UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d)
of the Securities Exchange Act of 1934

Date of report (Date of earliest event reported): September 16, 2021

AYALA PHARMACEUTICALS, INC.
(Exact name of registrant as specified in its charter)

Delaware	**001-39279**	**82-3578375**
(State or other jurisdiction of incorporation or organization)	**(Commission File Number)**	**(I.R.S. Employer Identification No.)**

Oppenheimer 4
Rehovot 7670104, Israel
(Address of principal executive offices) (Zip Code)

(857) 444-0553
(Registrant's telephone number, include area code)

N/A
(Former Name or Former Address, if Changed Since Last Report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, $0.01 par value per share	**AYLA**	**The Nasdaq Global Market**

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company ☒

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 8.01 Other Events

On September 16, 2021, Ayala Pharmaceuticals, Inc. (the "Company") announced preliminary clinical data from the 6 mg cohort in its ongoing Phase 2 ACCURACY clinical trial of AL101 for the treatment of recurrent/metastatic adenoid cystic carcinoma ("R/M ACC") harboring Notch-activating mutations and results from its preclinical study of AL101 in combination with approved cancer therapies for dual targeting of adenoid cystic carcinoma tumors.

Preliminary Safety and Efficacy Data from 6mg Cohort of ACCURACY Phase 2 Trial:

The Company presented new preliminary data from the 6mg cohort in its ongoing ACCURACY Phase 2 clinical trial evaluating the safety and efficacy of AL101 monotherapy for the treatment of patients with R/M ACC harboring Notch-activating mutations. The Phase 2 ACCURACY clinical trial is an open-label, single-arm, multi-center study to assess the clinical activity of AL101 using radiographic assessments of patients with R/M ACC demonstrating disease progression within 6 months prior to dosing.

As of July 9, 2021, all 42 patients enrolled in the 6mg cohort were treated and evaluable for safety and 33 were evaluable for efficacy.

Efficacy:

All evaluable patients were assessed for efficacy for a best response by investigators using RECIST 1.1 criteria.

- Disease control rate (defined as partial response and stable disease) was 70% (23/33 patients).
- Partial responses were observed in 3 patients (9%).
- Stable disease was observed in 20 patients (61%).
- Progressive disease was observed in 8 patients (24%).
- Two patients were determined to be evaluable per protocol but their scans were not available for analyses.
- Study is ongoing with several patients remaining on drug as of the cutoff date

Safety:

AL101 6mg dosed once weekly ("QW") in patients with R/M ACC was well tolerated with manageable side effects consistent with those observed in the 4mg QW cohort with no new adverse events ("AEs") specific to the 6mg cohort.

- Most common treatment-related AEs ("TRAEs") of any grade were diarrhea (76%), fatigue (48%), nausea (41%), hypophosphatemia (29%), vomiting (26%) and decreased appetite (26%).
- Treatment-related diarrhea was common and occurred in 32 patients (76%) and most were grades 1 and 2. Treatment-related serious diarrhea occurred in 6 patients (14%).
- Serious TRAEs were reported in 31% of patients with treatment-emergent AEs leading to discontinuation in 26% of patients.
- Two patients experienced a grade 4 TRAE: one patient experienced a seizure and one patient experienced drug-induced liver injury.
- Four treatment-emergent patient deaths occurred (10%), one of which was assessed by the investigator to be treatment related.

The Company plans to report additional data from the ACCURACY study in 2022.

Preclinical Results of AL101 Combined with Other Drugs for Dual Targeting of Notch Dysregulated Tumors:

In this preclinical study evaluating the potential of combination therapy of AL101 in PDX models of ACC, the Company compared the differential gene expression of ACC tumors versus normal matched tissue regardless of Notch activation status. Combination compounds were selected based on determination of the pathways that are implicated with approved oncology therapies, including inhibitors of Bcl2, HDAC, FGFR and CDK4/6. Based on a comparison of AL101 alone, each approved drug alone, and the combination of each drug with AL101, the Company observed additive or synergistic activity of AL101 combined with agents of various mechanisms of action. AL101 in combination demonstrated significant tumor growth inhibition, including regressions, compared to each drug alone, showing significant benefit with dual targeting of Notch and

other dysregulated pathways. Additionally, the study indicated that crosstalk between signaling pathways may increase the efficacy of AL101 in R/M ACC regardless of Notch mutational status. These preclinical results demonstrated a compelling rationale for potential expansion to a larger portion of ACC patients and to additional cancer indications.

Forward-Looking Statements

This Current Report on Form 8-K (the "Current Report") contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. All statements contained in this Current Report that do not relate to matters of historical fact should be considered forward-looking statements, including statements relating to our development of AL101, the promise and potential impact of our preclinical or clinical trial data, and the timing of additional data from clinical trials of AL101. 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: the impact of the COVID-19 pandemic on our operations, including our preclinical studies and clinical trials, and the continuity of our business; we have incurred significant losses, are not currently profitable and may never become profitable; our need for additional funding; our cash runway; our limited operating history and the prospects for our future viability; the lengthy, expensive, and uncertain process of clinical drug development, including potential delays in regulatory approval; our requirement to pay significant payments under product candidate licenses; the approach we are taking to discover and develop product candidates and whether it will lead to marketable products; the expense, time-consuming nature and uncertainty of clinical trials; enrollment and retention of patients; potential side effects of our product candidates; our ability to develop or to collaborate with others to develop appropriate diagnostic tests; protection of our proprietary technology and the confidentiality of our trade secrets; potential lawsuits for, or claims of, infringement of third-party intellectual property or challenges to the ownership of our intellectual property; risks associated with international operations; our ability to retain key personnel and to manage our growth; the potential volatility of our common stock; costs and resources of operating as a public company; unfavorable or no analyst research or reports; and securities class action litigation against us. 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 Current Report. Any such forward-looking statements represent management's estimates as of the date of this Current Report. 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 Current Report.

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

AYALA PHARMACEUTICALS, INC.

Date: September 16, 2021

By: /s/ Roni Mamluk
Roni Mamluk, Ph.D.
President and Chief Executive Officer