Ayala Pharmaceuticals Presents Updated AL102 Results from Phase 2 Clinical Trial in Desmoid Tumors at ESMO Congress 2023

October 23, 2023

AL102 1.2 mg once daily treatment achieved Overall Response Rate of 83% in the evaluable population

AL102 1.2 mg once daily treatment resulted in 88% reduction in tumor volume and 85% reduction in T2W signal intensity

REHOVOT, Israel and MONMOUTH JUNCTION, N.J., Oct. 23, 2023 (GLOBE NEWSWIRE) -- Ayala Pharmaceuticals, Inc. (OTCQX: ADXS), a clinical-stage oncology company, today announced that new data from the RINGSIDE study evaluating its lead investigational candidate AL102 for the treatment of desmoid tumors (DT) are being presented today at the European Society for Molecular Oncology (ESMO) Congress 2023, taking place October 20th to 24th in Madrid, Spain. The data are from Phase 2 (Part A) of the study and from the Open Label Extension (OLE). The results are featured in a poster being presented by Professor Robin Jones, Team Leader in Sarcoma Clinical Trials at The Institute of Cancer Research and Consultant Medical Oncologist at The Royal Marsden, UK.

“The RINGSIDE results continue to improve over time, with more patients in this latest Phase 2 and OLE data cut demonstrating responses to treatment with AL102,” said Kenneth Berlin, President and CEO of Ayala. “We are seeing impressive anti-tumor activity across multiple parameters and are particularly encouraged by the high response rates, including 83% in the 1.2 mg once daily arm, the dose being used in our Phase 3 study, and 64% across all three doses combined. Furthermore, in two other important efficacy parameters, patients receiving 1.2 mg daily dose experienced an 88% reduction in tumor volume and 85% reduction in T2W signal intensity in median best change from baseline. We are pleased to note that 29 of the 42 patients who participated in Phase 2 of RINGSIDE entered the OLE and that we are seeing new responses in some of the patients who were receiving dosing twice a week and are now receiving 1.2 mg once daily. The Phase 3 registration segment (Part B) of RINGSIDE continues to enroll patients globally at a good pace with greater than 70% of the 154 patients we aim to enroll already dosed. These latest results from Phase 2 and OLE reinforce our belief that AL102 has the potential to be a best-in-class gamma secretase inhibitor and may offer a promising new treatment option to patients with unresectable, recurrent or progressive desmoid tumors.”

Professor Robin Jones commented, “The outlook for patients with desmoid tumors appears to be improving, with one gamma secretase inhibitor already in registration with FDA, as an important new class of agents. These latest results on AL102 are unprecedented, showing meaningful clinical benefits across three key efficacy measures in a large proportion of treated patients as well as a manageable safety profile.”

Andres Gutierrez MD PhD., Executive VP and Chief Medical Officer of Ayala, added, “The data from the Phase 2 segment of RINGSIDE continue to show efficacy across all dose cohorts with the earliest and deepest responses observed in the 1.2 mg once daily arm, the dose being evaluated in the ongoing Phase 3 segment. The large reductions in T2 signal intensity, as measured by MRI, are noteworthy as they have been correlated with loss of tumor cellularity and symptom control in patients undergoing treatment for DT. AL102 continues to be generally well tolerated and has a manageable safety profile as seen in all three dose arms. The safety results appear consistent with the GSI class.”

RINGSIDE Study Phase 2 and OLE 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. Patients in Phase 2 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. Patients in the intermittent dosing arms were allowed to rollover to the Open Label Extension to receive 1.2 mg once daily after evaluations were completed in the Phase 2 part.

The results presented at ESMO reflect a cut-off date as of July 5, 2023.

Efficacy Results

- 1.2 mg once daily achieved ORR of 83% per RECIST in the evaluable population as assessed by MRI BICR (Blinded Independent Central Review)
- ORR per RECIST was 64% in evaluable patients across the 3 dose arms (n=36)
- Efficacy results continue to demonstrate a dose-response pattern favoring the 1.2 mg once daily arm
- First Partial Responses (PRs) observed at 16 weeks and 21 additional PRs and 1 Complete Response across all dose arms
- Early and deep volume (-52%) and T2 signal intensity (-58%) reductions within 16 weeks after starting 1.2 mg once daily
- Best overall median reductions of 88% and 85% in volume and T2 signal intensity, respectively, in the 1.2 mg once daily arm at 16.6 months of median time on treatment
- Reductions in volume and T2 signal intensity were also observed across biweekly dose arms

- 29 patients rolled over to the OLE between Oct 2022 and May 2023, with 27 still on study
- Three patients from the 4 mg BIW arm achieved PR after rolling over to the OLE where they received 1.2 mg once daily

