Advaxis, Inc.
Form 10-K
January 08, 2016

UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 10-K

[X] ANNUAL REPORT UNDER SECTION 13 OR 15(d)

OF THE SECURITIES EXCHANGE ACT OF 1934

FOR THE FISCAL YEAR ENDED - OCTOBER 31, 2015

OR

[ ] TRANSITION REPORT UNDER SECTION 13 OR 15 (d)

OF THE SECURITIES EXCHANGE ACT OF 1934

FOR THE TRANSITION PERIOD FROM _____ TO _____

COMMISSION FILE NUMBER 000-28489

ADVAXIS, INC.

(Name of Registrant in Its Charter)

Delaware *(State or Other Jurisdiction of Incorporation or Organization)*	02-0563870 *(I.R.S. Employer Identification No.)*
305 College Road East Princeton, New Jersey *(Address of Principal Executive Offices)*	08540 *(Zip Code)*

(609) 452-9813

(Issuer's Telephone Number)

Securities registered under Section 12(b) of the Exchange Act:	Common Stock - $.001 par value NASDAQ Capital Market
Securities registered under Section 12(g) of the Exchange 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 [X]

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Exchange Act.

Yes [ ] No [X]

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 [X] No [ ]

Indicate by check mark whether the registrant has submitted electronically and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted 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 and post such files).

Yes [X] No [ ]

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K (§ 229.405 of this chapter) is not contained herein, and will not be contained, to the best of registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. [ ]

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, or a smaller reporting company. See the definitions of "large accelerated filer", "accelerated filer," and "smaller reporting company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer [ ] Accelerated filer [X]

Non-accelerated filer [ ] Smaller reporting company [ ]

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act).

Yes [ ] No [X]

As of April 30, 2015, the aggregate market value of the voting common equity held by non-affiliates was approximately $445,644,000 based on the closing bid price of the registrant's Common Stock on the NASDAQ Capital Market. (For purposes of determining this amount, only directors, executive officers, and 10% or greater shareholders and their respective affiliates have been deemed affiliates). [X]

The registrant had 33,769,136 shares of Common Stock, par value $0.001 per share, outstanding as of January 7, 2016.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the Proxy Statement for the registrant's 2016 Annual Meeting of Stockholders (the "Proxy Statement") to be filed within 120 days of the end of the fiscal year ended October 31, 2015 are incorporated by reference in Part III hereof. Except with respect to information specifically incorporated by reference in this Form 10-K, the Proxy Statement is not deemed to be filed as a part hereof.

Table of Contents

Form 10-K Index

PART 1

PART II

PART III

Part IV

PART 1

FORWARD LOOKING STATEMENTS

This Annual Report on Form 10-K contains "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995. Such forward-looking statements involve known and unknown risks, uncertainties and other factors which may cause the actual results, performance or achievements of the Company, or industry results, to be materially different from any future results, performance or achievements expressed or implied by such forward-looking statements. When used in this Annual Report, statements that are not statements of current or historical fact may be deemed to be forward-looking statements. Without limiting the foregoing, the words "plan", "intend", "may," "will," "expect," "believe", "could," "anticipate," "estimate," or "continue" or similar expressions or oth comparable terminology are intended to identify such forward-looking statements. Readers are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date hereof. Except as required by law, the Company undertakes no obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise.

Item 1. Business.

General

Advaxis, Inc. ("Advaxis" or the "Company") is a clinical stage biotechnology company focused on the discovery, development and commercialization of proprietary *Lm*-LLO cancer immunotherapies. These immunotherapies are based on a platform technology that utilizes live attenuated *Listeria monocytogenes* ("*Lm*" or "Listeria") bioengineered to secrete antigen/adjuvant fusion proteins. These *Lm*-LLO strains are believed to be a significant advancement in immunotherapy as they integrate multiple functions into a single immunotherapy as they access and direct antigen presenting cells to stimulate anti-tumor T-cell immunity, stimulate and activate the immune system with the equivalent of multiple adjuvants, and simultaneously reduce tumor protection in the tumor microenvironment to enable the T-cells to eliminate tumors.

