiary's functional currency is the currency of the primary economic environment in which the subsidiary operates; normally, that is the currency of the environment in which a subsidiary primarily generates and expends cash. In making the determination of the appropriate functional currency for a subsidiary, the Company considers cash flow indicators, local market indicators, financing indicators and the subsidiary's relationship with both the parent company and other subsidiaries. For subsidiaries that are primarily a direct and integral component or extension of the parent entity's operations, the U.S. dollar is the functional currency.

The Company has determined the functional currency of its foreign subsidiary is the U.S. Dollar. The foreign operation is considered a direct and integral part or extension of the Company's operations. The day-to-day operations of the foreign subsidiary are dependent on the economic environment of the U.S. Dollar.

Accordingly, monetary accounts maintained in currencies other than the U.S. dollar are remeasured into U.S. dollars in accordance with Statement of the Accounting Standard Codification ("ASC") No. 830 "Foreign Currency Matters" ("ASC No. 830"). All transaction gains and losses of the remeasured monetary balance sheet items are reflected in the statements of operations as financial income or expenses as appropriate.

Principles of Consolidation

The consolidated financial statements include the accounts of the Company and the Subsidiary. Intercompany balances and transactions have been eliminated upon consolidation.

Cash and Cash Equivalents and Short-term restricted bank deposits

The Company considers all highly liquid certificates of deposits with original maturities of three months or less from the purchase date to be cash equivalents. Cash equivalents consist primarily of amounts invested in money market accounts in the United States and are stated at carrying value which approximate their fair values. Short-term restricted bank deposits consist of a bank deposit accounts that serves as collateral for a credit card agreement and lease agreements at one of the Company's financial institutions.

Property and Equipment, Net

Property and equipment are stated at cost, minus accumulated depreciation. Depreciation is calculated on a straight-line basis over the estimated useful lives of the related assets, at the following annual rates:

Computers and Software	33%
Lab Equipment	15%
Office Furniture and Equipment	7-9%

Leasehold improvements are amortized on a straight-line basis over the shorter of the assets' estimated useful life or the remaining term of the lease.

Maintenance and repair costs are expensed as incurred.

Impairment of Long-Lived Assets

The Company's long-lived assets are reviewed for impairment in accordance with ASC No. 360, "Property, Plant and Equipment," whenever events or changes in circumstances indicate that the carrying amount of an asset (assets group) may not be recoverable. If indicators of impairment exist and the undiscounted future cash flows that the assets (assets group) are expected to generate are less than the carrying value of the assets (assets group), the Company reduces the carrying amount of the assets through an impairment charge, to their estimated fair values. During the years ended December 31, 2022, and 2021, no impairment indicators have been identified.

Accrued Post-Employment Benefit

Under Israeli employment laws, employees of the Company are included under Section 14 of the Severance Compensation Act, 1963 ("Section 14") for a portion of their salaries. According to Section 14, these employees are entitled to monthly payments made by the Company on their behalf with insurance companies.

Payments in accordance with Section 14 release the Company from any future severance payments with respect to those employees. The obligation to make the monthly deposits is expensed as incurred. In addition, the aforementioned deposits are not recorded as an asset in the consolidated balance sheet, and there is no liability recorded as the Company does not have a future obligation to make any additional payments. Severance costs amounted to approximately $0.3 million and $0.3 million for the year ended December 31, 2022 and 2021, respectively.

The Company maintains a 401(k) retirement savings plan for its U.S. employees. Each eligible employee may elect to contribute a portion of the employee's compensation to the plan. As of December 31, 2022, and 2021, the Company has matched 100% of all employee contributions, up to 6% of the employee's base salary.

Leases

The Company's leases include offices for its facilities, as well as car leases, which are all classified as operating leases.. Short-term leases with a term of 12 months or less are not recorded on the balance sheet. The Company does not separate lease components from non-lease components.

At the inception of an arrangement, the Company determines whether the arrangement is or contains a lease. Operating lease liabilities and their corresponding right-of-use assets are recorded at commencement date. The Company records lease liabilities based on the present value of lease payments over the lease term. The ROU asset also includes any lease payments made and excludes lease incentives. The Company generally uses an incremental borrowing rate to discount its lease liabilities, as the rate implicit in the lease is typically not readily determinable. Certain lease agreements include renewal options that are under the Company's control. The Company includes optional renewal periods in the lease term only when it is reasonably certain that The Company will exercise its option.

Certain lease agreements contain variable payments, which are expensed as incurred and not included in the operating lease right-of-use ("ROU") assets and liabilities.

Fair Value of Financial Instruments:

The Company measures and discloses the fair value of financial assets and liabilities in accordance with ASC Topic 820, "Fair Value Measurement." Fair value is based on the price that would be received to sell an asset or paid to transfer a liability in an orderly transaction between market participants at the measurement date.

Valuation techniques used to measure fair value must maximize the use of observable inputs and minimize the use of unobservable inputs.

The accounting standard establishes a fair value hierarchy that prioritizes observable and unobservable inputs used to measure fair value into three broad levels, which are described below:

Level 1: Quoted prices (unadjusted) in active markets that are accessible at the measurement date for assets or liabilities. The fair value hierarchy gives the highest priority to Level 1 inputs.

Level 2: Observable inputs that are based on inputs not quoted on active markets but corroborated by market data.

Level 3: Unobservable inputs are used when little or no market data are available.

Restricted bank deposits, trade receivables, trade payables are stated at their carrying value, which approximates fair value due to the short time to the expected receipt or payment date.

Research and Development

Research and development costs are expensed as incurred. Research and development costs include payroll and personnel expenses, consulting costs, external contract research and development expenses, raw materials, drug product manufacturing costs, and allocated overhead including depreciation, rent, and utilities. Research and development costs that are paid in advance of performance are classified as a prepaid expense and amortized over the service period as the services are provided.

Acquired In-Process Research and Development

In an asset acquisition, the initial costs of rights to in-process research and development projects acquired are expensed as R&D in the consolidated statements of operations unless the in-process research and development has an alternative future use.

Clinical Trial Costs

Clinical trial costs are a component of research and development expenses. The Company bases its expenses related to Clinical Research Organization ("CRO") on the services received, and efforts expanded pursuant to agreements with them. The financial terms of these agreements are subject to negotiation, vary from contract to contract and may result in uneven payment flows. In instances where payments made to CROs exceed the level of services provided and result in a prepayment of the research and development expenses. For reoccurring services fees, the Company calculates the time period over which services will be performed and the level of effort to be expanded in each period. If the actual timing of the performance of services varies from the calculation, the Company adjusts the accrual or amount of prepaid expenses accordingly. Non-refundable advance payments for goods and services that will be used in future research and development activities are expensed when the activity has been performed or when the goods have been received rather than when the payment is made.

Patent Costs

Legal and related patent costs are expensed as incurred as their realization is uncertain. Costs related to patent registration are classified as general and administrative expenses, and costs related to acquired patents are classified as research and development expenses in the accompanying consolidated statements of operations.

Contingent Liabilities

The Company accounts for its contingent liabilities in accordance with ASC No. 450, "Contingencies". A provision is recorded when it is both probable that a liability has been incurred and the amount of the loss can be reasonably estimated. With respect to legal matters, provisions are reviewed and adjusted to reflect the impact of negotiations, estimated settlements, legal rulings, advice of legal counsel and other information and events pertaining to a particular matter. As of December 31, 2022, and 2021, the Company is not a party to any litigation that could have a material adverse effect on the Company's business, financial position, results of operations or cash flows.

Income Taxes

The Company accounts for income taxes in accordance with ASC 740, "Income Taxes". This standard prescribes the use of the liability method whereby deferred tax asset and liability account balances are determined based on differences between financial reporting and tax bases of assets and liabilities and are measured using the enacted tax rates and laws that will be in effect when the differences are expected to reverse. The Company provides a valuation allowance, if necessary, to reduce deferred tax assets to their estimated realizable value, if it is more likely than not that some portion of the entire deferred tax asset will not be realized.

The Company accounts for uncertain tax positions in accordance with the provisions of ASC 740-10, "Income Taxes". Accounting guidance addresses the determination of whether tax benefits claimed or expected to be claimed on a tax return should be recorded in the consolidated financial statements, under which a Company may recognize the tax benefit from an uncertain tax position only if it is more likely than not that the tax position will be sustained on examination by the taxing authorities, based on the technical merits of the position.

The tax benefits recognized in the consolidated financial statements from such a position should be measured based on the largest benefit that has a greater than fifty percent likelihood of being realized upon ultimate settlement.

Concentrations of Credit Risk

Financial instruments that potentially subject the Company to a concentration of credit risk consist primarily of cash and cash equivalents. Bank deposits are held by accredited financial institutions and these deposits may at times be in excess of insured limits. Money Market funds are of Prime A and only invested in government issued securities. The Company limits its credit risk associated with cash and cash equivalents by placing them with financial institutions that it believes are of high-quality credit rating. The Company has not experienced any losses on its deposits of cash or cash equivalents.

Company's trade receivables are from one customer as of December 31, 2022, and December 31, 2021. In addition, the potential risk of loss with any one counterparty resulting from this type of credit risk is monitored on an ongoing basis. The Company grants credit of 45 days to this one customer.

Stock-Based Compensation

The Company measures its stock-based payment awards made to employees, directors, and non-employee service providers based on estimated fair values. The fair value of each option award is estimated on the grant date using the Black-Scholes option pricing model. The Company recognizes compensation expenses based on the accelerated method over the requisite service period. The Company recognizes forfeitures of awards as they occur.

The Black-Scholes option pricing model requires a number of assumptions, of which the most significant are share price, expected volatility, expected option term (the time from the grant date until the options are exercised or expire), risk-free rate, and expected divided rate. After the IPO, the fair value of each ordinary share was based on the closing price of the Company's publicly traded ordinary shares as reported on the date of the grant.

Expected volatility

As the Company has a short trading history for its ordinary shares, the expected volatility is derived from the average historical share volatilities of several unrelated public companies within the Company's industry that the Company considers to be comparable to its own business over a period equivalent to the option's expected term.

Expected Dividend Yield

The Company has historically not paid dividends and has no foreseeable plans to pay dividends, therefore the Company uses an expected dividend yield of 0%.

