Ayala Pharmaceuticals Announces Updated RINGSIDE Phase 2 Results at 2023 American Society of Clinical Oncology (ASCO) Annual Meeting

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ASCO abstract highlights 50% partial response and 100% disease control rates in evaluable desmoid tumor patients treated with AL102 1.2 mg once daily (the selected Phase 3 dose)

Tumor response, volume and T2 signal reduction were observed earlier in the 1.2 mg once daily group, with deeper and sustained treatment responses

Registration-enabling Phase 3 segment of RINGSIDE is enrolling patients globally.

REHOVOT, Israel and MONMOUTH JUNCTION, N.J., May 25, 2023 (GLOBE NEWSWIRE) -- Ayala Pharmaceuticals, Inc. (OTCQX: ADXS), a clinical-stage oncology company, today announced updated results from Phase 2 (Part A segment) of the RINGSIDE study evaluating AL102 in desmoid tumors. The results are summarized in an abstract published today for the 2023 American Society of Clinical Oncology (ASCO) Annual Meeting. More detailed results will be featured in a poster session at ASCO on Saturday, June 3. AL102 is a once-daily, potent, selective, oral gamma-secretase inhibitor (GSI).

“This latest data cut includes data from all 42 patients enrolled in the Phase 2 study portion of this trial and shows compelling evidence of anti-tumor activity for all tested dose regimens of AL102 across multiple measures, including RECIST-based response rate, disease control rate and reduction in tumor volume per blinded independent central review,” said Andres Gutierrez, MD, PhD, Executive Vice President & Chief Medical Officer of Ayala. “In addition, there appears to be a consistent pattern of deeper and faster responses in the 1.2 mg once-daily group, the selected Phase 3 dose, versus the biweekly regimen groups. We are also encouraged to see that AL102 continues to be generally well tolerated and has a manageable safety profile as seen in all three dose arms. There have been no new safety signals, and the safety results appear consistent with the GSI class. Overall, the data continuing to emerge from RINGSIDE support our belief that AL102 has the potential to become a valuable treatment option for people living with desmoid tumors as it may have important clinical advantages along with convenient once-daily dosing, which may improve treatment adherence and patient satisfaction.”

RINGSIDE Study Highlights

The ongoing Phase 2/3 RINGSIDE clinical trial is a randomized, global multi-center study evaluating AL102 in patients with progressing desmoid tumors. The study consists of two parts: Phase 2 (Part A) is an open-label, dose regimen finding study, and Phase 3 (Part B) is a double blind, placebo-controlled study and Open Label Extension utilizing the 1.2 mg once daily dose regimen selected based on data from Phase 2.

Enrollment of all 42 patients into Phase 2 was completed as of March 2022. Patients were randomized to one of three dose regimens of AL102 (n=14 each), including 1.2 mg once-daily (QD), 4 mg twice a week (BIW) or 2 mg BIW. As of January 3, 2023, median time on study was 10.3 months (range 0.8 – 14.7) and 30 patients were still on study,10 of whom rolled over to the open label extension.

Efficacy Results

- In the evaluable patient population, partial responses were observed in 50% of patients (i.e., 6 out of 12) in the 1.2 mg QD group, 23.1% of patients (3/13) in the 4 mg BIW group, and 45.5% of patients (5/11) in the 2 mg BIW group. Responses were assessed by blinded independent central review (BICR).
- In the intention-to-treat (ITT) population, partial responses were observed in 43% of patients (i.e., 6/14) in the 1.2 mg QD group, 21.4% of patients (3/14) in the 4 mg BIW group, and 36% (5/14) in the 2 mg BIW group. Responses were assessed by BICR.
- Median volume changes, assessed by BICR, from baseline to week 16 were -51.9% for 1.2 mg QD, -9.5% for 4 mg BIW, and -15.2% for 2 mg BIW.
- Median tumor volume changes from baseline to week 28 were -76.4%, -35.5%, and -51.2%, respectively, for the 1.2 mg QD, 4 mg BIW and 2 mg BIW dose groups.
- Similar patterns were observed for percentage changes from baseline in T2 signal intensity, suggesting reduction of cell density within the tumor.
- Disease control rates (partial response + stable disease) were 100%, 91%, and 97% in the evaluable patients in the 1.2mg QD, 4 mg BIW and 2 mg BIW dose groups, respectively.