Axalimogene filolisbac (ADXS-HPV) is our lead *Lm*-LLO immunotherapy product candidate for the treatment of Human Papilloma Virus ("HPV") associated cancers. We completed a randomized Phase 2 study in 110 patients with recurrent cervical cancer that was shown to have a manageable safety profile, apparent improved survival and objective tumor responses. In addition, the Gynecologic Oncology Group ("GOG"), now part of NRG Oncology, is conducting a cooperative group sponsored Phase 2 open-label clinical study of axalimogene filolisbac in patients with persistent or recurrent cervical cancer with documented disease progression. The study, known as GOG-0265, has

successfully completed its first stage and has met the predetermined safety and efficacy criteria required to proceed into the second stage of patient recruitment. We plan to advance axalimogene filolisbac into a registrational clinical trial for the treatment of women with high-risk locally advanced cervical cancer.

Axalimogene filolisbac has received United States Food and Drug Administration ("FDA") orphan drug designation for three HPV-associated cancers: cervical, head and neck, and anal cancer, and has received European Medicines Agency ("EMA") orphan drug designation for anal cancer. It is being evaluated in Company-sponsored trials executed under an Investigational New Drug ("IND") which include the following: i) a Phase 1/2 clinical trial alone and in combination with MedImmune, LLC's ("MedImmune") investigational anti-PD-L1 immune checkpoint inhibitor, durvalumab (MEDI4736), in patients with previously treated metastatic cervical cancer and HPV-associated head and neck cancer; ii) a Phase 2 multi-center, open-label study alone and in combination with Incyte Corporation's ("Incyte") investigational oral indoleamine 2,3-dioxygenase 1 (IDO1) inhibitor, epacadostat (INCB24360) in patients with Stage I-IIa cervical cancer; iii) a Phase 1/2 study evaluating higher doses and repeat cycles of axalimogene filolisbac in patients with recurrent cervical cancer; iv) a single arm Phase 2 monotherapy study in patients with metastatic anal cancer; and v) a Phase 2 study in collaboration with and funded by Global BioPharma Inc. ("GBP"), under a development and commercialization license agreement applicable to Asia, HPV-associated non-small cell lung cancer. In addition to Company-sponsored trials, axalimogene filolisbac is also being evaluated in three ongoing investigator-initiated clinical trials as follows: locally advanced cervical cancer (GOG-0265), head and neck cancer (Mount Sinai), and anal cancer (Brown University).

ADXS-PSA is our *Lm*-LLO immunotherapy product candidate designed to target the Prostate Specific Antigen ("PSA") associated with prostate cancer. This Phase 1/2 clinical trial in combination with KEYTRUDA® (pembrolizumab), Merck & Co.'s ("Merck") humanized monoclonal antibody against PD-1, is in patients with previously treated metastatic castration-resistant prostate cancer.

ADXS-HER2 is our *Lm*-LLO immunotherapy product candidate designed for the treatment of Human Epidermal Growth Factor Receptor 2 ("HER2") expressing cancers, including human and canine osteosarcoma, breast, gastric and other cancers. This Phase 1b clinical trial is in patients with metastatic HER2 expressing solid tumors. We received orphan drug designation from both the FDA and EMA for ADXS-HER2 in osteosarcoma. Clinical research with ADXS-HER2 in canine osteosarcoma is being developed by our pet therapeutic partner, Aratana Therapeutics Inc. ("Aratana"), who holds exclusive rights to develop and commercialize ADXS-HER2 and three other *Lm*-LLO immunotherapies for pet health applications. Aratana has announced that a product license application for use of ADXS-HER2 in the treatment of canine osteosarcoma has been filed with the United States Department of Agriculture ("USDA"). Aratana received communication from the USDA in March 2015 stating that the previously submitted efficacy data for product licensure for AT-014 (ADXS-HER2), the cancer immunotherapy for canine osteosarcoma, was accepted and that it provides a reasonable expectation of efficacy that supports conditional licensure. While additional steps need to be completed, including in the areas of manufacturing and safety, Aratana anticipates that AT-014 could receive conditional licensure from the USDA in 2016.

In October of 2015, we received notification from the FDA that the INDs for axalimogene filolisbac were put on clinical hold in response to our submission of a safety report to the FDA. The clinical hold also included the INDs for ADXS-PSA and ADXS-HER2. Following discussions with the FDA and in accordance with their recommendations, we agreed to implement certain risk mitigation measures, including revised study protocol inclusion / exclusion criteria, post-administration antibiotic treatment and patient surveillance and monitoring measures. In December 2015, the FDA notified us that the hold has been lifted with respect to our INDs.