Risk-Free Interest Rate

The risk-free interest rate is based on the yield from U.S. Treasury zero-coupon bonds with an equivalent expected term.

Expected Term The expected option term is calculated for options granted to employees and directors using the "simplified" method. Under this approach, the expected term is presumed to be the midpoint between the weighted average vesting term and the contractual term of the option. The simplified method makes the assumption that the employee will exercise share options evenly over the period when the share options are vested and ending on the date when the share options expire. The expected option term for options granted to non-employees is based on the contractual term. Changes in the determination of each of the inputs can affect the fair value of the share options granted and the results of operations of the Company.

Restricted shares are value as fair value of shares on date of grant.

Basic and Diluted Net Loss per Share

Basic loss per share is computed by dividing the net loss by the weighted average number of shares of Common Stock outstanding during the period. Diluted loss per share is computed by dividing the net loss by the weighted average number of shares of Common Stock outstanding together with the number of additional shares of Common Stock that would have been outstanding if all potentially dilutive shares of Common Stock had been issued. Diluted net loss per share is the same as basic net loss per share in periods when the effects of potentially dilutive shares of Common Stock are anti-dilutive.

Segment Information

Financial information is available for evaluation by the chief operating decision maker, the Company's Chief Executive Officer, in making decisions regarding resource allocation and assessing performance. The Company views its operations and manages its business in one operating segment. Operating segments are defined as components of an enterprise in which separate financial information is evaluated regularly by the chief operating decision maker in deciding how to allocate resources and assessing performance.

Revenue Recognition

The Company recognizes revenue in accordance with ASC Topic 606, Revenue from Contracts with Customers, which applies to all contracts with customers. Under Topic 606, an entity recognizes revenue when its customer obtains control of promised goods or services, in an amount that reflects the consideration that the entity expects to receive in exchange for those goods or services. To determine revenue recognition for arrangements that an entity determines are within the scope of Topic 606, the entity performs the following five steps:

(i) identify the contract(s) with a customer;

(ii) identify the performance obligations in the contract;

(iii) determine the transaction price;

(iv) allocate the transaction price to the performance obligations in the contract; and

(v) recognize revenue when (or as) the entity satisfies a performance obligation.

At contract inception, once the contract is determined to be within the scope of Topic 606, the Company assesses the goods or services promised within the contract and determines those that are performance obligations and assesses whether each promised good or service is distinct.

Customer option to acquire additional goods or services gives rise to a performance obligation in the contract only if the option provides a material right to the customer that it would not receive without entering into that contract.

In a contract with multiple performance obligations, the Company develop estimates and assumptions that require judgment to determine the underlying stand-alone selling price for each performance obligation, which determines how the transaction price is allocated among the performance obligations.

The Company evaluates each performance obligation to determine if it can be satisfied at a point in time or over time.

Revenue is recognized when control of the promised goods or services is transferred to the customers, in an amount that reflects the consideration the Company expect to be entitled to receive in exchange for those goods or services.

In December 2018, the Company entered into an Evaluation Option to acquire License Agreement (the "Novartis Agreement") with Novartis International Pharmaceutical Limited ("Novartis") for which the company is paid for its research and development costs. For additional details regarding the Novartis Agreement, refer to Note 6.

The Company concluded that there is one distinct performance obligation under the Novartis Agreement: Research and development services, obligation which is satisfied over time.

Revenue associated with the research and development services in the amount of $0.6 million and $3.5 million was recognized in 2022 and 2021 respectively.

The Company concluded that progress towards completion of the research and development performance obligation related to the Novartis Agreement is best measured in an amount proportional to the expenses incurred from the total estimated expenses. The Company periodically reviews and updates its estimates, when appropriate, which may adjust revenue recognized for the period. The transaction price to be recognized as revenue under the Novartis Agreement consists of the reimbursable research and development costs.

Recently Adopted Accounting Pronouncements

In February 2016, the FASB issued the ASU No. 2016-02, *Leases (Topic 842)*. The standard outlines a comprehensive lease accounting model that supersedes the previous lease guidance and requires lessees to recognize lease liabilities and corresponding right-of-use ("ROU") assets for all leases with lease terms greater than 12 months. The guidance also changes the definition of a lease and expands the disclosure requirements of lease arrangements. The Company adopted the standard in the first quarter of 2022 using the modified retrospective method. Results for reporting periods beginning after December 31, 2021, have been presented in accordance with the standard, while results for prior periods have not been adjusted and continue to be reported in accordance with the Company's historical accounting. The cumulative effect of initially applying the new leases standard was recognized as an adjustment to the opening consolidated balance sheet as of January 1, 2022.

The Company elected a package of practical expedients for leases that commenced prior to January 1, 2022, and did not reassess historical conclusions on: (i) whether any expired or existing contracts are or contain leases; (ii) lease classification for any expired or existing leases; and (iii) initial direct costs capitalization for any existing leases.

This standard has a significant impact on the Company's consolidated balance sheet but did not have a significant impact on the Company's consolidated statements of operations. The most significant effects relate to the recognition ROU assets and lease liabilities on consolidated balance sheet for offices for its and car operating leases.

Upon adoption, the Company recognized lease liabilities and corresponding ROU assets, adjusted for the accrued rent and remaining lease incentives received on the adoption date, as follows:

	January 1, 2022	
	ROU assets	**Lease liabilities**
Offices	$ 1,448	$ 2,020
Cars	302	267
Total operating leases	**$ 1,750**	**$ 2,287**

See Note 4, *Leases* for further details.

In August 2020, the FASB issued ASU 2020-06, Debt - Debt with Conversion and Other Options (Subtopic 470-20) and Derivatives and Hedging - Contracts in Entity's Own Equity (Subtopic 815-40): Accounting for Convertible Instruments and Contracts in an Entity's Own Equity ("ASU 2020-06"). The final guidance issued by the FASB for convertible instruments eliminates two of the three models in ASC 470-20 that require separate accounting for embedded conversion features. Separate accounting is still required in certain cases. Additionally, among other changes, the guidance eliminates some of the conditions for equity classification in ASC 815-40-25 for contracts in an entity's own equity. The guidance also requires entities to use the if-converted method for all convertible instruments in the diluted earnings per share calculation and include the effect of share settlement for instruments that may be settled in cash or shares, except for certain liability-classified share-based payment awards. ASU 2020-06 is effective for fiscal years beginning after December 15, 2023, and interim periods within those fiscal years. Adoption of the standard did not have a material impact on the financial statements.

In December 2019, the FASB issued ASU No. 2019-12, Income Taxes (Topic 740): Simplifying the Accounting for Income Taxes, which simplifies the accounting for income taxes by removing a variety of exceptions within the framework of ASC 740. These exceptions include the exception to the incremental approach for intra-period tax allocation in the event of a loss from continuing operations and income or a gain from other items (such as other comprehensive income), and the exception to using general methodology for the interim period tax accounting for year-to-date losses that exceed anticipated losses. The guidance will be effective for the Company beginning January 1, 2022, and interim periods in fiscal years beginning January 1, 2023. Early adoption is permitted. The Company Adoption of the standard did not have a material impact on the financial statements.

Recently Issued Accounting Pronouncements Not Yet Adopted

As an "emerging growth company," the Jumpstart Our Business Startups Act ("JOBS Act") allows the Company to delay adoption of new or revised accounting pronouncements applicable to public companies until such pronouncements are made applicable to private companies. The Company has elected to use this extended transition period under the JOBS Act. The adoption dates discussed below reflects this election.

In June 2016, the FASB issued ASU No. 2016-13 (Topic 326), Financial Instruments—Credit Losses: Measurement of Credit Losses on Financial Instruments, which replaces the existing incurred loss impairment model with an expected credit loss model and requires a financial asset measured at amortized cost to be presented at the net amount expected to be collected. The guidance will be effective for the Company for fiscal years beginning after December 15, 2022. The Company believes adoption of the standard will not have a material impact on the financial statements.

3. Property and Equipment, net

Property and Equipment, net consists of the following:

	December 31, 2022	December 31, 2021
	(in thousands)	
Cost:		
Computers and Software	$ 73	$ 73
Lab Equipment	296	294
Office Furniture and Equipment	146	146
Leasehold Improvements	1,105	1,105
	1,620	**1,618**
Less: Accumulated Depreciation	660	498
Property and Equipment, Net	**$ 960**	**$ 1,120**

Depreciation expenses for the years ended December 31, 2022, and 2021 was approximately $162 thousands and $168 thousands, respectively.

4. Leases

In January 2019, the Company signed a new lease agreement. The term of the lease is for 63 months and includes an option to extend the lease for an additional 60 months. As part of the agreement, the lessor also provided the Company an amount of approximately $0.5 million paid in arrears for of leasehold improvements. The amount was recorded as an incentive and is taken into account when computing the ROU asset.

The Subsidiary obtained a bank guarantee in the amount of approximately $0.2 million for its new office lease agreement.

The Company has the following operating ROU assets and lease liabilities:

	December 31, 2022	
	ROU assets	Lease liabilities
Offices	$ 1,273	$ 1,612
Cars	189	139
Total operating leases	**$ 1,462**	**$ 1,751**

	December 31, 2022
	Lease liabilities
Current lease liabilities	$ 419
Non-current lease liabilities	1,332
Total lease liabilities	**$ 1,751**

The following table summarizes the lease costs recognized in the consolidated statement of operations:

	December 31, 2022
Operating lease cost	$ 442
Variable lease cost	10
Total lease cost	**$ 452**

As of December 31, 2022, the weighted-average remaining lease term and weighted-average discount rate for operating leases are 3.25 years and 7.7%, respectively. The following table presents supplementary cash flow information regarding the company's operating leases:

	December 31, 2022
Cash paid for amounts included in the measurement of lease liabilities	$ 444
Right of use assets obtained in exchange for operating lease liabilities	$ 1,751

The following table summarizes the future payments of the Company for its operating lease liabilities:

	December 31, 2022
2023	$ 445
2024	345
2025	309
2026	308
2027	308
After 2027	411
Total undiscounted lease payments	$ 2,126
Less: Interest	375
Total lease liabilities - operating	**$ 1,751**

Lease Disclosures Related to Periods Prior to the Adoption of ASU 2016-02 are as follows:

The Company leasing expense for the years ended December 2022 and 2021 was $0.4 million and $0.4 million, respectively.