Best overall responses for the three dose arms in the evaluable population of Part A and OLE, as determined by blinded independent central review (BICR), are summarized in the table below:

Evaluable population	**1.2 mg QD**	**4 mg BIW**	**2 mg BIW**	**All**
	(n=12)	(n=13)	(n=11)	(n=36)
ORR (CR + PR), n (%)	**10 (83)**	**8 (62)**	**5 (45)**	**23 (64)**
Complete Response (CR)	0	0	**1 (9)**	**1 (3)**
Partial Response (PR)	**10 (83)**	**8 (62)**	**4 (36)**	**22 (61)**
Stable Disease (SD)	2 (17)	5 (38)	5 (45)	12 (33)
Progressive Disease (PD)	0	0	1 (9)	1 (3)
Disease Control Rate	100%	100%	91%	97%
Time to objective response (months), median (range)	8.1	12	9.2	9.4
	(3.8-15)	(9.0-18)	(6.4-9.2)	(3.8-18)

The second table shows tumor responses as measured by volume reduction, T2W signal intensity and RECIST:

	Best median change from baseline across all dose groups as measured on MRI by BICR			
	1.2 mg QD	**4 mg BIW**	**2 mg BIW**	**Overall**
	(n=12)	(n=13)	(n=11)	(n=36)
Tumor Volume	-88	-70	-48[1]	-83[2]
T2W Signal Intensity (cellularity)	-85	-77	-53	-76
Central RECIST v1.1	-54	-36	-29	-38

[1] n=10 for tumor volume in the 2 mg BIW arm

[2] n=35 for tumor volume in the overall population

Safety

- AL102 was generally well tolerated with a manageable safety profile across all dose arms
- Adverse events (AEs) were consistent with gamma secretase inhibitors' (GSI) mechanism of action. The most frequent treatment-related AEs with 1.2 mg once daily included diarrhea (92.8%), nausea (57.1%), fatigue (50%), dry skin (50%), alopecia (50%), stomatitis (50%), dermatitis acneiform (42.9%), dry mouth (42.9%), hypophosphatemia (42.9%), rash maculopapular (37.7%) and aspartate aminotransferase increased (28.6%)
- Regardless of dose regimen, AEs were Grade 1 or Grade 2 in >95% of the cases
- There was one Grade 4 unrelated AE and no Grade 5 AEs. There were no treatment-related serious AEs
- Ovarian dysfunction was reported in 56% of pre-menopausal women in the 1.2 mg once daily arm and 61% of pre-menopausal women across all dose arms

The registration-enabling Phase 3 segment of RINGSIDE is now enrolling patients globally. Patients are receiving AL102 1.2mg once daily or placebo. For more information on RINGSIDE, please visit ClinicalTrials.gov and reference Identifier NCT04871282 (RINGSIDE).

A copy of the poster will be available on the Ayala corporate website, following the ESMO congress.

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. The Company's lead candidates under development are the oral gamma secretase inhibitor, AL102, for desmoid tumors, and aspacytarabine (BST-236), a novel proprietary anti-metabolite for first line treatment in unfit acute myeloid leukemia (AML). 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.

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Cautionary Statement Regarding Forward-Looking Statements

Certain statements contained in this filing may be considered forward-looking statements that involve a number of risks and uncertainties, 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: our ability to integrate the business of Biosight, Ltd., with which we recently consummated a merger ("Biosight"), successfully with ours and to achieve anticipated synergies; the possibility that other anticipated benefits of the merger with Biosight will not be realized, including without limitation, anticipated revenues, expenses, earnings and other financial results, and growth and expansion of the combined company's operations, and the anticipated tax treatment of the combination; potential litigation relating to the transaction that could be instituted against us, Biosight or our respective directors; possible disruptions from the merger with Biosight that could harm our and/or Biosight's respective businesses; the ability of us and Biosight to retain, attract and hire key personnel; potential adverse reactions or changes to relationships with customers, employees, suppliers or other parties resulting from the announcement or completion of the merger; the success and timing of clinical trials, including subject accrual, the ability to avoid and quickly resolve any clinical holds and the ability to obtain and maintain regulatory approval and/or reimbursement of product candidates for marketing; the ability to obtain the appropriate labeling of products under any regulatory approval; plans to develop and commercialize our products; our ability to continue as a going concern; our levels of available cash and our need to raise additional capital, including to support current and future planned clinical activities; 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 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; legislative, regulatory and economic developments; unpredictability and severity of catastrophic events, including, but not limited to, acts of terrorism or outbreak of war or hostilities, as well as management's response to any of the aforementioned factors; 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, 2022 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.