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): March 13, 2023

AVALO THERAPEUTICS, INC.

(Exact name of registrant as specified in its charter)

Delaware

(State or other jurisdiction of incorporation)

001-37590 (Commission File Number)

45-0705648 (IRS Employer Identification No.)

540 Gaither Road, Suite 400, Rockville, Maryland 20850 (Address of principal executive offices) (Zip Code)

Registrant's Telephone Number, Including Area Code: (410) 522-8707

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, \$0.001 Par Value	AVTX	Nasdaq Capital 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. \Box

Item 7.01. Regulation FD Disclosure.

On March 13, 2023, Avalo Therapeutics, Inc. (the "Company") posted on its website an updated investor presentation (the "Investor Presentation"). The Investor Presentation will be used from time to time in meetings with investors. A copy of the Investor Presentation is attached hereto as Exhibit 99.1 and is incorporated herein by reference.

The information set forth in this Item 7.01 and furnished hereto as Exhibit 99.1 shall not be deemed "filed" for purposes of Section 18 of the Securities and Exchange Act of 1934, as amended (the "Exchange Act"), and is not incorporated by reference into any of the Company's filings under the Security Act of 1933, as amended, or the Exchange Act, whether made before or after the date hereof, except as shall be expressly set forth by specific reference in any such filing.

Item 9.01. Financial Statements and Exhibits.

(d) Exhibits:

Exhibit No.	Description
99.1	Investor Presentation.
104	The cover pages of this Current Report on Form 8-K, formatted in Inline XBRL.

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SIGNATURE

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.

AVALO THERAPEUTICS, INC.

Date: March 13, 2023

By: /s/ Christopher Sullivan

Christopher Sullivan Chief Financial Officer

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Avalo Therapeutics, Inc. (AVTX)

Corporate Presentation

March 2023



Forward-Looking Statements

This presentation may include forward-looking statements made pursuant to the Private Securities Litigation Reform Act of 1995. Forward-looking statements are statements that are not historical facts. Such forward-looking statements are subject to significant risks and uncertainties that are subject to change based on various factors (many of which are beyond the control of Avalo Therapeutics, Inc. ("Avalo" or the "Company")), which could cause actual results to differ from the forward-looking statements. Such statements may include, without limitation, statements with respect to Avalo's plans, objectives, projections, expectations and intentions and other statements identified by words such as "projects," "may," "might," "will," "could," "would," "should," "continue," "seeks," "aims," "predicts," "believes," "expects," "anticipates," "estimates," "intends," "plans," "potential," or similar expressions (including their use in the negative), or by discussions of future matters such as: the future financial and operational outlook of the Company; the development of product candidates or products; timing and success of trial results and regulatory review; potential attributes and benefits of product candidates; and other statements that are not historical.

These statements are based upon the current beliefs and expectations of Avalo's management but are subject to significant risks and uncertainties, including: drug development costs, timing of trial results and other risks, including reliance on investigators and enrollment of patients in clinical trials, which might be slowed by the COVID-19 pandemic; Avalo's debt and cash position and the potential need for it to raise additional capital; reliance on key personnel; regulatory risks; general economic and market risks and uncertainties, including those caused by the COVID-19 pandemic and the war in Ukraine; and those other risks detailed in Avalo's filings with the Securities and Exchange Commission. Actual results may differ from those set forth in the forward-looking statements. Except as required by applicable law, Avalo expressly disclaims any obligations or undertaking to release publicly any updates or revisions to any forward-looking statements contained herein to reflect any change in Avalo's expectations with respect thereto or any change in events, conditions or circumstances on which any statement is based.



Avalo Therapeutics (AVTX)



Portfolio emphasizing potential high value, first-in-class biologics focused on dysregulated inflammation via the LIGHT-signaling network



AVTX-002 (anti-LIGHT mAb) completed enrollment in Non-Eosinophilic Asthma PEAK trial – Phase 2 topline data expected 2Q23; POC completed in COVID-19 ARDS and CD



AVTX-008 (BTLA agonist fusion protein) – IND 2024



Exclusive consulting arrangement with Carl Ware, PhD, Sanford Burnham Prebys (discoverer of the LIGHT-signaling network)

