

April 5, 2016



# Advaxis Combination Trial with Merck Completes First Two Dose-Escalation Cohorts

*Study Evaluating ADXS-PSA Launches Third Dose-Escalation Cohort*



*Part B Combination with 51 Patients to Begin Mid-Year*

PRINCETON, N.J., April 05, 2016 (GLOBE NEWSWIRE) -- [Advaxis, Inc.](#) (NASDAQ:ADXS), a clinical-stage biotechnology company developing cancer immunotherapies, and Merck & Co., Inc. (NYSE:MRK), today announced that they have completed the first two dose-escalation cohorts and launched the third dose-escalation cohort in their KEYNOTE-046 clinical trial. The Phase 1/2 study is evaluating the combination of ADXS-PSA (ADXS31-142) and KEYTRUDA<sup>®</sup> (pembrolizumab), the first anti-PD-1 (programmed death receptor-1) therapy approved in the United States, in patients with previously treated, metastatic castration-resistant prostate cancer (mCRPC).

The KEYNOTE-046 trial is the first-in-human study of Advaxis' *Lm* immunotherapy candidate for prostate cancer. It is the second study initiated to evaluate the use of KEYTRUDA in the treatment of advanced prostate cancer.

"We are one step closer to evaluating our *Lm* platform in combination with a PD-1 antibody and are excited to launch this next cohort," said Daniel J. O'Connor, President and Chief Executive Officer at Advaxis. "We are thrilled to continue our collaboration with Merck in pursuit of finding a treatment option for a form of prostate cancer where few options exist."

KEYNOTE-046 is a multicenter, dose determining, open-label Phase 1/2 study designed to evaluate the safety and efficacy of ADXS-PSA as a monotherapy and in combination with KEYTRUDA in 51 mCRPC patients. Part A of the study is a dose escalating study designed to establish the maximum tolerated dose of ADXS-PSA as a monotherapy. Part B of the study will commence mid-year and evaluate ADXS-PSA in combination with KEYTRUDA, followed by an expansion cohort phase. The primary objective is to evaluate the safety and tolerability of the two immunotherapies, with the secondary objective to

evaluate anti-tumor activity and progression-free survival.

The companies plan to submit an abstract to a major medical meeting on the dose-escalation portion of the study in the second half of the year. Further information about KEYNOTE-046 can be found on [ClinicalTrials.gov](https://clinicaltrials.gov), using Identifier NCT02325557.

### **About Prostate Cancer**

Prostate cancer is the second most common form of cancer affecting men in the United States: an estimated one in seven will be diagnosed with prostate cancer in his lifetime. The American Cancer Society estimates that approximately 180,890 new cases of prostate cancer will be diagnosed and about 26,120 men are expected to die of the disease this year.

### **About ADXS-PSA**

ADXS-PSA is an *Lm* Technology™ product candidate that is a multi-function immunotherapy designed to target prostate cancer. ADXS-PSA combines potent innate immune stimulation, triggering of STING receptors, and induction of T-cell response targeting prostate specific antigen (PSA) with tumor microenvironment effects. In a preclinical analysis this approach also inhibits the Treg and myeloid-derived suppressor cells (MDSCs) that contribute to immunologic tolerance of prostate cancer. Preclinical studies have shown ADXS constructs to be synergistic with checkpoint inhibitors like Keytruda.

### **About KEYTRUDA® (pembrolizumab)**

KEYTRUDA (pembrolizumab) is a humanized monoclonal antibody that blocks the interaction between PD-1 (programmed death receptor-1) and its ligands, PD-L1 and PD-L2. By binding to the PD-1 receptor and blocking the interaction with the receptor ligands, KEYTRUDA releases the PD-1 pathway-mediated inhibition of the immune response, including the anti-tumor immune response.