Future minimum lease commitments under non-cancellable operating leases as of December 31, 2021, are as follows:

Year ended December 31,	**(in thousands)**
2022	$ 360
2023	360
2024	120
	$ 840

5. Other account payables

Other account payables consist of the following:

	December 31, 2022	December 31, 2021
	(in thousands)	
Accrued Professional Fees	$ 487	$ 291
Accrued Research and Development Expenses	64	56
Tax Provision	1492	1,150
Accrued Payroll and Employee Benefits	994	1,761
Total Accrued Expenses	$ 3,037	$ 3,258

6. Commitments and Contingent Liabilities

Asset Transfer and License Agreement with Bristol-Myers Squibb Company.

In November 2017, the Company entered into a license agreement, or the BMS License Agreement, with Bristol-Myers Squibb Company, or BMS, under which BMS granted the Company a worldwide, non-transferable, exclusive, sublicensable license under certain patent rights and know-how controlled by BMS to research, discover, develop, make, have made, use, sell, offer to sell, export, import and commercialize AL101 and AL102, or the BMS Licensed Compounds, and products containing AL101 or AL102, or the BMS Licensed Products, for all uses including the prevention, treatment or control of any human or animal disease, disorder or condition.

Under the BMS License Agreement, the Company is obligated to use commercially reasonable efforts to develop at least one BMS Licensed Product. The Company has sole responsibility for, and bear the cost of, conducting research and development and preparing all regulatory filings and related submissions with respect to the BMS Licensed Compounds and/or BMS Licensed Products. BMS has assigned and transferred all INDs for the BMS Licensed Compounds to the Company. The Company is also required to use commercially reasonable efforts to obtain regulatory approvals in certain major market countries for at least one BMS Licensed Product, as well as to effect the first commercial sale of and commercialize each BMS Licensed Product after obtaining such regulatory approval. The Company has sole responsibility for, and bear the cost of, commercializing BMS Licensed Products. For a limited period of time, the Company may not, engage directly or indirectly in the clinical development or commercialization of a Notch inhibitor molecule that is not a BMS Licensed Compound.

As consideration of the rights granted by BMS to the Company under the BMS License Agreement, the Company paid BMS a payment of $6 million and issued to BMS 1,125,929 shares of Series A Preferred Stock valued at approximately $7.3 million. The payment and transfer of intellectual property occurred in November 2017 at the time the BMS License Agreement was executed (the "Effective Date").

The Company is required to pay BMS payments upon the achievement of certain development or regulatory milestone events of up to $95 million in the aggregate with respect to the first BMS Licensed Compound to achieve each such event and up to $47 million in the aggregate with respect to each additional BMS Licensed Compound to achieve each such event. The Company is also obligated to pay BMS payments of up to $50 million in the aggregate for each BMS Licensed Product that achieves certain sales-based milestone events and tiered royalties on net sales of each BMS Licensed Product by the Company or its affiliates or sublicensees at rates ranging from a high single-digit to low teen percentage, depending on the total annual worldwide net sales of each such Licensed Product. If the Company sublicenses or assigns any rights to the licensed patents, the BMS Licensed Compounds and/or the BMS Licensed Products, the Company is required to share with BMS a portion of all consideration received from such sublicense or assignment, ranging from a mid-teen to mid-double-digit percentage, depending on the development stage of the most advanced BMS Licensed Compound or BMS Licensed Product that is subject to the applicable sublicense or assignment, but such portion may be reduced based on the milestone or royalty payments that are payable by the Company to BMS under the BMS License Agreement.

Under the terms of the BMS Agreement, the Company was obligated to issue to BMS additional shares of preferred stock as would be required for BMS to maintain its 8% equity ownership in Company, subject to certain exceptions. This right terminated upon the closing of the sale of the Company's Series B Preferred Stock. The Company estimates the fair value of this anti-dilution commitment using the probability weighted expected return method ("PWERM"). At the date of BMS Agreement, the Company recorded liability associated with the anti-dilution right in the amount of approximately $0.5 million, according to its fair value. For the year ended December 31, 2018, the Company recorded an income of approximately $0.5 million for the reassessment of the liability, within financial income, net, in the consolidated statement of operations.

The Company accounted for the acquisition of the rights granted by BMS as an asset acquisition because it did not meet the definition of a business. The Company recorded the total consideration transferred and value of shares issued to BMS as research and development expense in the consolidated statement of operations as incurred since the acquired the rights granted by BMS represented in-process research and development and had no alternative future use.

The Company accounts for contingent consideration payable upon achievement of sales milestones in such asset acquisitions when the underlying contingency is resolved.

The BMS License Agreement remains in effect, on a country-by-country and BMS Licensed Product-by-BMS Licensed Product basis, until the expiration of royalty obligations with respect to a given BMS Licensed Product in the applicable country. Royalties are paid on a country-by-country and BMS Licensed Product-by-BMS Licensed Product basis from the first commercial sale of a particular BMS Licensed Product in a country until the latest of 10 years after the first commercial sale of such BMS Licensed Product in such country, (b) when such BMS Licensed Product is no longer covered by a valid claim in the licensed patent rights in such country, or (c) the expiration of any regulatory or marketing exclusivity for such BMS Licensed Product in such country. Any inventions, and related patent rights, invented solely by either party pursuant to activities conducted under the BMS License Agreement shall be solely owned by such party, and any inventions, and related patent rights, conceived of jointly by the Company and BMS pursuant to activities conducted under the BMS License Agreement shall be jointly owned by the Company and BMS, with BMS's rights thereto included in the Company's exclusive license. The Company has the first right—with reasonable consultation with, or participation by, BMS—to prepare, prosecute, maintain and enforce the licensed patents, at the Company's expense.

BMS has the right to terminate the BMS License Agreement in its entirety upon written notice to the Company (a) for insolvency-related events involving the Company, (b) for the Company's material breach of the BMS License Agreement if such breach remains uncured for a defined period of time, for the Company's failure to fulfill its obligations to develop or commercialize the BMS Licensed Compounds and/or BMS Licensed Products not remedied within a defined period of time following written notice by BMS, or (d) if the Company or its affiliates commence any action challenging the validity, scope, enforceability or patentability of any of the licensed patent rights. The Company has the right to terminate the BMS License Agreement for convenience upon prior written notice to BMS, the length of notice dependent on whether a BMS Licensed Project has received regulatory approval, (b) upon immediate written notice to BMS for insolvency-related events involving BMS, (c) for BMS's material breach of the BMS License Agreement if such breach remains uncured for a defined period of time, or (d) on a BMS Licensed Compound-by-BMS Licensed Compound and/or BMS Licensed Product-by-BMS Licensed Product basis upon immediate written notice to BMS if the Company reasonably determine that there are unexpected safety and public health issues relating to the applicable BMS Licensed Compounds and/or BMS Licensed Products.

Upon termination of the BMS License Agreement in its entirety by the Company for convenience or by BMS, the Company grants an exclusive, non-transferable, sublicensable, worldwide license to BMS under certain of its patent rights that are necessary to develop, manufacture or commercialize BMS Licensed Compounds or BMS Licensed Products. In exchange for such license, BMS must pay the Company a low single-digit percentage royalty on net sales of the BMS Licensed Compounds and/or BMS Licensed Products by it or its affiliates, licensees or sublicensees, provided that the termination occurred after a specified developmental milestone for such BMS Licensed Compounds and/ or BMS Licensed Products.

Option and License Agreement with Novartis International Pharmaceutical Ltd.

In December 2018, the Company entered into an evaluation, option and license agreement, or the Novartis Option Agreement, with Novartis International Pharmaceutical Limited, or Novartis, pursuant to which Novartis agreed to conduct certain studies to evaluate AL102 in combination with its B-cell maturation antigen, or BCMA, therapies in multiple myeloma, and the Company agreed to supply AL102 for such studies. All supply and development costs associated with such evaluation studies are fully borne by Novartis.

Under the Novartis Option Agreement, the Company granted Novartis an exclusive option to obtain an exclusive (including as to the Company and its affiliates), sublicensable (subject to certain terms and conditions), worldwide license and sublicense (as applicable) under certain patent rights and know-how controlled by the Company (including applicable patent rights and know-how that are licensed from BMS pursuant to the BMS License Agreement) to research, develop, manufacture (subject to the Company's non-exclusive right to manufacture and supply AL102 or the Novartis Licensed Product for Novartis) and commercialize AL102 or any pharmaceutical product containing AL102 as the sole active ingredient, or the Novartis Licensed Product, for the diagnosis, prophylaxis, treatment, or prevention of multiple myeloma in humans. The Company also granted Novartis the right of first negotiation for the license rights to conduct development or commercialization activities with respect to the use of AL102 for indications other than multiple myeloma. Additionally, from the exercise by Novartis of its option until the termination of the Novartis Option Agreement, the Company may not, either itself or through its affiliates or any other third parties, directly or indirectly research, develop or commercialize certain BCMA-related compounds for the treatment of multiple myeloma.

According to the agreement, Novartis shall pay the Company a low eight figure option exercise fee in order to exercise its option and activate its license, upon which the Company will be eligible to receive development, regulatory and commercial milestone payments of up to $245 million in the aggregate and tiered royalties on net sales of Novartis Licensed Products by Novartis or its affiliates or sublicensees at rates ranging from a mid-single-digit to low double-digit percentage, depending on the total annual worldwide net sales of Novartis Licensed Products. Royalties will be paid on a country-by-country and Novartis Licensed Product-by-Novartis Licensed Product basis from the first commercial sale of a particular Novartis Licensed Product in a country until the latest of (a) 10 years after the first commercial sale of such Novartis Licensed Product in such country, (b) when such Novartis Licensed Product is no longer covered by a valid claim in the licensed patent rights in such country, or (c) the expiration of any regulatory or marketing exclusivity for such Novartis Licensed Product in such country. Contemporaneously with the Novartis Option Agreement, the Company entered into a stock purchase agreement and associated investment agreements, or the SPA, with Novartis' affiliate, Novartis Institutes for BioMedical Research, Inc., or NIBRI, pursuant to which NIBRI acquired a $10 million equity stake in the Company.