Safety

- AL102 was generally well tolerated with a manageable safety profile across all dose arms. The safety profile was consistent with the GSI class of drugs.

- Regardless of dose regimen, adverse events (AEs) were predominantly Grade 1 (~70%) or Grade 2 (~20%). There were no Grade 4 or Grade 5 related AEs. Serious AEs were reported in 6 of 42 patients (14%) and assessed as unrelated to AL102 by investigators. There were no new safety signals.
- Discontinuation due to AEs occurred in 6 of 42 (14%) patients. These were due to Grade 2 rash, keratitis, stomatitis, diarrhea, ALT elevation. All occurred within 3 months of treatment initiation.
- Ovarian dysfunction was reported in 11 of 23 (48%) women of childbearing potential across all dose arms, but in only 3 of 9 (33%) women who received the 1.2 mg once-daily dose.

The registration-enabling Phase 3 segment is enrolling patients globally. For more information on RINGSIDE, please visit ClinicalTrials.gov and reference Identifier NCT04871282 (RINGSIDE).

Poster Presentation Details

The poster (abstract # 11515, Poster Bd # 449 in Hall A) will be available for viewing 1.15pm - 4:15pm CT Saturday, June 3, 2023. In addition to the presentation of the study in the poster hall, Elizabeth J. Davis, M.D. of Vanderbilt University Medical Center, will highlight and discuss this and other selected abstracts in the Poster Discussion Session S404 Primary track: Sarcoma, 4:30 pm CT on the same day. The focus of this session will be on how the findings apply to clinical practice and future research. Dr. Davis and the abstract presenters will answer questions during a moderated panel discussion.

A copy of the poster will be available on the Ayala corporate website, under Events & Presentations, following the presentation at ASCO.

About Desmoid Tumors

Desmoid tumors, also called aggressive fibromatosis or desmoid-type fibromatosis, are rare connective tissue tumors that typically arise in the upper and lower extremities, abdominal wall, head and neck area, mesenteric root, and chest wall, or other parts of the body. Desmoid tumors do not metastasize, but often aggressively infiltrate neurovascular structures and vital organs. People living with desmoid tumors are often limited in their daily life due to chronic pain, functional deficits, general decrease in their quality of life and organ dysfunction. Desmoid tumors have an annual incidence of approximately 1,700 patients in the United States and typically occur in patients between the ages of 15 and 60 years. They are most commonly diagnosed in young adults between 30-40 years of age and are more prevalent in females. Today, surgery is no longer regarded as the cornerstone treatment of desmoid tumors due to surgical morbidity and a high rate of recurrence post-surgery. There are currently no FDA-approved systemic therapies for the treatment of unresectable, recurrent or progressive desmoid tumors.

About AL102

AL102 is an investigational small molecule gamma secretase inhibitor (GSI) that is designed to potently and selectively inhibit Notch 1, 2, 3 and 4, and is currently being evaluated in the Phase 2/3 RINGSIDE clinical studies in patients with progressing desmoid tumors. AL102 is designed to inhibit the expression of Notch gene targets by blocking the final cleavage step by the gamma secretase required for Notch activation. Ayala obtained an exclusive, worldwide license to develop and commercialize AL102 from Bristol-Myers Squibb Company in November 2017. AL102 was granted U.S. FDA Fast Track Designation for the treatment of DT.

About Ayala Pharmaceuticals, Inc.