LIGHT, Lymphotoxin-like, exhibits Inducible expression, and competes with HSV Glycoprotein D for HVEM, a receptor expressed by T lymphocytes; mAb, monoclonal antibody; CD, Crohn's Disease; NEA, non-eosinophilic asthma; POC, Proof of concept studies; COVID-19 ARDS, SARS-COV2 associated acute respiratory distress syndrome (ARDS); IBD, Inflammatory bowel disease; PEAK trial, A Phase 2, Randomized, Double-Blind, Placebo-Controlled, Parallel Group Study to Evaluate the Safety and Efficacy of AVTX-002 for the Treatment of Poorly Controlled Non-Eosinophilic Asthma K; BTLA, B and T Lymphocyte Attenuator, Ig superfamily checkpoint



Pipeline

				Development Stage				
Program	Mechanism of Action	Indication	Designation	Preclinical	Phase 1	Phase 2	Phase 3/Pivotal	Anticipated Milestone
Core Programs:	Immune Dysregulation Di	sorders						
		NEA	-					Phase 2 Topline Data 2Q 2023 (Enrollment Complete)
AVTX-002	Anti-LIGHT mAb	Crohn's Disease	-					
		COVID-19 ARDS	Fast Track				>	*
AVTX-008	BTLA agonist fusion protein	Immunoregulatory disorders	-					IND 2024
Other								
AVTX-803	Fucose replacement	LAD II (SLC35C1-CDG)	ODD RPDD Fast Track					Pivotal Trial Data Timing under evaluation

* The Company will assess the next stage of development for these indications, as well as potentially others, upon or close to data readout of the Phase 2 PEAK trial in NEA.

ARDS, acute respiratory distress syndrome; BTLA, B and T lymphocyte attenuator, Ig superfamily checkpoint; CDG, congenital disorder of glycosylation; LAD, leukocyte adhesion deficiency; LIGHT, Lymphotxin-like, exhibits Inducible expression, and competes with HSV Glycoprotein D for HVEM, a receptor expressed by T lymphocytes; mAb, monoclonal antibody; NEA, non-eosinophilic asthma; ODD, orphan drug designation; RPDD, rare pediatric disease designation





LIGHT is a Key Driver of Acute & Chronic Inflammation

- Proinflammatory cytokine in the TNF superfamily
- Key component of a larger immunoregulatory network, including BTLA
- Critical for neutrophil, NK, T & B cell function
- Two primary receptors: LTβR, HVEM
- Pivotal role in body "barriers": lung, gut, skin
- We believe modulating LIGHT can moderate immune dysregulation in many acute and chronic inflammatory disorders



Ware, C., Croft, M., and Neil, G. J.Exp Med. 2022 Jul 4;219(7):e20220236. 10.1084/jem.20220236.

CD4Tem, CD4 effector-memory T cells; DC, dendritic cell; HVEM, herpes virus entry mediator; LT\$R, Lymphotoxin beta receptor; MAC, macrophage; NK, natural killer cell; Tfh, T follicular helper cells; TNF, tumor necrosis factor



AVTX-002: First-in-Class Neutralizing Anti-LIGHT mAb

- Fully human monoclonal antibody to LIGHT
- CMC at 2,000 L scale; 6-month toxicology study near completion
- POC in two indications:
 - COVID-19 ARDS
 - Crohn's Disease
- Currently in Phase 2 (POC) for NEA
- Additional indications in immune dysregulation under consideration

CMC, Chemistry, manufacturing and control







TNF SuperFamily of Ligands (TNFSF) and Receptors (TNFRSF)

C. F. Ware, Ruddle, N.H. TNF Superfamily of Cytokines and Receptors. M. F. Flajnik ed. Paul's Fundamental Immunology. Publisher: Wolters Kluwer Health 2022 8th ed. Vol. Ch 10, 308-343. Cardinale CJ, et al., Targeted resequencing identifies defective variants of decoy receptor 3 in pediatric-onset inflammatory bowel disease. Genes Immun. 2013 Oct;14(7):447-52. doi: 10.1038/gene.2013.43. Epub 2013 Aug 22

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POC Demonstrated in Phase 2 COVID-19 ARDS Trial