We have focused our development efforts on understanding our platform technology and establishing a drug development pipeline that incorporates this technology into therapeutic cancer immunotherapies, with clinical trials currently targeting HPV-associated cancer (cervical cancer, head and neck cancer and anal cancer), prostate cancer, and HER2-expressing cancers. Although no immunotherapies have been commercialized to date, we continue to invest in research and development to advance the technology and make it available to patients with many different types of cancer. Pipeline development and the further exploration of the technology for advancement entails risk and expense. We anticipate that our ongoing operational costs will increase significantly as we continue conducting and expanding our clinical development program. In addition to our existing single antigen vectors that target one tumor associated antigen, we are actively engaged in the development of new constructs that will address multiple targets that are common to tumor types, as well as mutation-associated neo-epitopes that are specific to an individual patient's tumor. Lastly, we are developing certain internal capabilities to produce supplies for our neoepitope and our other programs.

Clinical Pipeline

We are a clinical-stage biotechnology company focused on the discovery, development and commercialization of proprietary *Lm*-LLO cancer immunotherapies. These immunotherapies are based on a platform technology that utilizes live attenuated *Listeria monocytogenes* bioengineered to secrete antigen/adjuvant fusion proteins. These *Lm*-LLO strains are believed to be a significant advancement in immunotherapy as they integrate multiple functions into a single immunotherapy as they access and direct antigen presenting cells to stimulate anti-tumor T-cell immunity, stimulate and activate the immune system with the equivalent of multiple adjuvants, and simultaneously reduce tumor protection in the tumor microenvironment to enable the T-cells to eliminate tumors.

Axalimogene filolisbac Franchise

Axalimogene filolisbac is an *Lm*-LLO immunotherapy directed against HPV and designed to target cells expressing the HPV. It is currently under investigation or planned investigation in four HPV-associated cancers: cervical cancer, head and neck cancer, anal cancer, and lung cancer, either as a monotherapy or in combination.

Cervical Cancer

There are 527,624 new cases of cervical cancer caused by HPV worldwide every year, and 14,377 new cases in the U.S. alone, according to the WHO Human Papillomavirus and Related Cancers in the World Summary Report 2014 ("WHO"). Current preventative vaccines cannot protect the 20 million women who are already infected with HPV. Challenges with acceptance, accessibility, and compliance have resulted in approximately a third of young women being vaccinated in the United States and even less in other countries around the world.

We completed a randomized Phase 2 clinical study (*Lm*-LLO-E7-15), conducted exclusively in India, in 110 women with recurrent/refractory cervical cancer. The final results were presented at the 2014 American Society of Clinical Oncology ("ASCO") Annual Meeting, and showed that 32% (35/109) of patients were alive at 12 months, 22% (24/109) of patients were Long-term Survivors ("LTS") alive greater than 18 months, and 18% (16/91) evaluable with adequate follow-up) of patients were alive for more than 24 months. Of the 109 patients treated in the study, LTS included not only patients with tumor shrinkage but also patients who had experienced stable disease or increased tumor burden. 17% (19/109) of the patients in the trial had recurrence of disease after at least two prior treatments for their cervical cancer; these patients comprised 8% (2/24) of LTS. Among the LTS, 25% (3/12) of patients had a baseline ECOG performance status of 2, a patient population that is often times excluded from clinical trials. Furthermore, a 10% objective response rate (including 5 complete responses and 6 partial responses) and a disease control rate of 38% (42/109) were observed. The addition of cisplatin chemotherapy to axalimogene filolisbac in this study did not significantly improve overall survival or objective tumor response (p =0.9981).

In this study, 109 patients received 254 doses of axalimogene filolisbac. Axalimogene filolisbac was found to be well tolerated with 38% (41/109) of patients experiencing mild to moderate Grade 1 or 2 transient adverse events associated with infusion; 1 patient experienced a Grade 3 Serious Adverse Events ("SAE"). All observed treatment related adverse events either self-resolved or responded readily to symptomatic treatment.

The GOG (now a member of NRG Oncology), under the sponsorship of the Cancer Therapy Evaluation Program ("CTEP") of the National Cancer Institute ("NCI"), is independently conducting GOG-0265, an open-label, single arm Phase 2 study of axalimogene filolisbac in persistent or recurrent cervical cancer (patients must have received at least 1 prior chemotherapy regimen for the treatment of their recurrent/metastatic disease, not including that administered as a component of primary treatment) at 21 clinical sites in the U.S. The first stage of enrollment in GOG-0265 has successfully been completed with 26 patients treated and has met the predetermined safety and efficacy criteria required to proceed into the second stage of patient enrollment. Clinical data from the first stage of GOG-0265 was presented at the American Gynecological & Obstetrical Society ("AGOS") annual meeting on September 17, 2015. Overall survival at 12 months was 38.5% (10/26) (the predefined criteria for 12-month survival was ≥20%), and, among patients who had received the full treatment regimen of 3 doses of axalimogene filolisbac, the 12-month survival rate was 55.6% (10/18). The adverse events observed in the first stage of the study have been consistent with those reported in other clinical studies with axalimogene filolisbac. It was well-tolerated, with Grade 1-2 fatigue, chills, and fever the most commonly reported Adverse Events ("AE"); six patients experienced a treatment-related Grade 3 or Grade 4 AE, which was considered possibly-related to axalimogene filolisbac. The second stage of the study will include approximately 37 additional patients; it has been amended to permit only one prior chemotherapy regimen for the treatment of recurrent/metastatic disease and allows patients to continue to receive repeat cycles of therapy until disease progression.