KEYTRUDA is indicated in the United States at a dose of 2 mg/kg administered as an intravenous infusion over 30 minutes every three weeks for the treatment of patients with unresectable or metastatic melanoma and disease progression following ipilimumab and, if BRAF V600 mutation positive, a BRAF inhibitor. This indication is approved under accelerated approval based on tumor response rate and durability of response. An improvement in survival or disease-related symptoms has not yet been established. Continued approval for this indication may be contingent upon verification and description of clinical benefit in the confirmatory trials.

Merck is advancing a broad and fast-growing clinical development program for KEYTRUDA with more than 70 clinical trials – across more than 30 tumor types and over 8,000 patients – both as a monotherapy and in combination with other therapies.

### **Selected Important Safety Information for KEYTRUDA**

Pneumonitis occurred in 12 (2.9%) of 411 patients with advanced melanoma receiving

KEYTRUDA (the approved indication in the United States), including Grade 2 or 3 cases in 8 (1.9%) and 1 (0.2%) patients, respectively. Monitor patients for signs and symptoms of pneumonitis. Evaluate suspected pneumonitis with radiographic imaging. Administer corticosteroids for Grade 2 or greater pneumonitis. Withhold KEYTRUDA for Grade 2; permanently discontinue KEYTRUDA for Grade 3 or 4 pneumonitis.

Colitis (including microscopic colitis) occurred in 4 (1%) of 411 patients, including Grade 2 or 3 cases in 1 (0.2%) and 2 (0.5%) patients respectively, receiving KEYTRUDA. Monitor patients for signs and symptoms of colitis. Administer corticosteroids for Grade 2 or greater colitis. Withhold KEYTRUDA for Grade 2 or 3; permanently discontinue KEYTRUDA for Grade 4 colitis.

Hepatitis (including autoimmune hepatitis) occurred in 2 (0.5%) of 411 patients, including a Grade 4 case in 1 (0.2%) patient, receiving KEYTRUDA. Monitor patients for changes in liver function. Administer corticosteroids for Grade 2 or greater hepatitis and, based on severity of liver enzyme elevations, withhold or discontinue KEYTRUDA.

Hypophysitis occurred in 2 (0.5%) of 411 patients, including a Grade 2 case in 1 and a Grade 4 case in 1 (0.2% each) patient, receiving KEYTRUDA. Monitor for signs and symptoms of hypophysitis. Administer corticosteroids for Grade 2 or greater hypophysitis. Withhold KEYTRUDA for Grade 2; withhold or discontinue for Grade 3; and permanently discontinue KEYTRUDA for Grade 4 hypophysitis.

Nephritis occurred in 3 (0.7%) patients receiving KEYTRUDA, consisting of one case of Grade 2 autoimmune nephritis (0.2%) and two cases of interstitial nephritis with renal failure (0.5%), one Grade 3 and one Grade 4. Monitor patients for changes in renal function. Administer corticosteroids for Grade 2 or greater nephritis. Withhold KEYTRUDA for Grade 2; permanently discontinue KEYTRUDA for Grade 3 or 4 nephritis.

Hyperthyroidism occurred in 5 (1.2%) of 411 patients, including Grade 2 or 3 cases in 2 (0.5%) and 1 (0.2%) patients respectively, receiving KEYTRUDA. Hypothyroidism occurred in 34 (8.3%) of 411 patients, including a Grade 3 case in 1 (0.2%) patient, receiving KEYTRUDA. Thyroid disorders can occur at any time during treatment. Monitor patients for changes in thyroid function (at the start of treatment, periodically during treatment, and as indicated based on clinical evaluation) and for clinical signs and symptoms of thyroid disorders. Administer corticosteroids for Grade 3 or greater hyperthyroidism. Withhold KEYTRUDA for Grade 3; permanently discontinue KEYTRUDA for Grade 4 hyperthyroidism. Isolated hypothyroidism may be managed with replacement therapy without treatment interruption and without corticosteroids.

