



## **Ayala Pharmaceuticals, MD Anderson Cancer Center and the Adenoid Cystic Carcinoma Research Foundation Announce Initiation of Enrollment in Window of Opportunity Study of AL101 in Adenoid Cystic Carcinoma**

March 8, 2022

### **Window of Opportunity Study is Evaluating AL101 Administered Prior to Surgery in Patients with Advanced, Notch-activated ACC**

REHOVOT, Israel and WILMINGTON, Del., March 08, 2022 (GLOBE NEWSWIRE) -- Ayala Pharmaceuticals, Inc. (Nasdaq: AYLA), together with M.D. Anderson Cancer Center and the Adenoid Cystic Carcinoma (ACC) Research Foundation are pleased to announce that the first five patients have been enrolled in a "Window of Opportunity" study for individuals with an aggressive, Notch-activated form of Adenoid Cystic Carcinoma. Under the leadership of Dr. Renata Ferrarotto at M.D. Anderson, this study is focused on determining the effects of AL101, a gamma-secretase inhibitor being developed by Ayala for the treatment of ACC and other cancers, on the biology of ACC tumors.

In this study, participants will have a biopsy to confirm the diagnosis of ACC with Notch activation and will then receive AL101 for 6 to 8 weeks prior to surgery to remove the tumor. AL101 has already shown monotherapy activity in the treatment of individuals with advanced, Notch-activated ACC. The study is being funded by the Department of Defense, the ACC Research Foundation, and Ayala.

"It has been established that mutations in Notch are tumorigenic drivers in ACC and correlate with poorer prognosis. AL101, as a  $\gamma$ -secretase inhibitor, can extinguish Notch signaling in these mutant tumors and has the potential to reduce recurrence and improve long-term patient outcomes," said Dr. Renata Ferrarotto, Associate Professor and Director of Head and Neck Oncology Clinical Research at M.D. Anderson Cancer Center. "This study allows us to monitor changes in the tumor caused by AL101 and to better understand how it affects the biology of the disease."

Dr. Roni Mamluk, Chief Executive Officer of Ayala commented, "There is a compelling rationale for the inhibition of the Notch signaling pathway in ACC. We have already demonstrated clinical proof of concept with AL101 in this disease. The goals of this study are to better understand the mechanism of AL101, help us determine the most successful treatment regime, and generate data that will inform the future development strategy."

Jeffrey Kaufman, Executive Director of the ACC Research Foundation stated, "ACC can be treated with surgery and radiation following initial diagnosis, resulting in relatively high 5-year survival rates. However, late disease recurrence is common and can occur many years after initial treatment. Unfortunately, there are no approved therapies for patients with recurrent/metastatic disease, and the 10 to 20-year survival rates for ACC remain very low. We are very encouraged by the excellent work being conducted by Ayala and M.D. Anderson Cancer Center and the promise that AL101 holds in improving outcomes for patients. We are pleased to support this important study."

For more information on the study, refer to Clinicaltrials.gov identifier [NCT04973683](https://clinicaltrials.gov/ct2/show/study/NCT04973683).

### **About Adenoid Cystic Carcinoma (ACC)**

ACC is a rare malignancy of the secretory glands including salivary glands, accounting for about 10% of all salivary gland tumors with an annual incidence of 3,400 in the U.S. There is currently no approved standard of care for patients with recurrent/metastatic ACC. Patients with locoregional disease undergo surgery and radiation therapy, with recurring disease treated by chemotherapy. ACC is an immunologically "cold" tumor that is refractory to chemotherapy, with a recurrence rate of about 60% after initial surgery. 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 the M.D. Anderson Cancer Center**

The [University of Texas MD Anderson Cancer Center](https://www.mdanderson.org) is one of the world's most respected centers devoted exclusively to cancer patient care, research, education and prevention. Its mission is to eliminate cancer in Texas, the nation, and the world through outstanding programs that integrate patient care, research and prevention, and through education for undergraduate and graduate students, trainees, professionals, employees and the public.

### **About the ACC Research Foundation**

The [ACC Research Foundation](https://www.accrf.org) is the leading organization for the support of individuals with ACC and research to help cure this disease.

### **About Ayala Pharmaceuticals**

Ayala Pharmaceuticals, Inc. is a clinical-stage oncology company focused on developing and commercializing small molecule therapeutics for patients suffering from rare and aggressive cancers, primarily in genetically defined patient populations. Ayala's approach is focused on predicating, identifying and addressing tumorigenic drivers of cancer through a combination of its bioinformatics platform and next-generation sequencing to deliver targeted therapies to underserved patient populations. The company has two product candidates under development, AL101 and AL102, targeting the aberrant activation of the Notch pathway with gamma secretase inhibitors to treat a variety of tumors including Adenoid Cystic Carcinoma, Triple Negative Breast Cancer (TNBC), T-cell Acute Lymphoblastic Leukemia (T-ALL), Desmoid Tumors and Multiple Myeloma (MM) (in collaboration with Novartis). AL101, has received Fast Track Designation and Orphan Drug Designation from the U.S. FDA and is currently in a Phase 2 clinical trial for patients with ACC ([ACCURACY](#)) bearing Notch activating mutations and in a Phase 2 clinical trial for patients with TNBC ([TENACITY](#)) bearing Notch activating mutations and other gene rearrangements. AL102 is currently in a Pivotal Phase 2/3 clinical trials for patients with desmoid tumors ([RINGSIDE](#)) and is being evaluated in a Phase 1 clinical trial in combination with Novartis' BMCA targeting agent, WVT078, in Patients with relapsed/refractory Multiple

Myeloma. For more information, visit [www.avalapharma.com](http://www.avalapharma.com).