Ayala Pharmaceuticals, Inc. is a clinical-stage oncology company primarily focused on developing and commercializing small molecule therapeutics for people living with rare tumors and aggressive cancers and is also developing proprietary *Lm*-based antigen delivery products for patients suffering from more common cancers. The Company's lead candidates under development are the oral gamma secretase inhibitor, AL102, for desmoid tumors; ADXS-504, a *Lm*-based therapy for early-stage prostate cancer; and the intravenous gamma secretase inhibitor, AL101, for adenoid cystic carcinoma. AL102 has received Fast Track Designation from the U.S. FDA and is currently in the Phase 3 segment of a pivotal study for patients with desmoid tumors (RINGSIDE). For more information, visit www.ayalapharma.com.

Contacts:

Ayala Pharmaceuticals:
+1-857-444-0553
info@ayalapharma.com

Media:

Tim McCarthy
LifeSci Advisors, LLC
tim@lifesciadvisors.com
917-679-9282

Cautionary Statement Regarding Forward-Looking Statements

Certain statements contained in this filing may be considered forward-looking statements within the meaning of the U.S. Private Securities Litigation Reform Act of 1995, including statements regarding the future conduct of our studies and the potential efficacy and success of product candidates. Forward-looking statements generally include statements that are predictive in nature and depend upon or refer to future events or conditions, and include words such as "may," "will," "should," "would," "expect," "anticipate," "plan," "likely," "believe," "estimate," "project," "intend," and other similar expressions among others. Statements that are not historical facts are forward-looking statements. Forward-looking statements are based on current beliefs and assumptions that are subject to risks and uncertainties and are not guarantees of future performance. Actual results could differ materially from those contained in any forward-looking statement as a result of various factors, including, without limitation: the success and timing of our clinical trials, including subject accrual; our ability to avoid and quickly resolve any clinical holds; our ability to obtain and maintain regulatory approval and/or reimbursement of our product candidates for marketing; our ability to obtain the appropriate labeling of our products under any regulatory approval; our

plans to develop and commercialize our products; the successful development and implementation of our sales and marketing campaigns; the size and growth of the potential markets for our product candidates and our ability to serve those markets; our ability to successfully compete in the potential markets for our product candidates, if commercialized; regulatory developments in the United States and other countries; the rate and degree of market acceptance of any of our product candidates; new products, product candidates or new uses for existing products or technologies introduced or announced by our competitors and the timing of these introductions or announcements; market conditions in the pharmaceutical and biotechnology sectors; our available cash, including to support current and planned clinical activities; uncertainties as to our ability to obtain a listing of our common stock on Nasdaq; our ability to integrate our various business areas successfully and to achieve anticipated synergies following our recent merger and the possibility that other anticipated benefits of the transaction will not be realized; potential litigation relating to the transaction; the accuracy of our estimates regarding expenses, future revenues, capital requirements and needs for additional financing; our ability to obtain additional funding; our ability to obtain and maintain intellectual property protection for our product candidates; the success and timing of our preclinical studies including IND-enabling studies; the timing of our IND submissions; our ability to get FDA approval for study amendments; the timing of data read-outs; the ability of our product candidates to successfully perform in clinical trials; our ability to initiate, enroll, and execute pilots and clinical trials; our ability to maintain our existing collaborations; our ability to manufacture and the performance of third-party manufacturers; the performance of our clinical research organizations, clinical trial sponsors and clinical trial investigators; our ability to successfully implement our strategy; and such other factors as are set forth in our periodic public filings with the SEC, including but not limited to those described under the heading “Risk Factors” in the Form 10-K for the fiscal year ended December 31, 2021 of Old Ayala, Inc. (f/k/a Ayala Pharmaceuticals, Inc.) and the Form 10-K for the fiscal year ended October 31, 2022 of Ayala Pharmaceuticals, Inc. (f/k/a Advaxis, Inc.) (“Ayala” or “we,” “us” or “our”), and such entities’ periodic public filings with the SEC, including but not limited to those described under the heading “Risk Factors” in Ayala’s Form 10-K for the fiscal year ended October 31, 2022. Except as required by applicable law, we undertake no obligation to revise or update any forward-looking statement, or to make any other forward-looking statements, whether as a result of new information, future events or otherwise.