Novartis shall own any inventions, and related patent rights, invented solely by it or jointly with the Company in connection with activities conducted pursuant to the Novartis Option Agreement. The Company will maintain first right to prosecute and maintain any patents licensed to Novartis, both before and after its exercise of its option. The Company maintain the first right to defend and enforce its patents prior to Novartis's exercise of its option, upon which Novartis gains such right with respect to patents included in the license.

The option granted to Novartis will remain in effect until the earlier of (a) 60 days following the last visit of the last subject in the evaluation studies, the termination of the Novartis Option Agreement, or (c) 36 months following the delivery by the Company to Novartis of sufficient amounts of clinical evaluation materials to conduct the anticipated clinical studies. The Novartis Option Agreement remains in effect until such time as no Novartis Licensed Product is being developed or commercialized by Novartis, its affiliates, or sublicensees (including distributors or commercial partners), unless terminated earlier. The Company has the right to terminate the Novartis Option Agreement (a) for Novartis's material breach if such breach remains uncured for 60 days (such cure period shall be extended for an additional period during which Novartis is making good faith efforts to cure such breach) or (b) for Novartis's failure to use commercially reasonable efforts to develop or commercialize AL102 and/or the Novartis Licensed Product not remedied within four months following written notice to Novartis. Novartis has the right to terminate the Novartis Option Agreement (a) in its entirety or on a country-by-country basis for convenience, upon 60 days written notice to us, (b) for Company's material breach if such breach remains uncured for 60 days (such cure period shall be extended for an additional period during which Novartis is making good faith efforts to cure such breach) or (c) upon immediate written notice to the Company for insolvency-related events involving the Company.

On June 2, 2022, Novartis informed the Company that Novartis does not intend to exercise its option to obtain an exclusive license for AL102, thereby terminating the agreement.

7. Fair Value Measurements

As of December 31, 2022, the Company had no financial liabilities measured at fair value.

The following tables summarize the fair value measurements of our financial instruments as of December 31, 2022:

	Fair Value Measurements at December 31, 2022			
	Quoted Prices in Active Markets for Identical Assets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)	Total
		($in thousands)		
Cash equivalents:				
Money market funds	$ 1,200	$ —	$ —	$ 1,200
Total cash equivalents	$ 1,200	$ —	$ —	$ 1,200

The following tables summarize the fair value measurements of our financial instruments as of December 31, 2021:

	Fair Value Measurements at December 31, 2021			
	Quoted Prices in Active Markets for Identical Assets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)	Total
		($in thousands)		
Cash equivalents:				
Money market funds	$ 32,900	$ —	$ —	$ 32,900
Total cash equivalents	$ 32,900	$ —	$ —	$ 32,900

8. Common Stock

The Common Stock confer upon the holders the right vote in annual and special meetings of the Company, and to participate in the distribution of the surplus assets of the Company upon liquidation of the Company, after the distribution of the preferred stock liquidation preference. No dividends have been declared as of December 31, 2022 and 2021.

On February 19, 2021, we entered into a Securities Purchase Agreement (the "2021 Purchase Agreement") with the purchasers named therein (the "Investors"). Pursuant to the 2021 Purchase Agreement, we agreed to issue (i) an aggregate of 333,333 shares of our common stock (the "Private Placement Shares"), par value $0.01 per share, together with warrants to purchase an aggregate of 116,666 shares of our common stock with an exercise price of $18.10 per share (the "Common Warrants"), for an aggregate purchase price of $4,999,995.00 and (ii) pre-funded warrants to purchase an aggregate of 1,333,333 shares of our common stock with an exercise price of $0.01 per share (the "Pre-Funded Warrants" and collectively with the Common Warrants, the "Private Placement Warrants"), together with an aggregate of 466,666 Common Warrants, for an aggregate purchase price of $19,986,661.67 (collectively, the "Private Placement"). The Private Placement closed on February 23, 2021. The Company had issuance costs of approximately $1.715 million. The Private Placement closed on February 23, 2021. The warrants were classified as a component of permanent equity pursuant to ASC 480 "Distinguishing Liabilities from Equity" and ASC 815 "Derivatives and Hedging." As of December 31, 2021, the 1,799,999 warrants are all outstanding.

In June 2021, we entered into an Open Market Sales Agreement, or the Sales Agreement, with Jefferies LLC, or Jefferies, as sales agent, pursuant to which we may, from time to time, issue and sell common stock with an aggregate value of up to $200.0 million in "at-the-market" offerings, under our Registration Statement on Form S-3 (File No. 333-256792) filed with the SEC on June 4, 2021 (the "ATM"). Sales of common stock, if any, pursuant to the Sales Agreement, may be made in sales deemed to be an "at the market offering" as defined in Rule 415(a) of the Securities Act, including sales made directly through The Nasdaq Global Market or on any other existing trading market for our common stock. Pursuant to the Sales Agreement, during the twelve months ended December 31, 2021, the Company issued a total of 827,094 shares of common stock for total gross proceeds of approximately $10.4 million.

Total shares of Common Stock reserved for issuance are summarized as follows:

	December 31, 2022	December 31, 2021
Options Outstanding	1,056,015	900,789
Warrants for common shares of the company.	1,799,999	1,799,999
Shares available for future option grants	547,085	593,040
Total shares of Common Stock reserved for Issuance	3,403,099	3,293,828

Composition of Capital Stock:

	December 31, 2022		December 31, 2021	
	Authorized	Issued and outstanding	Authorized	Issued and outstanding
Shares of USD 0.01 par value:				
Common Stock	200,000,000	14,381,361*	200,000,000	13,956,035*

* Does not include 431,376 and 124,348 shares of restricted Common Stock issued but not outstanding in 2022 and 2021, respectively.

9. Stock-Based Plans

In 2017, the Company's board of directors adopted the 2017 Stock Incentive Plan (the "Plan"). According to the Plan, share awards, including restricted stock, restricted stock units or other stock-based awards, or options to purchase shares may be granted to employees, directors, consultants and other service providers of the Company or any affiliate of the Company.

As of December 31, 2022, a total of 2,404,255 shares of Common Stock were authorized for issuance in accordance with the provisions of the 2017 Plan, of which 547,085 shares were then available for future awards (whether as share awards or as options to purchase shares of common stock of the Company). Each option granted under the Plan expires no later than 10 years from the date of grant. The options vest primarily over four to five years of employment.

The following table set forth the parameters used in the computation of the fair value of options granted to employees:

	Year ended December 31,	
	2022	2021
Expected volatility	80%	80%
Expected dividends	0%	0%
Expected term (in years)	6.34	6.34
Risk free rate	0.98%-3.53%	0.50%-1.08%

Expected Volatility:

As the Company was privately owned in part of 2020, there was not sufficient historical volatility for the expected term of the stock options. Therefore, the Company used an average historical share price volatility based on an analysis of reported data for a peer group of comparable publicly traded companies which were selected based upon industry similarities.

Expected term (years):

Expected term represents the period that the Company's option grants are expected to be outstanding. There is not sufficient historical share exercise data to calculate the expected term of the stock options. Therefore, the Company elected to utilize the simplified method to value option grants. Under this approach, the weighted-average expected life is presumed to be the average of the shortest vesting term and the contractual term of the option.

Risk-free interest rate:

The Company determined the risk-free interest rate by using a weighted-average equivalent to the expected term based on the U.S. Treasury yield curve in effect as of the date of grant.

Expected dividend yield:

The Company does not anticipate paying any dividends in the foreseeable future.

The Company recorded stock-based compensation for the period indicated as follows (in thousands):

	Year ended December 31, 2022	Year ended December 31, 2021
Research and Development	$ 717	$ 1,097
General and Administrative	1,527	1,587
Total Stock-Based Compensation	$ 2,244	$ 2,684

The Company recognizes compensation expenses for the value of its awards granted based on the accelerated method over the requisite service period of each of the awards.

A summary of the Company's stock option activity granted to employees under the Plan is as follows:

	Year ended December 31, 2022			
	Number of options	Weighted average exercise price	Weighted average remaining contractual term (in years)	Aggregate intrinsic value
Outstanding at Beginning of Year	900,789	$ 7.41	7.25	$ 1,695,276
Granted	318,830	8.37		
Forfeited	(107,943)	6.28		
Expired	(55,661)	7.58		
Outstanding, December 31, 2022	1,056,015	$ 7.53	4.91	$ -
Exercisable Options, December 31, 2022	550,850	$ 6.34	5.92	$ -

The weighted-average grant date per-share fair value of stock options granted during 2022 and 2021 was $5.74 and $7.98, respectively. The aggregate intrinsic value of stock options exercised during the year ended December 31, 2022 and 2021 was $ 0 and $55, respectively. As of December 31, 2022, there was approximately $1.2 million of total unrecognized compensation cost related to non-vested stock-based compensation arrangements granted under the Plan. That cost is expected to be recognized over a weighted-average period of 0.94 years.

Company's restricted shares:

In January 2021, the Company granted 71,253 restricted shares to officers and employees of the Company. The restricted shares vest over three years starting January 4, 2022.

In May 2022, the Company granted 427,160 restricted shares to officers and employees of the Company. The restricted shares vest over three years starting May 15, 2022.

In August 2022, the Company granted 26,400 restricted shares to employees of the Company. The restricted shares vest over four years starting Aug 14, 2022.

The following table summarizes information relating to restricted shares, as well as changes to such awards during the fiscal years ended December 31, 2022 and 2021:

	Year ended December 31, 2022	Year ended December 31, 2021
Outstanding at beginning of Year	124,348	101,929
Granted	453,560	71,253
Forfeited	(31,623)	-
Vested	(114,909)	(48,834)
Outstanding at end of Year	431,376	124,348

The weighted average fair values at grant date of restricted shares granted for the years ended December 31, 2022 and 2021 was $2.00 and $11.26, per share respectively.

The total fair value of shares vested during each of 2022 and 2021 was approximately $0.7 million and $0.6 million, respectively. As of December 31, 2022, the Company had approximately $0.6 million of unrecognized compensation expense related to non-vested restricted shares, expected to be recognized over a weighted average period of 0.84 years.

Restricted shares are subject to a repurchase right by the Company on certain occasions. Under the repurchase right, the Company may reacquire restricted shares, for no consideration, if certain conditions occur including the employees' end of service with the Company.