- Demonstrated target engagement: Single-dose rapidly reduced serum free-LIGHT levels by 80%¹
- Well-tolerated; no increase in serious adverse events vs. placebo¹
- Evidence of clinically important anti-inflammatory effect in the lung¹
- Granted Fast Track Designation by FDA
- Potential for benefit in other causes of ARDS and other lung inflammation



Significant Reduction in COVID-19 Induced Respiratory Failure and Mortality





Non-Eosinophilic Asthma

Patient Population	 US prevalence of asthma ≤ 25M¹ NEA accounts for ≤ 47% of asthma^{2,3} Majority of patients with asthma remain uncontrolled⁴ Higher need in underserved populations¹
Signs and Symptoms ⁴	 Asthma symptoms often more severe/resistant to treatment⁵ Associated with smoking, pollution, infections, obesity⁵
Treatment Approach ⁴	 Standard therapies for asthma; many NEA patients remain uncontrolled^{6,7} Currently no approved targeted therapies for NEA
Rationale for AVTX-002	 Sputum LIGHT levels negatively associated with lung function (FEV and FVC) in asthma^{8,9} Higher LIGHT levels in sputum in asthma patients with neutrophilia⁸ Neutrophils have high, pre-formed LIGHT levels¹⁰

1. Asthma and Allergy Foundation of America. Asthma facts and figures. https://www.aafa.org/asthma-facts/. Accessed January 3, 2022; 2. McGrath KW et al., Am J Resp Crit Care Med. 2012;185(6):612-619; 3. Jiang Y et al., Allergy Asthma Clin Immunol. 2021;17(1):45; 4. Centers for Disease Control and Prevention. AsthmaStats: Uncontrolled asthma among adults, 2016. https://www.cdc.gov/asthma/asthma_stats/uncontrolled-asthma-adults.htm. Accessed January 3, 2022; 5. Carr, T. F., Zeki, A. A. & Kraft, M. Eosinophilic and Noneosinophilic Asthma. Am J Resp Crit Care 197, 22–37 (2017); 6. Esteban-Gorgojo I et al., J Asthma Allergy. 2018;11:267-281; 7. ClearView Healthcare Partners Analysis, June 2021; 8. Hastie AT et al., J Allergy Clin Immunol. 2010;125(5):1028-1036; 9. Romeo J et al., J Allergy Clin Immunol. 2013;131(2 Suppl):AB203. Abstract 725; 10. Rørvig et al., J Leukocyte Biol 94, 711–721 (2013).

FEV, forced expiratory volume in 1 second; FVC, forced vital capacity



LIGHT (TNFSF14) in Asthma and Pulmonary Fibrosis



Human Patients*

- LIGHT expression in lung inflammatory cells (T and NK cells), alveolar epithelial, fibroblasts, goblet cells
- · LIGHT expression in lungs of patients with persistent airflow limitation
- IL-8, IL-19, MMP2, osteopontin associated with high LIGHT immunoreactivity
- · LIGHT-positive cells correlate with increased PMN, macrophages in sputum
- Intense immunoreactivity of LIGHT is negatively associated with decreased forced expiratory volume

Asthma Models**

- Signaling receptors $\mbox{LT}\beta\mbox{R}$ and HVEM expressed in lung fibroblasts, goblet and epithelial cells
- · Pharmacological inhibition or gene deletion of LIGHT:
 - Reduces Lung fibrosis, smooth muscle hyperplasia, airway hyperresponsiveness
 - LIGHT inhibition limits lung expression of IL13, TGFb, TSLP
 - $\mbox{LT}\beta\mbox{R}$ controls airway smooth muscle deregulation and asthmatic lung dysfunction
 - LIGHT induces inflammatory activation of lung fibroblasts
 - LIGHT promotes differentiation of proinflammatory lung fibroblasts through LTβR

Conclusion: LIGHT is a profibrogenic cytokine in asthma acting through the $LT\beta R$

*Gaddis, LungMAP Portal Ecosystem: Am J Respir Cell Mol Biol doi: 10.1165/rcmb.2022-0165OC; Hirano, Respir Investig 2021 doi: 10.1016/j.resinv.2021.05.011
**Mouse models of asthma induced by antigen, bleomycin or Rhinovirus