Other clinically important immune-mediated adverse reactions can occur. The following clinically significant, immune-mediated adverse reactions occurred in less than 1% of patients treated with KEYTRUDA: exfoliative dermatitis, uveitis, arthritis, myositis, pancreatitis, hemolytic anemia, partial seizures arising in a patient with inflammatory foci in brain parenchyma, adrenal insufficiency, myasthenic syndrome, optic neuritis, and rhabdomyolysis.

For suspected immune-mediated adverse reactions, ensure adequate evaluation to confirm etiology or exclude other causes. Based on the severity of the adverse reaction,

withhold KEYTRUDA and administer corticosteroids. Upon improvement of the adverse reaction to Grade 1 or less, initiate corticosteroid taper and continue to taper over at least 1 month. Restart KEYTRUDA if the adverse reaction remains at Grade 1 or less. Permanently discontinue KEYTRUDA for any severe or Grade 3 immune-mediated adverse reaction that recurs and for any life-threatening immune-mediated adverse reaction.

Based on its mechanism of action, KEYTRUDA may cause fetal harm when administered to a pregnant woman. If used during pregnancy, or if the patient becomes pregnant during treatment, apprise the patient of the potential hazard to a fetus. Advise females of reproductive potential to use highly effective contraception during treatment and for 4 months after the last dose of KEYTRUDA.

For the treatment of advanced melanoma, KEYTRUDA was discontinued for adverse reactions in 6% of 89 patients who received the recommended dose of 2 mg/kg and 9% of 411 patients across all doses studied. Serious adverse reactions occurred in 36% of patients receiving KEYTRUDA. The most frequent serious adverse drug reactions reported in 2% or more of patients were renal failure, dyspnea, pneumonia, and cellulitis.

The most common adverse reactions (reported in  $\geq 20\%$  of patients) were fatigue (47%), cough (30%), nausea (30%), pruritus (30%), rash (29%), decreased appetite (26%), constipation (21%), arthralgia (20%), and diarrhea (20%).

The recommended dose of KEYTRUDA is 2 mg/kg administered as an intravenous infusion over 30 minutes every three weeks until disease progression or unacceptable toxicity. No formal pharmacokinetic drug interaction studies have been conducted with KEYTRUDA. It is not known whether KEYTRUDA is excreted in human milk. Because many drugs are excreted in human milk, instruct women to discontinue nursing during treatment with KEYTRUDA. Safety and effectiveness of KEYTRUDA have not been established in pediatric patients.

Please see Prescribing Information for KEYTRUDA (pembrolizumab) at [http://www.merck.com/product/usa/pi\\_circulars/k/keytruda/keytruda\\_pi.pdf](http://www.merck.com/product/usa/pi_circulars/k/keytruda/keytruda_pi.pdf) and the Medication Guide for KEYTRUDA at [http://www.merck.com/product/usa/pi\\_circulars/k/keytruda/keytruda\\_mg.pdf](http://www.merck.com/product/usa/pi_circulars/k/keytruda/keytruda_mg.pdf).

### **About Advaxis, Inc.**

Located in Princeton, N.J., Advaxis, Inc. is a clinical-stage biotechnology company developing multiple cancer immunotherapies based on its proprietary *Lm* Technology™. The *Lm* Technology™, using bioengineered live attenuated *Listeria monocytogenes* (*Lm*) bacteria, is the only known cancer immunotherapy agent shown in preclinical studies to both generate cancer fighting T-cells directed against cancer antigens and neutralize Tregs and myeloid-derived suppressor cells (MDSCs) that protect the tumor microenvironment from immunologic attack and contribute to tumor growth. Advaxis' lead *Lm* Technology™ immunotherapy, axalimogene filolisbac, targets human papillomavirus (HPV)-associated cancers and is in clinical trials for three potential indications: Phase 2 in invasive cervical cancer, Phase 1/2 in head and neck cancer, and Phase 1/2 in anal cancer. The U.S. Food and Drug Administration (FDA) has granted axalimogene filolisbac

orphan drug designation for each of these three clinical settings. Advaxis has two additional immunotherapy products: ADXS-PSA in prostate cancer and ADXS-HER2 in HER2 expressing solid tumors, in human clinical development.