10. Taxes on Income

The Company records income tax expense related to profits realized in the United States and realized by its subsidiary in Israel.

United States:

On December 22, 2017, the United States enacted the Tax Cuts and Jobs Act (the "U.S. Tax Reform"); a comprehensive tax legislation that includes significant changes to the taxation of business entities. These changes, most of which are effective for tax years beginning after December 31, 2017, include several key tax provisions that might impact the Company, among others: (i) a permanent reduction to the statutory federal corporate income tax rate from 35% (top rate) to 21% (flat rate) effective for tax years beginning after December 31, 2017 (ii) a new tax deduction in the amount of 37.5% of "foreign derived intangible income" that effectively reduces the federal corporate tax on certain qualified foreign derived sales/licenses/leases and service income in excess of a base amount to 13.125% (as compared to the regular corporate income tax rate of 21%); (iii) stricter limitation on the tax deductibility of business interest expense; (iv) a shift of the U.S. taxation of multinational corporations from a tax on worldwide income to a territorial system (along with certain rules designed to prevent erosion of the U.S. income tax base) (v) a one-time deemed repatriation tax on accumulated offshore earnings held in cash and illiquid assets, with the latter taxed at a lower rate and (vi) an expansion of the U.S. controlled foreign corporation ("CFC") anti deferral starting with the CFC's first tax year beginning in 2018 intended to tax in the U.S. "global intangible low-taxed income" ("GILTI").

The Company recorded loss from continuing operations, before taxes on income for the period indicated as follows (in thousands):

	Year ended December 31, 2022	Year ended December 31, 2021
United States	$ (36,674)	$ (39,018)
Israel	(755)	(460)
Net loss before tax	$ (37,429)	$ (39,478)

Income tax expense is summarized as follows (in thousands):

	Year ended December 31, 2022	Year ended December 31, 2021
Current :		
Domestic	$ 57	$ -
Foreign	527	776
	$ 584	$ 776
Income tax expense	$ 584	$ 776

The effective income tax rate differed from the amount computed by applying the federal statutory rate to our loss before income taxes as follows:

	Year ended December, 31 2022	Year ended December, 31 2021
U.S. federal tax provision at statutory rate	21.00%	21.00%
State and local tax, net of federal benefit	0.72	4.01
Foreign rate differences	(0.06)	(0.09)
Non-deductible stock compensation	(1.26)	(1.43)
Section 951A GILTI	0.00	0.00
Effect of other permanent differences	(0.01)	(0.07)
Uncertain tax positions	(1.15)	(0.66)
Change in valuation allowance	(25.51)	(34.39)
Federal Tax Reform Rate Change	0.00	0.00
Tax Credits	4.14	6.01
Provision to Return	1.67	3.95
Other adjustments	(1.10)	(0.30)
Effective tax rate	(1.56)%	(1.97)%

Deferred Income Taxes

Deferred income taxes reflect the net tax effects of temporary differences between the carrying amounts of assets and liabilities for financial reporting purposes and the amounts used for income tax purposes. Significant components of the Company's deferred tax assets are as follows (in thousands):

	($ in thousands) As of December 31,	
	2022	2021
Deferred tax assets:		
Federal net operating loss carry forwards	$ 27,592	$ 22,614
Tax credit carry forwards	4,862	3,402
Intangible and other related assets	2,990	3,011
Research and Development Costs	3,074	-
Accrued expenses	72	169
Lease Liability	410	-
Total deferred tax assets before valuation allowance	39,000	29,196
Valuation allowance	(38,652)	(29,196)
Total deferred tax assets	348	-
Deferred tax liabilities:		
Right of Use Asset	348	-
Total deferred tax liabilities	348	-
Net deferred tax assets	$ -	$ -

As of December 31, 2022, the Company has provided a valuation allowance of approximately $38.7 million in respect of the Company's deferred tax assets resulting from tax loss carryforwards, tax credits and other temporary differences. Realization of deferred tax assets is dependent upon future earnings, if any, the time and amount of which are uncertain. As the Company is still in its development stage and has not yet generated revenues, it is more likely than not that sufficient taxable income will not be available for the tax losses to be utilized in the future. Therefore, a valuation allowance was recorded to reduce the deferred tax assets to their recoverable amounts.

Available Carryforward Tax Losses

As of December 31, 2022, we had net operating loss carryforwards, or NOLs, of $114.3 million for federal income tax purposes and $69.4 million for state income tax purposes, which may be available to offset our future taxable income, if any, and begin to expire in various amounts in 2037 and 2038, respectively, provided that NOLs generated in tax years ending after December 31, 2017 will not be subject to expiration. In general, under Sections 382 and 383 of the U.S. Internal Revenue Code of 1986, as amended, or the Code, a corporation that undergoes an "ownership change" is subject to limitations on its ability to use its pre-change NOLs to offset future taxable income. If the U.S. Internal Revenue Service challenges our determinations with respect to the existence of previous ownership changes or the effects thereof, or if we undergo an ownership change, our ability to use our NOLs could be limited by Section 382 of the Code. Future changes in our stock ownership, some of which are outside of our control, could also result in an ownership change under Sections 382 and 383 of the Code. In addition, for taxable years beginning after December 31, 2020, utilization of federal NOLs generated in tax years beginning after December 31, 2017 are limited to a maximum of 80% of the taxable income for such year, after taking into account utilization of NOLs generated in years beginning before January 1, 2018 and determined without regard to such NOL deduction. Furthermore, our ability to use NOLs of companies that we may acquire in the future may be subject to limitations. For these reasons, we may not be able to use a material portion of the NOLs, even if we attain profitability. The reduction of the corporate tax rate under recently-enacted U.S. tax legislation may cause a reduction in the economic benefit of our NOLs and other deferred tax assets available to us.

In addition, as of December 31, 2022, the Company had federal Orphan Drug research and development credit carryforwards of approximately $4,619 thousand and $66, respectively. If not utilized, the federal tax carryforwards which expire in 2039. The Company also had state research and development credit carryforward of approximately $0.1 million and will begin to expire in 2037 if not utilized.

Uncertain Tax Positions

The Company has reviewed the tax positions taken, or to be taken, in our tax returns for all tax years currently open to examination by a taxing authority. As of December 31, 2022, and 2021, the Company has recorded an uncertain tax position liability exclusive of interest and penalties of approximately $1.3 million, and $0.9 million, respectively. As of December 31, 2022, the Company has not accrued penalties for uncertain tax positions. A reconciliation of the Company's unrecognized tax benefits is below:

	2022	2021
	(in thousands)	(in thousands)
Uncertain tax position at the beginning of year	$ 858	$ 581
Additions for uncertain tax position of prior years (foreign exchange and interest)	36	17
Additions for tax positions of current year	429	260
Uncertain tax position at the end of the year	$ 1,323	$ 858

The Company remains subject to examination until the statute of limitations expires for each respective tax jurisdiction. The statute of limitations is currently open for 2017, 2018, 2019, 2020, 2021 and 2022 for all tax jurisdictions.

Israel:

In December 2016, the Israeli Parliament approved the Economic Efficiency Law (Legislative Amendments for Applying the Economic Policy for the 2017 and 2018 Budget Years) which reduces the corporate income tax rate from 25% to 24% effective from January 1, 2017, and to 23% effective from January 1, 2018.

The Israeli corporate income tax rate was 23% in 2022 and 2021. Income not eligible for Preferred Enterprise benefits is taxed at the regular corporate tax rates as described above.

11. Net Loss Per Share Attributable to Common Stockholders

The following table sets forth the computation of the loss per share for the period presented (in thousands, except for share data):

	Year ended December 31, 2022	Year ended December 31, 2021
Numerator:		
Net loss	$ 38,013	$ 40,254
Denominator:		
Weighted-average number of shares used to compute net loss per share, basic and diluted	15,448,931	14,398,905

The calculation of basic and diluted Loss Per Share includes 1,333,333 and 1,155,555 weighted average warrants with an exercise price of $0.01 for the year ended December 31, 2022 and 2021, respectively.

The following potentially dilutive common stock equivalents have been excluded from the calculation of diluted net loss per share for the period presented due to their anti-dilutive effect: 466,666 shares of common stock and 1,056,015options outstanding to purchase common stock as of December 31, 2022.

The following potentially dilutive common stock equivalents have been excluded from the calculation of diluted net loss per share for the period presented due to their anti-dilutive effect: 466,666 shares of common stock and 900,789 options outstanding to purchase common stock as of December 31, 2021.

12. Subsequent Events

On October 18, 2022, the Company entered into an Agreement of Merger (the “Merger Agreement”) with Advaxis, Inc., a Delaware corporation (“Advaxis”). The Merger Agreement provides, among other things, that on the terms and subject to the conditions set forth therein: (i) each share of the common stock, par value $0.01 per share, of the Company (the “Ayala Common Stock”) issued and outstanding immediately prior to the Merger shall be automatically converted into the right to receive 0.1874 shares (as such amount may be adjusted as provided in the Merger Agreement “Exchange Ratio”) of the common stock, par value $0.001 per share, of Advaxis (the “Advaxis Common Stock”), (iii) each outstanding option to purchase shares of the Ayala Common Stock (each, an “Ayala Option”) were substituted and converted automatically into an option (each, an “Advaxis Replacement Option”) to purchase the number of shares of Advaxis Common Stock equal to the product obtained by multiplying (a) the number of shares of Ayala Common Stock subject such Ayala Option immediately prior to the effective time of the Merger, by (b) the Exchange Ratio, with any fractional shares rounded down to the nearest whole share, with each such Advaxis Replacement Option to have an exercise price per share of Advaxis Common Stock equal to (x) the per share exercise price for the shares of Ayala Common Stock subject to the corresponding Ayala Option immediately prior to the effective time of the Merger, divided by (y) the Exchange Ratio, rounded up to the nearest whole cent, and (iv) each restricted stock unit of the Company (each, an “Ayala RSU”) outstanding immediately prior to the effective time of the Merger, whether or not vested or issuable, were substituted and converted automatically into a restricted stock unit award of Advaxis with respect to a number of shares of Advaxis Common Stock equal to the product obtained by multiplying (i) the total number of shares of Ayala Common Stock subject to such Ayala RSU immediately prior to the effective time of the Merger by (ii) the Exchange Ratio, with any fractional shares rounded down to the nearest whole share.