Miki J Allergy Clin Immunol 2022 DOI: 10.1016/j.jaci.2022.11.016; Mehta, Allergy 2018 DOI: 10.1111/all.13390; Da Silva Antunes Front Immunol 2018 DOI: 10.3389/fimmu.2018.00576; Herro, J Allergy Clin Immunol 2015 DOI: 10.1016/j.jaci.2014.12.1936; Doherty, Nat Med 2011 DOI: 10.1038/nm.2356

MMP2, matrix metalloproteinase-2; PMN, polymorphonuclear neutrophils



AVTX-002 for Treatment of NEA: Phase 2 Trial Design





The LIGHT-Signaling Network: A Key Immunoregulatory System



Arrow heads refer to mono and bidirectional signaling

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- BTLA B and T lymphocyte attenuator (Ig superfamily checkpoint)
 - Co-expressed with HVEM in T and B cells
 - "Dampens" the immune response
- LIGHT activates HVEM
 - Inhibits BTLA signaling, allowing immune stimulation
- LIGHT activates LTβR
 - Activates dendritic cells, macrophages, stromal cells
 - Recruits lymphocytes
 - Stimulates antigen presentation & lymphoid organization
- DcR3 inhibits/regulates LIGHT
- CD160 competes with BTLA for HVEM
 - Stimulated immune activation by restricting inhibitory signaling in NK, CTL, Tfh
- BTLA and CD160 can activate HVEM (bidirectional signaling)

Ward-Kavanagh et al., Immunity 2016. Šedý et al., Cold Spring Harb Perspect Biol 2014; Mintz & Cyster Immunol Rev 2020; Ware, C., Croft, M., and Neil, G. J.Exp Med. 2022 Jul 4;219(7):e20220236. 10.1084. DCR3, decoy receptor 3



AVTX-008 MOA: Distinct from Other Autoimmune Therapeutics

• Activation of the BTLA inhibitory receptor by its ligand HVEM turns on SHP phosphatases* limiting lymphocyte activation and inflammatory cytokine signaling



Ward-Kavanagh, et al., Immunity 2016; Ware, C., Croft, M., and Neil, G., J.Exp Med. 2022 Jul 4;219(7):e20220236. 10.1084; Xiaozheng Xu, et al., PD-1 and BTLA regulate T cell signaling differentially and only partially through SHP1 and SHP2. J Cell Biol 1 June 2020; 219 (6): e201905085. doi: https://doi.org/10.1083/jcb.201905085/jcb.201905085/

*Includes SHP-1 and SHP-2; SHP-1, sarcoma (SRC) homology 2 domain-containing protein tyrosine phosphatase 1; SHP-2, SRC homology 2 domain-containing protein tyrosine phosphatase 2





AVTX-008: BTLA Agonist Fusion Protein

Fully human, bioengineered HVEM, specific and high-affinity agonist for BTLA

Executive Summary

MOA	 Novel mechanism of action Inhibits lymphocyte activation and effector cells through BTLA
Unmet Need	 Immunoregulatory disorders: potentially SLE, GVHD and non-responders to TNF inhibitors
Stage	• IND 2024
Clinical Advantages	 Inhibition of inflammatory cytokine production predicts efficacy in patients not responsive to anti-TNF therapy Efficacy in murine lupus model excels compared to Abatacept Reduced risk of anti-drug response Proven modality of Fc fusion proteins: Orencia, Enbrel
Business Advantages	 Unique BTLA agonist fusion protein Exclusive license to portfolio of issue patents and patent applications SLE, Systemic lupus erythematosus; GVHD, graft-versus-host disease



JORAN

World Class Scientific Advisor

- Carl Ware, PhD, Head of Avalo Scientific Advisory Board
 - Director, Sanford Burnham Prebys (SBP) Infectious and Inflammatory Diseases Center
 - Professor, SBP Immunity and Pathogenesis Program
 - Director, SBP Laboratory of Molecular Immunology
- Discoverer of LIGHT-signaling network









Financial & Investor Information

Key Financial Highlights

NASDAQ: AVTX

The following data is as of December 31, 2022

- Cash and cash equivalents \$13.2M^{1, 2}
- Outstanding common shares 9.4M^{1, 2}
- Fully diluted shares³ 11.3M^{1, 2}
- Average daily trading volume 17K

¹Preliminary, has not been audited and subject to change.