We have completed an End-of-Phase 2 ("EOP2") meeting with the FDA. The purpose of the EOP2 meeting was to discuss axalimogene filolisbac preclinical data, Chemistry, Manufacturing and Controls ("CMC"), and clinical program, prior to moving axalimogene filolisbac forward into a registrational trial in cervical cancer. At the meeting, the FDA provided guidance on our CMC activities and clinical development plan. We have submitted our Phase 3 protocol for a Special Protocol Assessment ("SPA") request to the FDA. The SPA request included specific questions from Advaxis to facilitate a meaningful dialogue with the FDA on the proposed study design. We have received back from FDA initial comments and considerations for incorporation into our study design. Additional rounds of review and/or a formal meeting are anticipated, both of which can extend the review period and be beneficial in reaching agreement with the FDA on design elements. Based on the FDA's feedback, we may reach final agreement with FDA or may decide to incorporate the advice into the design of the Phase 3 clinical study without undergoing additional rounds of review. FDA's assessment of the SPA request, and all related feedback, will be very valuable in the development of axalimogene filolisbac. Contingent upon the outcome of the forgoing, we plan to initiate, in collaboration with the GOG/NRG Foundation, Inc., an independent international non-profit organization with the purpose of promoting excellence in the quality and integrity of clinical and basic scientific research in the field of gynecologic malignancies, a registrational clinical trial in cervical cancer in 2016 to support a Biologics License Application ("BLA") submission in the U.S. and in other territories around the world.

The planned registrational clinical trial will be a Phase 3 study of adjuvant axalimogene filolisbac, following primary treatment with chemoradiation, in patients with high-risk locally advanced cervical cancer compared to placebo alone. This population has a high recurrence rate and, once the disease has recurred, there are currently no available treatments. This study will evaluate both the time it takes for the cancer to recur as well as the overall survival. Our goal is to develop a treatment to prevent or reduce the risk of recurrence of cervical cancer after primary treatment interventions.

Biocon Limited ("Biocon"), our co-development and commercialization partner for axalimogene filolisbac in India and key emerging markets, filed a Marketing Authorization Application ("MAA") for licensure of this immunotherapy in India. The Drug Controller General of India ("DCGI") accepted this MAA for review. The filing of the MAA was driven by several factors: i) results from the *Lm* -LLO-E7-15 Phase 2 trial indicated that axalimogene filolisbac was well tolerated and showed significant clinical activity in recurrent/refractory cervical cancer; ii) cervical cancer is the second most common cancer among Indian women (according to WHO, there are 122,844 new cases per year with 67,544 deaths reported); and iii) current treatment options for non-operable refractory/recurrent disease are limited in India. As part of the MAA review process, Biocon met with the Scientific Expert Committee (the "Committee"). The Committee indicated that proof of concept for this novel immunotherapy has been established. The Committee advised Biocon to obtain data from a Phase 3 clinical trial in patients with recurrent cervical cancer who have failed prior chemo and radiation therapy. The face-to-face interaction with the Committee provided Biocon and Advaxis with valuable insight for future development and the companies are evaluating next steps.

We are conducting a Phase 1/2 trial evaluating higher doses and repeat cycles of axalimogene filolisbac in patients with recurrent cervical cancer. This Phase 1/2 study is designed to evaluate the safety, efficacy and immunological effect of the highest-tolerated dose of axalimogene filolisbac administered in repeat cycles to patients with cervical cancer whose disease has recurred after receiving one prior systemic dose cytotoxic treatment regimen. At present, a total of 27 cycles of therapy have been delivered at the 5 x 10^9 CFU dose level and 5 cycles at the high dose of 1 x 10^{10} CFU, which will now constitute the randomized Phase 2 dose. The AEs observed at the high dose are consistent with previous clinical experience with axalimogene filolisbac.