Upon completion of the Merger, the Company’s stockholders owned approximately 62.5 % of the combined company’s outstanding common stock and Advaxis stockholders will own approximately 37.5%.

As a result of the merger, the Company incurred issuance costs of 1,953 through the balance sheet date that are directly related to the Merger. The costs are accounted for as deferred issuance costs that will be charged to shareholder equity upon the completion of the transaction..

Closing of the Merger occurred on January 19th, 2023.

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

None.

Item 9A. Controls and Procedures.

Limitations on Effectiveness of Controls and Procedures

In designing and evaluating our disclosure controls and procedures, management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving the desired control objectives. In addition, the design of disclosure controls and procedures must reflect the fact that there are resource constraints and that management is required to apply judgment in evaluating the benefits of possible controls and procedures relative to their costs.

Evaluation of Disclosure Controls and Procedures

Our management, with the participation of our principal executive officer and principal financial officer, evaluated, as of the end of the period covered by this Annual Report on Form 10-K, the effectiveness of our disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act). Based on that evaluation, our principal executive officer and principal financial officer concluded that, as of December 31, 2021, our disclosure controls and procedures were effective at the reasonable assurance level.

Management's Annual Report on Internal Control over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over our financial reporting, as such term is defined in Rule 13a-15(f) under the Exchange Act. Our management conducted an assessment of the effectiveness of our internal control over financial reporting based on the criteria set forth in "Internal Control - Integrated Framework (2013)" issued by the Committee of Sponsoring Organizations of the Treadway Commission. Based on this assessment, our management concluded that, as of December 31, 2022, our internal control over financial reporting was effective.

Attestation Report of the Independent Registered Public Accounting Firm

This Annual Report on Form 10-K does not include an attestation report of our independent registered public accounting firm due to an exemption established by the JOBS Act for "emerging growth companies."

Changes in Internal control over Financial Reporting

There were no changes in our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) during the quarter ended December 31, 2022 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information.

Advaxis plans to file an amendment to its Form 8-K filed with the SEC on January 25, 2023, in which Advaxis expects to include pro forma financial information that contemplates the merger described in such 8-K being accounted for partially as a business combination and partially as a recapitalization, which differs from the pro forma financial information included in Advaxis's registration statement on Form S-4 (Commission file no. 333-268586), in which the transaction was accounted for solely as a business combination.

Item 9C. Disclosure Regarding Foreign Jurisdictions that Prevent Inspections.

Not applicable.

PART III

Item 10. Directors, Executive Officers and Corporate Governance.

Code of Ethics

Our board of directors has adopted a written Code of Business Conduct and Ethics applicable to all officers, directors and employees, including our principal executive officer, principal financial officer, principal accounting officer or controller, or persons performing similar functions. We have posted a current copy of our Code of Business Conduct and Ethics on our website at www.ayalapharma.com in the "Investors & Media" section under "Corporate Governance." We intend to satisfy the disclosure requirement under Item 5.05 of Form 8-K regarding amendment to, or waiver from, a provision of our Code of Business Conduct and Ethics, as well as The Nasdaq Global Market's requirement to disclose waivers with respect to directors and executive officers, by posting such information on our website at the address and location specified above. The information contained on our website is not incorporated by reference into this Annual Report on Form 10-K.

Executive Officers and Directors

Kenneth Berlin

Mr. Berlin has served as our President and Chief Executive Officer and is the sole Director of the Board since January 2023. Mr. Berlin served as New Ayala's Interim Chief Financial Officer from September 2020 to May 2022. Prior to joining New Ayala, Mr. Berlin served as President and Chief Executive Officer of Rosetta Genomics from November 2009 until April 2018. Prior to Rosetta Genomics, Mr. Berlin was Worldwide General Manager at cellular and molecular cancer diagnostics developer Veridex, LLC, a Johnson & Johnson company. At Veridex he grew the organization to over 100 employees, launched three cancer diagnostic products, led the acquisition of its cellular diagnostics partner, and delivered significant growth in sales as Veridex transitioned from an R&D entity to a commercial provider of oncology diagnostic products and services. Mr. Berlin joined Johnson & Johnson in 1994 and served as corporate counsel for six years. From 2001 until 2004 he served as Vice President, Licensing and New Business Development in the pharmaceuticals group, and from 2004 until 2007 served as Worldwide Vice President, Franchise Development, Ortho-Clinical Diagnostics. Mr. Berlin holds an A.B. degree from Princeton University and a J.D. from the University of California Los Angeles School of Law. Mr. Berlin's experience in life science companies, as well as his business experience in general, qualify him to service as our director.

Igor Gitelman

Mr. Gitelman has served as our Interim Chief Financial Officer since January 2023. Mr. Gitelman served as New Ayala's VP of Finance since November 2020 and Chief Accounting Officer since February 2021. Prior to joining New Ayala, Mr. Gitelman served as CFO Executive Financial Consultant for Accu Reference Medical Labs, a clinical diagnostic laboratory. Before that, from February 2017 through November 2018, Mr. Gitelman served as a chief accounting officer of Cancer Genetics, Inc., a drug discovery, preclinical oncology, and immuno-oncology services company. Prior to that, Mr. Gitelman served as an Assistant to Vice President (AVP) of Finance and Tax at clinical diagnostic laboratory, BioReference Laboratories, Inc., from October 2005 to October 2016. During this time at BioReference Laboratories, Inc., Mr. Gitelman held various positions of increasing responsibility managing the company's internal audit function, SEC financial reporting, tax, and corporate finance functions.

Andres Gutierrez, M.D., Ph.D.

Dr. Gutierrez has served as our Executive Vice President and Chief Medical Officer since January 2023. Prior to joining New Ayala, Dr. Gutierrez served as Chief Medical Officer for Oncolytics Biotech, Inc. from November 2016 to April 2018. Prior to Oncolytics, Dr. Gutierrez was Chief Medical Officer at SELLAS Life Sciences Group from November 2015 to September 2016 and was Medical Director, Early Development Immuno-Oncology at BMS from October 2012 to November 2015, where he oversaw the development of translational and clinical development of immuno-oncology programs in solid tumors and hematological malignancies. Earlier, Dr. Gutierrez was Medical Director for several biotechnology companies, including Sunesis Pharmaceuticals, BioMarin Pharmaceutical, Proteolix and Oculus Innovative Sciences, leading key programs with talazoparib and carfilzomib, among others. Prior to Oculus, he served as Director of the Gene & Cell Therapy Unit at the National Institutes of Health in Mexico City and as a consultant physician at the Hospital Angeles del Pedregal.

Item 11. Executive Compensation.

Following the merger Dr. Roni Mamluk, Mr. Yossi Maimon and Dr. Gary Gordon are no longer with the company, Mr. Kenneth Berlin, Mr. Igor Gitelman and Dr. Andres Gutierrez are the current officers, however they did not work in the company during 2021 and 2022.

	Year	Salary (1)	Bonus	Stock Awards (5)	Option Awards (5)	Non-Equity Incentive Plan Compensation	All Other (6) (7)	Total
Roni Mamluk, Ph.D. (2)	2022	369,236	-	240,000	815,364	-	135,997	1,560,597
Former Chief Executive Officer	2021	387,698	-	383,741	596,711	157,541	146,817	1,672,507
Yossi Maimon, C.P.A., M.B.A. (3)	2022	294,286	-	100,000	203,841	-	119,036	717,163
Former Chief Financial Officer	2021	309,000	-	95,935	149,178	125,562	121,869	801,544
Gary Gordon, M.D., Ph.D. (4)	2022	386,250	-	100,000	203,841	-	49,431	739,522
Former Chief Medical Officer	2021	386,250	-	95,935	149,178	154,500	36,646	822,509
Kenneth Berlin	2022	-	-	-	-	-	-	-
President, Chief Executive Officer	2021	-	-	-	-	-	-	-
Igor Gitelman	2022	-	-	-	-	-	-	-
Interim Chief Financial Officer and Vice President of Finance	2021	-	-	-	-	-	-	-
Andres Gutierrez	2022	-	-	-	-	-	-	-
Senior VP, Chief Medical Officer	2021	-	-	-	-	-	-	-

(1) Amounts reported for the named executive officer and paid in New Israeli Shekels are converted from New Israeli Shekels to U.S. dollars using an exchange rate of 3.36 New Israeli Shekels to 1 U.S. dollar.

(2) Dr. Mamluk is based in Israel.

(3) Mr. Maimon is based in Israel.

(4) Dr. Gordon is based in the United States.

(5) Amounts reflect the full grant-date fair value of stock awards and stock options granted during the year computed in accordance with ASC Topic 718, rather than the amounts paid to or realized by the named individual. We provide information regarding the assumptions used to calculate the value of all stock awards and option awards made to named executive officers in Note 8 to the consolidated financial statements included in our Annual Report for the fiscal year ended December 31, 2022.

(6) Consists of contributions to Dr. Mamluk's and Mr. Maimon's severance funds, pension funds and educational funds, in each case, under Israeli law, and the use of a leased company car.

(7) Amount represents matching 401(k) contributions, travel allowance, cell phone use and reimbursement of certain other items relating to Dr. Gordon's use of a home office.

Grants outstanding. as of December 31, 2022

Name	Number of Shares of Ayala Restricted Stock	Number of Ayala Options
Executive Officers		
Roni Mamluk, Ph.D., Former President and Chief Executive Officer	164,632(1)	251,767(1)
Yossi Maimon, CPA, M.B.A., Former Chief Financial Officer	55,587(1)	131,068(1)
Gary Gordon, M.D., Ph.D., Former Chief Medical Officer	50,625	140,113
Directors		
Vered Bisker-Leib, Ph.D., M.B.A.	—	21,244
Murray A. Goldberg	—	42,492
David Sidransky, M.D.	—	24,995
Todd Sone(2)	—	42,492
Robert Spiegel, M.D., F.A.C.P.	—	6,249

(1) Equity compensation award will vest in full upon the completion of the Merger or upon an agreed termination of employment occurring immediately following the Merger.

(2) Mr. Sone resigned from the Ayala Board effective July 28, 2021.

