Ayala Pharmaceuticals Presents Encouraging Preliminary Safety And Efficacy Data In Patients With Recurrent/Metastatic Adenoid Cystic Carcinoma With Progressing Disease And Notch Activating Mutations From Ongoing Phase 2 Clinical Trial At ESMO

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– 22% Response Rate; 61% Disease Control Observed –

REHOVOT, Israel & WILMINGTON, Del., September 30, 2019 – (BUSINESS WIRE) – Ayala Pharmaceuticals, Inc., a clinical-stage biopharmaceutical company dedicated to developing targeted cancer therapies for people living with cancer, today announced preliminary results from its ongoing Phase 2 ACCURACY study of lead investigational new drug candidate, AL101, in patients with recurrent/metastatic adenoid cystic carcinoma (ACC) with progressing disease and Notch activating mutations. The data were presented in a poster session at the European Society for Medical Oncology (ESMO) 2019 Congress in Barcelona, Spain.

“ACC is a devasting rare cancer that affects more than 1,300 people in the U.S. annually. Currently, there is no standard drug therapy for ACC and new treatments are desperately needed. ACC with activating NOTCH mutations represent a particularly aggressive disease subtype that can be associated with a poorer prognosis,” said Alan L. Ho., M.D., Ph.D., lead investigator in the ACCURACY study. “Ayala has taken the important step of attempting to personalize therapy for ACC patients by developing AL101, a drug designed to block NOTCH activation. It has been exciting to see the encouraging disease control rates and favorable safety profile emerging from the trial to date and I look forward to continuing to help further explore the clinical utility of AL101.”

“We are very pleased by the initial data from our study as we have seen early signs of biological and clinical activity and a potentially strong safety profile from AL101 in this extremely difficult to treat patient population. AL101 has been well tolerated by ACC patients, most significantly in relation to diarrhea, which has traditionally been difficult to control with previous Notch pathway inhibitors,” said Gary Gordon, M.D., Ph.D., Chief Medical Officer of Ayala. “Furthermore, we are encouraged by the 22% response rate and 61% disease control rate, as most ACC patients do not respond to treatment at all. To have observed some responses after only eight weeks on therapy is a noteworthy achievement.”

AL101 is an investigational small molecule, gamma-secretase inhibitor that potently and selectively inhibits Notch 1, 2, 3 and 4. AL101 inhibits the expression of Notch gene targets by blocking the final cleavage step by the gamma secretase required for Notch activation.

Trial Design:
The ongoing Phase 2 ACCURACY clinical trial is a Simon 2-stage optimal design, noncomparative, open-label, single-arm, multi-center study to assess the clinical activity of AL101 using radiographic assessments in patients with recurrent/metastatic ACC with progressing disease and Notch activating mutations. Patients were treated with 4 mg of once-weekly IV AL101 and underwent radiographic assessments every eight weeks, with an end of study visit 30 days after the last treatment and long-term follow-up every three months thereafter. Stage 1 of the study has completed enrollment and Stage 2 is ongoing. A total of 38 patients were screened and 27 have been dosed with AL101.

As of August 31, 2019, 18 of the 27 patients dosed with AL101 and had at least one pre-dosing and one post-dosing radiological evaluation. Seven patients are currently undergoing dosing and have not yet had a post-dosing radiological evaluation. Two patients began treatment, but discontinued prior to the first post-dosing radiological evaluation due to non-treatment related adverse events (AEs) and are considered to be non-evaluable for efficacy.

Preliminary Safety Results:
At the time of the cut off for data collection, treatment-related AEs were reported in ≥ 15% in patients dosed with AL101. The most common AEs included nausea (59%), diarrhea (56%, most reports were Grades 1 and 2 with one Grade 3 and zero Grade 4 events reported), fatigue (13%), cough (including productive cough) (11%), vomiting (9%), and epistaxis (6%).

Investigators reported Grade 3 AEs in three patients who experienced nausea, diarrhea and hypophosphatemia. Three treatment-related serious adverse events (SAEs) were observed, including two episodes of infusion reaction in one patient and one case of keratoacanthoma. There were two on-study, non-treatment related deaths.

Preliminary Efficacy Results:
Data presented at ESMO were from 18 patients with recurrent/metastatic ACC with progressing disease and Notch activating mutations treated with AL101 as of the data collection cut-off date of August 31, 2019. Based on RECIST 1.1 or modified MDA Bone Response Criteria, at the time of the cut-off date for data collection, four patients achieved a partial response (PR, 22%), seven patients achieved stable disease (SD, 39%), for a disease control rate of 61% and seven patients had progressive disease (PD, 39%).

About AL101
AL101 is an investigational small molecule, gamma-secretase inhibitor that potently and selectively inhibits Notch 1, 2, 3 and 4. AL101 inhibits the expression of Notch gene targets by blocking the final cleavage step by the gamma secretase required for Notch activation. It has the potential to inhibit tumor growth as demonstrated by three Phase 1 studies conducted by Bristol-Myers Squibb. AL101 is currently in a Phase 2 clinical trial in adenoid cystic carcinoma (ACC), as well as planned Phase 2 clinical trials for triple-negative breast cancer (TNBC) and T-Cell acute lymphoblastic leukemia (T-ALL).

About Adenoid Cystic Carcinoma (ACC)
ACC is a rare malignancy of the salivary glands, accounting for about 10% of all salivary gland tumors with an annual incidence of 1,300 in the U.S. There is currently no approved standard of care for patients with recurrent/metastatic ACC and as a result, patients undergo surgery and radiation therapy, with recurring disease treated by chemotherapy. ACC is an immunologically “cold” tumor that is refractory to chemotherapy (ORR 8%-11%), with a recurrence rate of about 60% after initial surgery.

About the Notch Signaling Pathway
The Notch signaling pathway functions as a mediator of short-range cell to cell communication and plays a fundamental role in a variety of tissue types. The gain or loss of Notch signaling aspects has been associated with a wide range of disorders, developmental syndromes and cancers, both hematological and solid tumors. The Notch pathway is involved in several hallmarks of cancer including: cellular proliferation, survival, migration, invasion, epithelial to mesenchymal transition and drug resistance, increased angiogenesis and metastasis. The Notch pathway has been determined to be an oncogenic driver of ACC and its dysregulation plays a key role in tumorigenesis and correlates with a distinct pattern of metastasis and a poor prognosis.

About Ayala Pharmaceuticals
Ayala Pharmaceuticals, Inc. is a clinical-stage biopharmaceutical company dedicated to developing targeted cancer therapies for people living with genetically defined cancers. Ayala is broadly developing its product candidates, AL101 and AL102, best-in-class gamma secretase inhibitors, with clinical and preclinical studies underway in both solid tumors (AL101) and hematologic malignancies (AL102). Ayala’s lead product candidate, AL101, is currently in phase 2 for adenoid cystic carcinoma patients with tumor bearing Notch activating mutations (ACCURACY).

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