We have entered into a clinical trial collaboration agreement with MedImmune, the global biologics research and development arm of AstraZeneca, and are conducting a Phase 1/2, open-label, multicenter, two-part study to evaluate the safety and immunogenicity of our investigational *Lm*-LLO cancer immunotherapy, axalimogene filolisbac, in combination with MedImmune's investigational anti-PD-L1 immune checkpoint inhibitor, durvalumab, as a combination treatment for patients with metastatic squamous or non-squamous carcinoma of the cervix and metastatic HPV-associated Squamous Cell Carcinoma of the Head and Neck ("SCCHN"). For the axalimogene filolisbac and durvalumab dose escalation portion of the study, Cohort 1 has been completed allowing for advancement to the next dose level. Once the dose escalation has been completed, the recommended combination doses will be advanced further into the study.

We have entered into a clinical trial collaboration agreement with Incyte where we plan to conduct a Phase 2, open-label, multicenter study to evaluate the safety and immunogenicity of axalimogene filolisbac as a monotherapy and in combination with Incyte's investigational oral indoleamine 2,3-dioxygenase 1 (IDO1) inhibitor, epacadostat (INCB24360), in patients with Stage I-IIa cervical cancer. Incyte plans to enroll patients in this Phase 2 trial in 2016.

Axalimogene filolisbac has received FDA orphan drug designation for invasive Stage II-IV cervical cancer. (Axalimogene filolisbac was not granted orphan drug designation for cervical cancer in the EMA).

Head and Neck Cancer

SCCHN is the most frequently occurring malignant tumor of the head and neck and is a major cause of morbidity and mortality worldwide. More than 90% of SCCHNs originate from the mucosal linings of the oral cavity, pharynx, or larynx and 60-80% of these cancers are caused by HPV. According to the American Cancer Society, head and neck cancer accounts for about 3% to 5% of all cancers in the United States with an increasing incidence of HPV-associated head and neck cancers. Approximately 12,000 new cases will be diagnosed in the United Stated in 2016 according to the Surveillance, Epidemiology, and End Results ("SEER") database.

The safety and immunogenicity of axalimogene filolisbac is being evaluated in a Phase 2 study under an investigator-sponsored IND at Mount Sinai, in patients with HPV-positive head and neck cancer. This clinical trial is the first study to evaluate the effects of axalimogene filolisbac in patients when they are initially diagnosed with HPV-associated head and neck cancer.

As stated above, we have entered into a clinical trial collaboration agreement with MedImmune to collaborate on a Phase 1/2, open-label, multicenter, two part study to evaluate safety and immunogenicity of durvalumab (MEDI4736) in combination with axalimogene filolisbac as a combination treatment for patients with metastatic squamous or non-squamous carcinoma of the cervix and metastatic HPV-associated SCCHN.

Axalimogene filolisbac has received FDA orphan drug designation for HPV-associated head and neck cancer.

Anal Cancer

According to the American Cancer Society, nearly all squamous cell anal cancers are linked to infection by HPV, the same virus that causes cervical cancer. According to the SEER database, approximately 7,500 new cases will be diagnosed in the United States in 2016.

The safety and efficacy of axalimogene filolisbac is being evaluated in a Phase 2 study under an investigator-sponsored IND by Brown University in patients with high-risk locally advanced anal cancer. Preliminary data indicates all patients who have completed the treatment regimen have experienced a six-month complete response, with no disease recurrence. In consideration of these preliminary data, the investigator at Brown University is evaluating the opportunity to transition this study into a NCI-funded cooperative group trial to evaluate the safety and efficacy of axalimogene filolisbac in a pivotal Phase 2/3 anal cancer trial, to be conducted by NRG Oncology. In advance of the foregoing, we have entered into a clinical trial collaboration agreement with the Radiation Therapy Oncology Group ("RTOG") Foundation for the conduct of such study.

We plan to enroll patients in a Company sponsored Phase 2 study in patients with persistent/recurrent, loco-regional or metastatic squamous cell carcinoma of the anorectal canal in 2016.

Axalimogene filolisbac has received FDA and EMA orphan drug designation for anal cancer.

Lung Cancer

Lung cancer is the leading cause of cancer death in Taiwan, China, and worldwide. Histologically, Non-Small Cell Lung Cancer ("NSCLC"), including squamous cell carcinoma, adenocarcinoma, and large cell carcinoma, comprises more than 80% of lung cancers. Cigarette smoking is the primary risk factor and accounts for approximately 85% of all lung cancer cases. For those who have never smoked, HPV infection is considered to be an important cause of lung cancer in Asia. In a recent international pooled analysis of data on HPV-associated lung cancers, the prevalence in Asia was found to be 5% of all lung cancers.