Securities Authorized for Issuance under Equity Compensation Plans

Equity Compensation Plan Information

The following table includes information related to shares available and outstanding awards under our equity incentive plans as of December 31, 2022:

Plan Category	Number of Securities to be issued upon Exercise of outstanding Options, Warrants and Rights (#)	Weighted-average Exercise Price of Outstanding Options, Warrants and Rights ($)	Number of Securities Remaining Available for Future Issuance Under Equity Compensation Plans (#)
Equity Compensation Plans approved by security holders	1,056,015	$ 7.53	547,085
Equity Compensation Plans not approved by security holders	-	-	-
TOTAL:	1,056,015	$ 7.53	547,085

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

Name of Beneficial Owner	Total # of Shares Beneficially Owned	Percentage of Ownership
Ayala Pharmaceuticals, Inc.[1]	1	100%
Kenneth Berlin	0	0%
Igor Gitelman	0	0%
Andres Gutierrez	0	0%

(1) Chief Executive Officer Kenneth Berlin and Acting Chief Financial Officer Igor Gitelman hold shared voting and dispositive power over the share.

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

Certain Relationships and Related Transactions

Our policy is to enter into transactions with related parties on terms that, on the whole, are no more favorable, or no less favorable, than those available from unaffiliated third parties. Based on our experience in the business sectors in which we operate and the terms of our transactions with unaffiliated third parties, we believe that all transactions that we enter will meet this policy standard at the time they occur. Presently, we have no such related party transactions.

Director Independence

Our sole director Kenneth Berlin is not independent.

Item 14. Principal Accounting Fees and Services.

Fee Category	2022	2021
Audit Fees	$ 525,000	$ 280,00
Audit-Related Fees	45,000	—
Tax Fees	14,000	10,000
All Other Fees	—	—
Total Fees	$ 584,000	$ 290,000

PART IV

Item 15. Exhibits and Financial Statement Schedules.

(a)(1) Financial Statements.

The financial statements required by this item are listed in Item 8, "Financial Statements and Supplementary Data" herein.

(a)(2) Financial Statement Schedules.

All financial statement schedules have been omitted because they are not applicable, not required or the information required is shown in the financial statements or the notes thereto.

(a)(3) Exhibits.

The following is a list of exhibits filed as part of this Annual Report on Form 10-K.

Exhibit Index

Exhibit Number	Description	Form	File No.	Exhibit	Filing Date	Filed/Furnished Herewith
3.1	Restated Certificate of Incorporation of Ayala Pharmaceuticals, Inc.	8-K	001-39279	3.1	5/12/2020	
3.2	Amended and Restated Bylaws of Ayala Pharmaceuticals, Inc.	8-K	001-39279	3.2	5/12/2020	
4.1	Amended and Restated Investors' Rights Agreement	S-1/A	333-236942	4.1	5/4/2020	
4.2	Specimen Stock Certificate evidencing the shares of common stock	S-1/A	333-236942	4.2	5/4/2020	
4.3	Description of Securities					*
4.4	Form of Common Warrant	8-K	001-39279	4.1	2/22/2021	
4.5	Form of Pre-Funded Warrant	8-K	001-39279	4.2	2/22/2021	
4.6	Form of Indenture	S-3	333-256792	4.3	6/4/2021	
21.1	Subsidiaries of Ayala Pharmaceuticals, Inc.	S-1	333-236942	21.1	3/6/2020	
23.1	Consent of Independent Registered Public Accounting Firm					*
31.1	Certification of Principal Executive Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.					*
31.2	Certification of Principal Financial Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.					*
32.1	Certification of Principal Executive Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.					**
32.2	Certification of Principal Financial Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.					**
99.1	Definitive Proxy Statement of Old Ayala (f/k/a Ayala Pharmaceuticals, Inc.). Incorporated by reference to the description of the business of Old Ayala set forth in pages 233-273 of the Definitive Proxy Statement of Old Ayala for the Special Meeting of Stockholders of Old Ayala held on January 13, 2023, filed with the SEC on December 12, 2022 (File No. 001-39279).	10-K	001-36138	99.1	2/10/2023	
101.INS	Inline XBRL Instance Document—the instance document does not appear in the Interactive Data File because its XBRL tags are embedded within the Inline XBRL document					*
101.SCH	Inline XBRL Taxonomy Extension Schema Document					*
101.CAL	Inline XBRL Taxonomy Extension Calculation Linkbase Document					*
101.DEF	Inline XBRL Taxonomy Extension Definition Linkbase Document					*
101.LAB	Inline XBRL Taxonomy Extension Label Linkbase Document					*
101.PRE	Inline XBRL Taxonomy Extension Presentation Linkbase Document					*
104	Cover Page Interactive Data File (formatted as Inline XBRL and contained in Exhibit 101)					*

* Filed herewith.
** Furnished herewith.
# Indicates management contract or compensatory plan.
† Portions of this exhibit have been redacted in compliance with Regulation S-K Item 601(b)(10)(iv).

Item 16. Form 10-K Summary

None.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, as amended, the Registrant has duly caused this Report to be signed on its behalf by the undersigned, thereunto duly authorized**.**

Ayala Pharmaceuticals, Inc.

Date: March 31, 2023

By: /s/ Kenneth Berlin.
Kenneth Berlin
President and Chief Executive Officer

Date: March 31, 2023

By: /s/ Igor Gitelman.
Igor Gitelman
Interim Chief Financial Officer and VP of Finance

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, this Report has been signed below by the following persons on behalf of the Registrant in the capacities and on the dates indicated.

Name	Title	Date
/s/ Kenneth Berlin **Kenneth Berlin**	President, Chief Executive Officer and Director *(principal executive officer)*	March 31, 2023
/s/ Igor Gitelman. **Igor Gitelman**	*Interim Chief Financial Officer and VP of Finance* *(principal financial and accounting officer)*	March 31, 2023

Exhibit 4.3

DESCRIPTION OF THE REGISTRANT'S SECURITIES REGISTERED PURSUANT TO SECTION 12 OF THE SECURITIES EXCHANGE ACT OF 1934, AS AMENDED

As of December 31, 2022, Ayala Pharmaceuticals, Inc. had one class of securities registered under Section 12 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"). References herein to "we," "us," "our" and the "Company" refer to Ayala Pharmaceuticals, Inc. and not to any of its subsidiaries.

General

The following description summarizes some of the terms of our restated certificate of incorporation and restated bylaws, the amended and restated investors' rights agreement and of the General Corporation Law of the State of Delaware. Because it is only a summary, it does not contain all the information that may be important to you. For a complete description, you should refer to our restated certificate of incorporation, restated bylaws and the amended and restated investors' rights agreement, copies of which have been filed with the Securities and Exchange Commission, as well as the relevant provisions of the General Corporation Law of the State of Delaware.

Our authorized capital stock consists of 200,000,000 shares of common stock, par value $0.01 per share, and 10,000,000 shares of preferred stock, par value $0.01 per share.

Common Stock

Holders of our common stock are entitled to one vote for each share held on all matters submitted to a vote of stockholders and do not have cumulative voting rights. An election of directors by our stockholders shall be determined by a plurality of the votes cast by the stockholders entitled to vote on the election. Subject to the supermajority votes for some matters, other matters shall be decided by the affirmative vote of our stockholders having a majority in voting power of the votes cast by the stockholders present or represented and voting on such matter. Our restated certificate of incorporation and restated bylaws also provide that our directors may be removed only for cause and only by the affirmative vote of the holders of at least two-thirds in voting power of the outstanding shares of capital stock entitled to vote thereon. In addition, the affirmative vote of the holders of at least two-thirds in voting power of the outstanding shares of capital stock entitled to vote thereon is required to amend or repeal, or to adopt any provision inconsistent with, several of the provisions of our restated certificate of incorporation. See below under "—Anti-Takeover Effects of Delaware Law and Our Certificate of Incorporation and Bylaws—Amendment of Charter Provisions." Holders of common stock are entitled to receive proportionately any dividends as may be declared by our board of directors, subject to any preferential dividend rights of any series of preferred stock that we may designate and issue in the future.

In the event of our liquidation or dissolution, the holders of common stock are entitled to receive proportionately our net assets available for distribution to stockholders after the payment of all debts and other liabilities and subject to the prior rights of any outstanding preferred stock. Holders of common stock have no preemptive, subscription, redemption or conversion rights. Our outstanding shares of common stock are validly issued, fully paid and nonassessable. The rights, preferences and privileges of holders of common stock are subject to and may be adversely affected by the rights of the holders of shares of any series of preferred stock that we may designate and issue in the future.

Preferred Stock

Under the terms of our restated certificate of incorporation, our board of directors is authorized to direct us to issue shares of preferred stock in one or more series without stockholder approval. Our board of directors has the discretion to determine the rights, preferences, privileges and restrictions, including voting rights, dividend rights, conversion rights, redemption privileges and liquidation preferences, of each series of preferred stock.

The purpose of authorizing our board of directors to issue preferred stock and determine its rights and preferences is to eliminate delays associated with a stockholder vote on specific issuances. The issuance of preferred stock, while providing flexibility in connection with possible acquisitions, future financings and other corporate purposes, could have the effect of making it more difficult for a third party to acquire, or could discourage a third party from seeking to acquire, a majority of our outstanding voting stock. There are no shares of preferred stock outstanding, and we have no present plans to issue any shares of preferred stock.

Registration Rights

Certain of our stockholders are entitled to certain rights with respect to the registration of such shares for public resale under the Securities Act, pursuant to an amended and restated investors' rights agreement by and among us and certain of our stockholders, until the rights otherwise terminate pursuant to the terms of the investors' rights agreement. Additionally, holders of warrants to purchase our common stock are entitled to certain rights with respect to the registration for public resale under the Securities Act of shares of our common stock issued or issuable upon exercise of such warrants, pursuant to a securities purchase agreement by and among certain purchasers named therein. The registration of shares of common stock as a result of the following rights being exercised would enable holders to trade these shares without restriction under the Securities Act when the applicable registration statement is declared effective.

Piggyback Registration Rights

If we propose to register any shares of our common stock under the Securities Act, subject to certain exceptions, the holders of registrable securities will be entitled to notice of the registration and to include their shares of registrable securities in the registration. If our proposed registration involves an underwriting, the managing underwriter of such offering will have the right to limit the number of shares to be underwritten for reasons related to the marketing of the shares.