²On February 7, 2023, Avalo closed an underwritten public offering of 3,770,000 shares of its common stock and warrants to purchase up to an aggregate of 3,770,000 shares of common stock for gross proceeds of \$15 million, which is not included above.

³Based on shares of common stock outstanding and common stock underlying outstanding warrants and outstanding options.



Experienced Management Team

Decades of successful leadership, product development, and commercialization in pharma and biotech





Garry A. Neil, MD **Chief Executive Officer** Chairman of the Board







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Chief Financial Officer





EY





Lisa Hegg, PhD SVP, Program Management, Corporate Infrastructure









Colleen Matkowski SVP, Global Regulatory Affairs, **Quality Assurance**



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FDA



Dino C. Miano, PhD SVP, CMC, **Technical Operations**





Avalo Therapeutics (AVTX)

Portfolio emphasizing potential high value, first-in-class biologics focused on dysregulated inflammation via the LIGHT-signaling network

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AVTX-008 (BTLA agonist fusion protein) - IND 2024

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Exclusive consulting arrangement with Carl Ware, PhD, Sanford Burnham Prebys (discoverer of the LIGHT-signaling network)







AVTX-803: Leukocyte Adhesion Disorders (LAD II)

LAD Type II: Absence of sialyl Lewis X of E-selectin (SLC35C1 mutation)

Overview

Patient Population	 Ultra-orphan disease: worldwide prevalence ~10-20 pt Nonfunctional GDP-fucose transporter with decreased fucosylation Absence of sialyl Lewis X (CD15a) expression
Signs and Symptoms	 Facial dysmorphism/growth & cognitive impairment Recurrent bacterial infections due to neutrophil dysfunction
Diagnosis/ Evaluation	 Flow cytometry for sialyl Lewis X (CD15a) expression Leukocytosis/neutrophil function assay H antigen expression (for pharmacodynamic effect)
Treatment	 Currently no FDA-approved treatment; patients use OTC fucose AVTX-803 granted orphan drug, Fast Track & Rare Pediatric Disease designations
	AVTX-803 is an oral formulation of fucose that seeks to enhance fuco

LAD II (SLC35C1-CDG) Pathophysiology



- Type II (LAD II) caused by LOF mutation in SLC35C1 gene resulting in the inability to fucosylate certain critical proteins
- Absence of sialyl Lewis X results in neutrophil dysfunction

AVTX-803 is an oral formulation of fucose that seeks to enhance fucosylation of proteins in the absence of a functioning GDP-fucose transporter, partially restoring protein function



AVTX-803 (fucose) for LAD II (SLC35C1-CDG): Pivotal Trial Design





TNF SuperFamily: Proven Target-rich Opportunities



BVBIC

C. F. Ware, Ruddle, N.H. TNF Superfamily of Cytokines and Receptors. M. F. Flajnik ed. Paul's Fundamental Immunology. Publisher: Wolters Kluwer Health 2022 8th ed. Vol. Ch 10, 308-343.



Efficacy Signal Observed in Crohn's Disease Phase 1b Proof of Concept Trial

- Phase 1b Escalating Dose, Open-Label, Signal-Finding Trial to Evaluate the Safety, Tolerability, and Short-Term Efficacy of the Anti-Light Monoclonal Antibody AVTX-002 in Adults with Moderate to Severe Active Crohn's Disease (CD) who have Failed Prior Treatment with an Anti-TNFα Agent
- Rapid reduction in serum free LIGHT levels
- · Well-tolerated: no drug-related serious adverse events observed
- · Clinically meaningful mucosal healing signal observed
 - 3 out of 7 patients demonstrated evidence of mucosal healing as determined by colonoscopy and adjudicated by a central reader
 - One patient (1/7) achieved remission (SES-CD = 0)

 $^{1}\text{TNF}\alpha,$ tumor necrosis factor alpha; $^{1}\text{SES-CD},$ Simple Endoscopic Score for Crohn's Disease

AVTX-002 Crohn's Disease Phase 1b, Proof of Concept Trial Design



* SES-CD, Simple Endoscopic Score for Crohn's Disease; * CDAI, Crohn's Disease Activity Index; * IBDQ, Inflammatory Bowel Disease Questionnaire;

- Heavily pre-treated
- Dose escalation starting at 1mg/kg every 2 weeks