GBP, our development and commercialization partner in Asia, is planning to conduct a randomized Phase 2, open-label, controlled study in HPV-associated NSCLC in patients following first-line induction chemotherapy. Pending Taiwanese FDA approval, the study is planned to initiate in 2016 and will enroll up to 124 patients. This trial will be fully funded exclusively by GBP.

ADXS-PSA Franchise

Prostate Cancer

According to the American Cancer Society, prostate cancer is the second most common type of cancer found in American men. Prostate cancer is the second leading cause of cancer death in men, behind only lung cancer. One man in seven will get prostate cancer during his lifetime, and one man in 36 will die of this disease. About 210,000 new cases will be diagnosed in the United States in 2016 according to the SEER database.

ADXS-PSA is an *Lm*-LLO immunotherapy designed to target the PSA antigen commonly overexpressed in prostate cancer.

We have 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® (pembrolizumab), Merck's anti PD-1 antibody, in a Phase 1/2, open-label, multicenter, two part study in patients with previously treated metastatic, castration-resistant prostate cancer. For ADXS-PSA monotherapy dose escalation portion of the study, Cohort 1 and Cohort 2 have been completed allowing for advancement into Cohort 3, the third and final dose level. Once the dose escalation has been completed, the recommended dose will be advanced into the combination portion of the study.

ADXS-HER2 Franchise

HER2 Expressing Solid Tumors

HER2 is overexpressed in a percentage of solid tumors such as breast, gastric, bladder, brain, pancreatic, ovarian and osteosarcoma. According to the SEER database and recent published literature, the percentage of HER2 expression varies by cancer type, with approximately 70,000 new cases of invasive HER2 positive breast cancer diagnosed each year in the US; approximately 5,000 new cases of HER2 positive gastric cancer; approximately 22,000 new cases of HER2 positive bladder cancer; approximately 20,000 new cases of HER2 positive pancreatic cancer; approximately 2,500 new cases of HER2 positive ovarian cancer; and approximately 600 new cases of HER2 positive osteosarcoma.

ADXS-HER2 is an *Lm*-LLO immunotherapy designed to target HER2 expressing solid tumors such as human and canine osteosarcoma, breast, gastric and other cancers. The FDA has cleared our IND application and we have

initiated a Phase 1b study in patients with metastatic HER2-expressing cancers. Thereafter, we intend to initiate a clinical development program with ADXS-HER2 for the treatment of pediatric osteosarcoma.

Osteosarcoma

Osteosarcoma affects about 400 children and teens in the U.S. every year, representing a small but significant unmet medical need that has seen little therapeutic improvement in decades. Osteosarcoma is considered a rare disease and may qualify for regulatory incentives including, but not limited to, orphan drug designation, patent term extension, market exclusivity, and development grants. Given the limited availability of new treatment options for osteosarcoma, and that it is an unmet medical need affecting a very small number of patients in the U.S. annually, we believe that, subject to regulatory approval, the potential to be on the market may be accelerated.

Based on encouraging data discussed below from a veterinarian clinical study in which pet dogs with naturally occurring osteosarcoma were treated with ADXS-HER2, we intend to initiate a clinical development program with ADXS-HER2 for the treatment of human osteosarcoma. Both veterinary and human osteosarcoma specialists consider canine osteosarcoma to be the best model for human osteosarcoma.

ADXS-HER2 has received FDA and EMA orphan drug designation for osteosarcoma.

Canine Osteosarcoma

Osteosarcoma is the most common primary bone tumor in dogs, accounting for roughly 85% of tumors on the canine skeleton. Approximately 10,000 dogs a year (predominately middle to older-aged dogs and larger breeds) are diagnosed with osteosarcoma in the United States. This cancer initially presents as lameness and oftentimes visible swelling on the leg. Current standard of care treatment is amputation immediately after diagnosis, followed by chemotherapy. Median survival time with standard of care is ten to twelve months. For dogs that cannot undergo amputation, palliative radiation and analgesics are frequently employed and median survival times range from three to five months.