Form S-3 Registration Rights

If, at any time after we become entitled under the Securities Act to register our shares on a registration statement on Form S-3, the holders of at least 20% of the registrable securities then outstanding request in writing that we effect a registration with respect to all or part of such registrable securities then outstanding and having an anticipated aggregate offering amount, net of expenses, of at least $3,000,000, we will be required to effect such registration.

Private Placement Form S-3 Registration Rights

We have also agreed to use reasonable best efforts to register certain shares of our common stock issued, or issuable upon exercise of certain warrants, for public resale pursuant to the Securities Act on a registration statement on Form S-3 promptly following the date such form is available for use by us, but in no event later than June 15, 2021. On June 6, 2021, we registered such shares on a registration statement on Form S-3 (File No. 333-256793).

Expenses and Indemnification

Ordinarily, other than underwriting discounts and commissions, we will be required to pay all expenses incurred by us related to any registration effected pursuant to the exercise of these registration rights. These expenses may include all registration and filing fees, printing expenses, fees and disbursements of our counsel, reasonable fees and disbursements of a counsel for the selling securityholders and blue sky fees and expenses. Additionally, we have agreed to indemnify selling stockholders for damages, and any legal or other expenses reasonably incurred, arising from or based upon any untrue statement of a material fact contained in any registration statement, an omission or alleged omission to state a material fact in any registration statement or necessary to make the statements therein not misleading, or any violation or alleged violation by the indemnifying party of securities laws, subject to certain exceptions.

Termination of Registration Rights

The registration rights terminate upon the earlier of the date that is five years after the closing of our initial public offering, such time as Rule 144 or another similar exemption under the Securities Act is available for the sale of all of such holders' shares without limitation during a three-month period without registration and the closing of a deemed liquidation event, as defined in the investors' rights agreement.

Anti-Takeover Effects of Delaware Law and Our Certificate of Incorporation and Bylaws

Some provisions of Delaware law, our restated certificate of incorporation and our restated bylaws could make the following transactions more difficult: an acquisition of us by means of a tender offer; an acquisition of us by means of a proxy contest or otherwise; or the removal of our incumbent officers and directors. It is possible that these provisions could make it more difficult to accomplish or could deter transactions that stockholders may otherwise consider to be in their best interest or in our best interests, including transactions which provide for payment of a premium over the market price for our shares.

These provisions, summarized below, are intended to discourage coercive takeover practices and inadequate takeover bids. These provisions are also designed to encourage persons seeking to acquire control of us to first negotiate with our board of directors. We believe that the benefits of the increased protection of our potential ability to negotiate with the proponent of an unfriendly or unsolicited proposal to acquire or restructure us outweigh the disadvantages of discouraging these proposals because negotiation of these proposals could result in an improvement of their terms.

Undesignated Preferred Stock

The ability of our board of directors, without action by the stockholders, to issue up to 10,000,000 shares of undesignated preferred stock with voting or other rights or preferences as designated by our board of directors could impede the success of any attempt to change control of us. These and other provisions may have the effect of deferring hostile takeovers or delaying changes in control or management of our company.

Stockholder Meetings

Our restated certificate of incorporation and restated bylaws provide that a special meeting of stockholders may be called only by our chairman of the board, chief executive officer or president (in the absence of a chief executive officer), or by a resolution adopted by a majority of our board of directors.

Requirements for Advance Notification of Stockholder Nominations and Proposals

Our restated bylaws establish advance notice procedures with respect to stockholder proposals to be brought before a stockholder meeting and the nomination of candidates for election as directors, other than nominations made by or at the direction of the board of directors or a committee of the board of directors.

Elimination of Stockholder Action by Written Consent

Our restated certificate of incorporation eliminates the right of stockholders to act by written consent without a meeting.

Staggered Board

Our board of directors is divided into three classes. The directors in each class serve for a three-year term, one class being elected each year by our stockholders. This system of electing and removing directors may tend to discourage a third party from making a tender offer or otherwise attempting to obtain control of us, because it generally makes it more difficult for stockholders to replace a majority of the directors.

Removal of Directors

Our restated certificate of incorporation provides that no member of our board of directors may be removed from office by our stockholders except for cause and, in addition to any other vote required by law, upon the approval of the holders of at least two-thirds in voting power of the outstanding shares of stock entitled to vote in the election of directors.

Stockholders Not Entitled to Cumulative Voting

Our restated certificate of incorporation does not permit stockholders to cumulate their votes in the election of directors. Accordingly, the holders of a majority of the outstanding shares of our common stock entitled to vote in any election of directors can elect all of the directors standing for election, if they choose, other than any directors that holders of our preferred stock may be entitled to elect.

Delaware Anti-Takeover Statute

We are subject to Section 203 of the General Corporation Law of the State of Delaware, which prohibits persons deemed to be "interested stockholders" from engaging in a "business combination" with a publicly held Delaware corporation for three years following the date these persons become interested stockholders unless the business combination is, or the transaction in which the person became an interested stockholder was, approved in a prescribed manner or another prescribed exception applies. Generally, an "interested stockholder" is a person who, together with affiliates and associates, owns, or within three years prior to the determination of interested stockholder status did own, 15% or more of a corporation's voting stock. Generally, a "business combination" includes a merger, asset or stock sale, or other transaction resulting in a financial benefit to the interested stockholder. The existence of this provision may have an anti-takeover effect with respect to transactions not approved in advance by the board of directors.

Choice of Forum

Our restated certificate of incorporation provides that, unless we consent in writing to the selection of an alternative form, the Court of Chancery of the State of Delaware will be the sole and exclusive forum for: (1) any derivative action or proceeding brought on our behalf; (2) any action asserting a claim of breach of a fiduciary duty or other wrongdoing by any of our directors, officers, employees or agents to us or our stockholders; (3) any action asserting a claim against us arising pursuant to any provision of the General Corporation Law of the State of Delaware or our certificate of incorporation or bylaws; (4) any action to interpret, apply, enforce or determine the validity of our certificate of incorporation or bylaws; or (5) any action asserting a claim governed by the internal affairs doctrine. Under our restated certificate of incorporation, this exclusive forum provision will not apply to claims which are vested in the exclusive jurisdiction of a court or forum other than the Court of Chancery of the State of Delaware, or for which the Court of Chancery of the State of Delaware does not have subject matter jurisdiction. For instance, the provision would not apply to actions arising under federal securities laws, including suits brought to enforce any liability or duty created by the Securities Act, Exchange Act, or the rules and regulations thereunder. Our restated certificate of incorporation further provides that, unless we consent in writing to the selection of an alternative forum, the federal district courts of the United States of America shall, to the fullest extent permitted by law, be the sole and exclusive forum for the resolution of any complaint asserting a cause of action arising under the Securities Act. Our restated certificate of incorporation also provides that any person or entity purchasing or otherwise acquiring any interest in shares of our capital stock will be deemed to have notice of and to have consented to these choice of forum provisions. It is possible that a court of law could rule that either or both of the choice of forum provisions contained in our restated certificate of incorporation is inapplicable or unenforceable if it is challenged in a proceeding or otherwise.

Amendment of Charter Provisions

The amendment of any of the above provisions, except for the provision making it possible for our board of directors to issue preferred stock and the provision prohibiting cumulative voting, would require approval by holders of at least two-thirds in voting power of the outstanding shares of stock entitled to vote thereon.

The provisions of Delaware law, our restated certificate of incorporation and our restated bylaws could have the effect of discouraging others from attempting hostile takeovers and, as a consequence, they may also inhibit temporary fluctuations in the market price of our common stock that often result from actual or rumored hostile takeover attempts. These provisions may also have the effect of preventing changes in the composition of our board and management. It is possible that these provisions could make it more difficult to accomplish transactions that stockholders may otherwise deem to be in their best interests.

Stock Exchange Listing

Our stock is not listed on a national securities exchange. In connection with the Merger, The Nasdaq Capital Markets filed a Form 25 delisting the Company's stock.

Exhibit 23.1

Consent of Independent Registered Public Accounting Firm

We consent to the incorporation by reference in the Registration Statement (Form S-3) of Ayala Pharmaceuticals, Inc. and in the related Prospectus of our report dated March 30, 2022 (which contains an explanatory paragraph describing conditions that raise substantial doubt about the Company's ability to continue as a going concern as described in Note 1 to the consolidated financial statements), with respect to the consolidated financial statements of Ayala Pharmaceuticals, Inc., included in this Annual Report (Form 10-K) for the year ended December 31, 2022.

Tel-Aviv, Israel
March 30, 2023

/s/ Kost, Forer, Gabbay & Kasierer
KOST, FORER, GABBAY & KASIERER
A Member of EY Global

Exhibit 31.1

CERTIFICATION

I, Kenneth Berlin, certify that:

1. I have reviewed this Annual on Form 10-K of Ayala Pharmaceuticals, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 31, 2023

By: /s/ Kenneth Berlin

Kenneth Berlin
Chief Executive Officer
(principal executive officer)

Exhibit 31.2

CERTIFICATION

I, Igor Gitelman, certify that:

1. I have reviewed this Annual Report on Form 10-K of Ayala Pharmaceuticals, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 31, 2023

By: /s/ Igor Gitelman.

Igor Gitelman.
Interim Chief Financial Officer and VP of Finance
(principal financial officer)

Exhibit 32.1

CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350, AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Annual Report on Form 10-K of Ayala Pharmaceuticals, Inc. (the "Company") for the period ended December 31, 2022 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I certify, pursuant to 18 U.S.C. § 1350, as adopted pursuant to § 906 of the Sarbanes-Oxley Act of 2002, that:

(1) The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended; and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: March 31, 2023

By: /s/ Kenneth Berlin
Kenneth Berlin
President and Chief Executive Officer
(principal executive officer)

Exhibit 32.2

CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350, AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Annual Report on Form 10-K of Ayala Pharmaceuticals, Inc. (the "Company") for the period ended December 31, 2022 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I certify, pursuant to 18 U.S.C. § 1350, as adopted pursuant to § 906 of the Sarbanes-Oxley Act of 2002, that:

(1) The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended; and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: March 31, 2023

By: /s/ Igor Gitelman.

Igor Gitelman.
Interim Chief Financial Officer and VP of Finance
(principal financial officer)