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**Forward-Looking Statements**

This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. All statements contained in this press release that do not relate to matters of historical fact should be considered forward-looking statements, including statements relating to our development of AL101 and AL102, the promise and potential impact of our preclinical or clinical trial data, the timing of and plans to initiate additional clinical trials of AL101 and AL102, the timing and results of any clinical trials or readouts, the sufficiency of cash to fund operations, and the anticipated impact of COVID-19, on our business. These forward-looking statements are based on management's current expectations. The words "may," "will," "should," "expect," "plan," "anticipate," "could," "intend," "target," "project," "estimate," "believe," "predict," "potential" or "continue" or the negative of these terms or other similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words.

These statements are neither promises nor guarantees, but involve known and unknown risks, uncertainties and other important factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements, including, but not limited to, the following: we have incurred significant losses since inception and anticipate that we will continue to incur losses for the foreseeable future. We are not currently profitable, and we may never achieve or sustain profitability; we will require additional capital to fund our operations, and if we fail to obtain necessary financing, we may not be able to complete the development and commercialization of AL101 and AL102; we have a limited operating history and no history of commercializing pharmaceutical products, which may make it difficult to evaluate the prospects for our future viability; we are heavily dependent on the success of AL101 and AL102, our most advanced product candidates, which are still under clinical development, and if either AL101 or AL102 does not receive regulatory approval or is not successfully commercialized, our business may be harmed; due to our limited resources and access to capital, we must prioritize development of certain programs and product candidates; these decisions may prove to be wrong and may adversely affect our business; the outbreak of COVID-19, may adversely affect our business, including our clinical trials; our ability to use our net operating loss carry forwards to offset future taxable income may be subject to certain limitations; our product candidates are designed for patients with genetically defined cancers, which is a rapidly evolving area of science, and the approach we are taking to discover and develop product candidates is novel and may never lead to marketable products; we were not involved in the early development of our lead product candidates; therefore, we are dependent on third parties having accurately generated, collected and interpreted data from certain preclinical studies and clinical trials for our product candidates; enrollment and retention of patients in clinical trials is an expensive and time-consuming process and could be made more difficult or rendered impossible by multiple factors outside our control; if we do not achieve our projected development and commercialization goals in the timeframes we announce and expect, the commercialization of our product candidates may be delayed and our business will be harmed; our product candidates may cause serious adverse events or undesirable side effects, which may delay or prevent marketing approval, or, if approved, require them to be taken off the market, require them to include safety warnings or otherwise limit their sales; the market opportunities for AL101 and AL102, if approved, may be smaller than we anticipate; we may not be successful in developing, or collaborating with others to develop, diagnostic tests to identify patients with Notch-activating mutations; we have never obtained marketing approval for a product candidate and we may be unable to obtain, or may be delayed in obtaining, marketing approval for any of our product candidates; even if we obtain FDA approval for our product candidates in the United States, we may never obtain approval for or commercialize them in any other jurisdiction, which would limit our ability to realize their full market potential; we have been granted Orphan Drug Designation for AL101 for the treatment of ACC and may seek Orphan Drug Designation for other indications or product candidates, and we may be unable to maintain the benefits associated with Orphan Drug Designation, including the potential for market exclusivity, and may not receive Orphan Drug Designation for other indications or for our other product candidates; although we have received Fast Track designation for AL101, and may seek Fast Track designation for our other product candidates, such designations may not actually lead to a faster development timeline, regulatory review or approval process; we face significant competition from other biotechnology and pharmaceutical companies and our operating results will suffer if we fail to compete effectively; we are dependent on a small number of suppliers for some of the materials used to manufacture our product candidates, and on one company for the manufacture of the active pharmaceutical ingredient for each of our product candidates; our existing collaboration with Novartis is, and any future collaborations will be, important to our business. If we are unable to maintain our existing collaboration or enter into new collaborations, or if these collaborations are not successful, our business could be adversely affected; enacted and future healthcare legislation may increase the difficulty and cost for us to obtain marketing approval of and commercialize our product candidates, if approved, and may affect the prices we may set; if we are unable to obtain, maintain, protect and enforce patent and other intellectual property protection for our technology and products or if the scope of the patent or other intellectual property protection obtained is not sufficiently broad, our competitors could develop and commercialize products and technology similar or identical to ours, and we may not be able to compete effectively in our markets; we may engage in acquisitions or in-licensing transactions that could disrupt our business, cause dilution to our stockholders or reduce our financial resources; and risks related to our operations in Israel could materially adversely impact our business, financial condition and results of operations.

These and other important factors discussed under the caption "Risk Factors" in our Annual Report on Form 10-K for the year ended December 31, 2020 filed with the U.S. Securities and Exchange Commission (SEC) on March 24, 2021 and our other filings with the SEC, could cause actual results to differ materially from those indicated by the forward-looking statements made in this press release. Any such forward-looking statements represent management's estimates as of the date of this press release. New risk factors and uncertainties may emerge from time to time, and it is not possible to predict all risk factors and uncertainties. While we may elect to update such forward-looking statements at some point in the future, except as required by law, we disclaim any obligation to do so, even if subsequent events cause our views to change. Although we believe the expectations reflected in such forward-looking statements are reasonable, we can give no assurance that such expectations will prove to be correct. These forward-looking statements should not be relied upon as representing our views as of any date subsequent to the date of this press release.