Under the direction of Dr. Nicola Mason, the University of Pennsylvania School of Veterinary Medicine is conducting studies in companion dogs evaluating the safety and efficacy of ADXS-HER2 in the treatment of naturally occurring canine osteosarcoma. In the initial study, the primary endpoint was to determine the maximum tolerated dose of ADXS-HER2. Secondary endpoints for the study were progression-free survival and overall survival. The findings of the Phase 1 clinical trial in dogs with osteosarcoma suggest that ADXS-HER2 is safe and well tolerated at doses up to 3×10^9 CFU with no evidence of significant cardiac, hematological, or other systemic toxicities. The study determined that ADXS-HER2 is able to delay or prevent metastatic disease and significantly prolong overall survival in dogs with osteosarcoma that had minimal residual disease following standard of care (amputation and follow-up chemotherapy). Dr. Mason presented data at the 2014 American College of Veterinary Internal Medicine ("ACVIM") Forum which showed that 80% of the dogs treated (n=15) were still alive and median survival had not yet been reached. A second study is currently being conducted by Dr. Mason and data was presented at the 2015 ACVIM Forum obtained from pet dogs (n=12) with primary osteosarcoma unsuitable for amputation. Repeat doses of ADXS-HER2 administered after palliative radiation were well tolerated with no systemic or cardiac toxicity.

On March 19, 2014, we entered into a definitive Exclusive License Agreement with 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 has been filed by Aratana for ADXS-HER2 (also known as AT-014 by Aratana) for the treatment of canine osteosarcoma with the USDA. Aratana received communication from the USDA in March 2015 stating that the previously submitted efficacy data for product licensure for AT-014 (ADXS-HER2), the cancer immunotherapy for canine osteosarcoma, was accepted and that it provides a reasonable expectation of efficacy that supports conditional licensure. While additional steps need to be completed, including in the areas of manufacturing and safety, Aratana anticipates that AT-014 could receive conditional licensure from the USDA in 2016. Aratana has been granted exclusive worldwide rights by us to develop and commercialize ADXS-HER2 in animals. Aratana is further responsible for the conduct of clinical research with ADXS-Survivin in canine/feline lymphoma, as well as pending investigations of two additional Advaxis constructs in animals.

ADXS-NEO Franchise (preclinical)

We intend to file an IND application for ADXS-NEO and to initiate Company-sponsored studies, as well as external collaborations.

We have entered into a research collaboration with Memorial Sloan Kettering Cancer Center ("MSK") to advance the study of neoepitope-based, personalized cancer therapy. The goal of the collaboration, titled "MINE™" (My Immunotherapy Neo-Epitopes), is to use our *Lm*-LLO cancer immunotherapy technology to develop neo-epitope immunotherapies based on an individual patient's tumor ("ADXS-NEO"). MINE™ will first focus on a preclinical study of our new construct approach to evaluate the immunologic effects and anti-tumor activity of a personalized immunotherapy in a mouse tumor model. We will use learnings from the MINE™ collaboration to identify and target neoepitopes using *Lm*-LLO technology and later develop patient specific immunotherapy constructs that incorporate

the neoepitope sequences identified in the patient's tumor cells. Clinical studies using ADXS-NEO, to be conducted at MSK, are in development.

ADXS-TNBC Franchise (preclinical)

We are developing a construct that targets antigens specific to Triple-Negative Breast Cancer ("TNBC"), which accounts for ~15-20% of all diagnosed breast cancer cases and has not been amenable to targeted therapies directed toward estrogen, progesterone, or HER2 receptors. A majority of TNBC patients' still exhibit poor outcomes, with only 30-45% of patients achieving a pathological complete response from conventional chemotherapeutic and radiation therapy. The heterogeneous nature of this cancer type, the presence of mutations in multiple pathways, and the development of resistance to single agents make combination therapy much more attractive and suggest the need for agents that address more than one antigen/target.

Lm-LLO Combination Franchise

Axalimogene filolisbac and Durvalumab

As stated above, we have entered into a clinical trial collaboration agreement with MedImmune to conduct a Phase 1/2, open-label, multicenter, two part study to evaluate safety and immunogenicity of our investigational *Lm*-LLO cancer immunotherapy, axalimogene filolisbac, in combination with MedImmune's investigational anti-PD-L1 immune checkpoint inhibitor, durvalumab (MEDI4736) for the treatment of patients with metastatic squamous or non-squamous carcinoma of the cervix and metastatic HPV-associated SCCHN. Preliminary patient responses have been observed in Cohort 1. For the axalimogene filolisbac and durvalumab (MEDI4736) dose escalation portion of the study, Cohort 1 has been completed allowing for advancement to the next dose level. Once the dose escalation has been completed, the recommended combination doses will be advanced further into the study.