For additional information on Advaxis, visit [www.advaxis.com](http://www.advaxis.com) and connect on [Twitter](#), [LinkedIn](#), [Facebook](#), [YouTube](#) and [Google+](#).

## **Merck's Focus on Cancer**

Our goal is to translate breakthrough science into biomedical innovations to help people with cancer worldwide. For Merck Oncology, helping people fight cancer is our passion, supporting accessibility to our cancer medicines is our commitment, and pursuing research in immuno-oncology is our focus to potentially bring new hope to people with cancer. For more information about our oncology clinical trials, visit [www.merck.com/clinicaltrials](http://www.merck.com/clinicaltrials).

## **About Merck**

Today Merck is a global healthcare leader working to help the world be well. Merck is known as MSD outside the United States and Canada. Through our prescription medicines, vaccines, biologic therapies and animal health products, we work with customers and operate in more than 140 countries to deliver innovative health solutions. We also demonstrate our commitment to increasing access to healthcare through far-reaching policies, programs and partnerships. For more information, visit [www.merck.com](http://www.merck.com) and connect with us on [Twitter](#), [Facebook](#) and [YouTube](#).

## **Advaxis Forward-Looking Statement**

This media statement contains forward-looking statements, including, but not limited to: statements regarding Advaxis' ability to develop the next generation of cancer immunotherapies; and the safety and efficacy of Advaxis' proprietary immunotherapies. These forward-looking statements are subject to a number of risks, including the risk factors set forth from time to time in Advaxis' SEC filings, including but not limited to its report on Form 10-K for the fiscal year ended October 31, 2015, which is available at <http://www.sec.gov>. Advaxis undertakes no obligation to publicly release the result of any revision to these forward-looking statements, which may be made to reflect the events or circumstances after the date hereof or to reflect the occurrence of unanticipated events, except as required by law. You are cautioned not to place undue reliance on any forward-looking statements.

## **Merck Forward-Looking Statement**

This news release includes "forward-looking statements" within the meaning of the safe harbor provisions of the United States Private Securities Litigation Reform Act of 1995. These statements are based upon the current beliefs and expectations of Merck's management and are subject to significant risks and uncertainties. If underlying assumptions prove inaccurate or risks or uncertainties materialize, actual results may differ materially from those set forth in the forward-looking statements.

Risks and uncertainties include, but are not limited to, general industry conditions and competition; general economic factors, including interest rate and currency exchange rate fluctuations; the impact of pharmaceutical industry regulation and healthcare legislation in the United States and internationally; global trends toward healthcare cost containment; technological advances, new products and patents attained by competitors; challenges inherent in new product development, including obtaining regulatory approval; Merck's ability to accurately predict future market conditions; manufacturing difficulties or delays; financial instability of international economies and sovereign risk; dependence on the effectiveness of Merck's patents and other protections for innovative products; and the exposure to litigation, including patent litigation, and/or regulatory actions.

Merck undertakes no obligation to publicly update any forward-looking statement, whether as a result of new information, future events or otherwise. Additional factors that could cause results to differ materially from those described in the forward-looking statements can be found in Merck's 2014 Annual Report on Form 10-K and the company's other filings with the Securities and Exchange Commission (SEC) available at the SEC's Internet site ([www.sec.gov](http://www.sec.gov)).

KEYTRUDA® is a registered trademark of Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Whitehouse Station, N.J., USA.

**CONTACTS:**

**Company:**

[Advaxis, Inc.](http://Advaxis, Inc.)

Greg Mayes, Executive Vice President and COO

[mayes@advaxis.com](mailto:mayes@advaxis.com)

609.250.7515

**Media Contact:**

[JPA Health Communications](http://JPA Health Communications)

Sally Bain

[Sally@jpa.com](mailto:Sally@jpa.com)

617.945.5183

**ADVAXIS**  
IMMUNOTHERAPIES™

Source: Advaxis