Axalimogene filolisbac and Epacadostat

As stated above, we have entered into a clinical trial collaboration agreement with Incyte where we plan to collaborate on a Phase 2, open-label, multicenter, preoperative window-study to evaluate the safety and immunogenicity of axalimogene filolisbac as a monotherapy and in combination with Incyte's investigational oral indoleamine 2,3-dioxygenase 1 (IDO1) inhibitor, epacadostat (INCB24360), in patients with Stage I-IIa cervical cancer. Incyte plans to enroll patients in this Phase 2 in 2016.

ADXS-PSA and KEYTRUDA® (pembrolizumab)

As stated above, we have entered into a clinical trial collaboration agreement with Merck to evaluate the safety and efficacy of ADXS-PSA as monotherapy and in combination with KEYTRUDA® (pembrolizumab), Merck's anti PD-1 antibody, in a Phase 1/2, open-label, multicenter, two part study in patients with previously treated metastatic, castration-resistant prostate cancer. For the ADXS-PSA monotherapy dose escalation portion of the study, Cohort 1 and Cohort 2 have been completed allowing for advancement to next dose level. Once the dose escalation has been completed, the recommended dose will be advanced into the combination portion of the study.

Lm-LLO Immunotherapy and Sorrento

We have entered into a non-exclusive research and clinical trial collaboration agreement with Sorrento Therapeutics, Inc. ("Sorrento") to evaluate our *Lm*-LLO cancer immunotherapy technology in combination with Sorrento's fully human antibodies, which may include GITR, OX40, LAG-3 and/or TIM-3, in two clinical trials.

Lm-LLO Immunotherapy (preclinical)

We have various preclinical collaborations with academic and other centers of excellence.

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 Advaxis, Inc., 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 Advaxis, the stockholders of Advaxis and us. As a result of the Share Exchange, Advaxis 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 Advaxis, Inc. 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.

Our principal executive offices are located at 305 College Road East, Princeton, New Jersey 08540 and our telephone number is (609) 452-9813. We maintain a website at www.advaxis.com which contains descriptions of our technology, our product candidates and the trial 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. You may read and copy any materials we file at the SEC's Public Reference Room at 100 F Street, N.E., Washington, D.C. 20549 on official business days during the hours of 10:00 a.m. to 3:00 p.m. Please call the SEC at 1-800-SEC-0330 for information on the Public Reference Room. Additionally, 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 and extensive patent portfolio that protects our product candidates and Lm -based immunotherapy technology. Currently, we own or have rights to 200 patents and applications, which are owned, licensed from, or co-owned with Penn, Merck, NIH, and/or Georgia Regents University. We continuously grow this portfolio by filing new applications to protect our ongoing research and development efforts. We aggressively prosecute and defend our patents and proprietary technology. Our patents

are directed to the compositions of matter, use, and methods thereof, of our Lm -LLO immunotherapies for our product candidates, axalimogene filolisbac, ADXS-PSA, and ADXS-HER2.

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.

We successfully defended our intellectual property concerning our Lm -based technology by contesting a challenge made by Anza Therapeutics, Inc. (now known as Aduro BioTech), to our patent position in Europe on a claim not available in the United States. The European Patent Office ("EPO") Board of Appeals in Munich, Germany ruled in favor of the Trustees of Penn and us, Penn's exclusive licensee, and reversed a patent ruling that revoked a technology patent that had resulted from an opposition filed by Anza. The ruling of the EPO Board of Appeals is final and cannot be appealed. The granted claims, the subject matter of which was discovered by Dr. Yvonne Paterson, are directed to the method of preparation and composition of matter of recombinant bacteria expressing tumor antigens for the treatment of patients with cancer. The successful development of our immunotherapies will include our ability to create and maintain intellectual property related to our product candidates.

Issued patents which are directed to our product candidates axalimogene filolisbac, ADXS-PSA, and ADVX-HER2 in the United States, will expire between 2017 and 2032. Issued patents directed to our product candidates axalimogene filolisbac, ADXS-PSA, and ADXS-HER2 outside of the United States, will expire in 2028. Issued patents directed to our Lm -based immunotherapy platform in the United States, will expire between 2016 and 2030. Issued patents directed to our Lm -based immunotherapy platform outside of the United States, will expire between 2021 and 2030.

We have issued patents directed to methods of using our product candidates axalimogene filolisbac, ADXS-PSA and ADXS-HER2 in the United States, which will expire between 2017 and 2032. Issued patents directed to use of our product candidates: axalimogene filolisbac, ADXS-PSA and ADXS-HER2 for indications outside of the United States, will expire between 2018 and 2028.