# 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 9, 2021**

# AVALO THERAPEUTICS, INC.

**(Exact name of registrant as specified in its charter)**

**Delaware**
**(State or other jurisdiction of incorporation)**

| **001-37590** | **45-0705648** |
|---|---|
| **(Commission File Number)** | **(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. ☐

**Item 7.01 Regulation FD Disclosure.**

On September 9, 2021, Avalo Therapeutics, Inc. (the "Company") released 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 on this Item 7.01 and furnished hereto as Exhibit 99.1 shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), and is not incorporated by reference into any of the Company's filings under the Securities 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 8K, formatted in Inline XBRL |



**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: September 9, 2021

By: /s/ Schond L. Greenway
Schond L. Greenway
Chief Financial Officer


## 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: its future financial and operational outlook; the development of product candidates or products; potential attributes and benefits of product candidates; strategic alternatives for Millipred; 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: reliance on and integration of key personnel; drug development costs, timing and other risks, including reliance on investigators and enrollment of subjects in clinical trials, which might be slowed by the COVID-19 pandemic; regulatory risks; Avalo's cash position and the need for it to raise additional capital; risks related to potential strategic alternatives for Millipred; general economic and market risks and uncertainties, including those caused by the COVID-19 pandemic 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.

# Pipeline Highlights

- Avalo has a pipeline of six novel, first-in-class assets in eight clinical development programs across Immunology, Immuno-oncology, and Rare Genetic Diseases
- All assets have demonstrated mechanistic rationale, biomarkers, or established proof-of-concept (POC) to increase probability of success
- AVTX-002 (anti-LIGHT mAb*) demonstrated clinically meaningful endoscopic improvement in 75% (3/4) of subjects in the initial results (Cohort 1) of a Phase 1b moderate to severe Crohn's disease clinical trial
- AVTX-002 demonstrated statistically significant improvement in the primary endpoint of alive and free of respiratory failure status in a Phase 2 COVID-19 ARDS clinical trial
- Currently, four assets have been designated ODD* and RPDD* enabling Priority Review Vouchers (would provide non-dilutive financing of the pipeline)
- Multiple data readouts anticipated in the second half of 2021

*Orphan Drug Designation, Rare Pediatric Disease Designation; eligibility for Priority Review Voucher Upon Approval.
mAb, monoclonal antibody.




# Clinical-Stage Pipeline

| Program | Mechanism of Action | Lead Indication | Designation | Clinical Development Stage | | | Anticipated Milestone |
|---|---|---|---|---|---|---|---|
| | | | | Early-Stage | Mid-Stage | Late-Stage | |
| **Immunology/Immuno-oncology** | | | | | | | |
| AVTX-002 | Anti-LIGHT mAb | COVID-19 ARDS | Fast Track | | | | Received Fast Track Designation* |
| | | Inflammatory bowel disease | – | | | | Crohn's Top-line Data 2H 2021 |
| AVTX-007 | Anti-IL-18 mAb | Still's disease | – | | | | Initial Data 4Q 2021 |
| | | Multiple myeloma | – | | | | Top-line Data 2H 2021 |
| **Rare Genetic Diseases** | | | | | | | |
| AVTX-006 | Dual mTOR inhibitor | Complex lymphatic malformations | ODD RPDD PRV eligible | | | | Initial Data 4Q 2021 |
| AVTX-801 | D-Galactose replacement | PGM1-CDG | ODD RPDD PRV eligible Fast Track | | | | Pivotal Trial Data 2022 |
| AVTX-802 | D-Mannose replacement | MPI-CDG | | | | | Pivotal Trial Data 2022 |
| AVTX-803 | L-Fucose replacement | LAD II (SLC35C1-CDG) | | | | | Pivotal Trial Data 1H 2022 |

*Avalo remains in dialogue with the FDA and is working through feedback to determine the trial design for a registrational study and accompanying timelines, including the potential expansion to a larger patient population in broader ARDS.

ARDS, acute respiratory distress syndrome; CDG, congenital disorder of glycosylation; IL, interleukin; IND, Investigational New Drug; LAD, leukocyte adhesion deficiency; mAb, monoclonal antibody; MPI, mannose phosphate isomerase; mTOR, mammalian target of rapamycin; ODD, orphan drug designation; PGM1, phosphoglucomutase 1; PRV, priority review voucher; RPDD, rare pediatric disease designation.

# AVTX-002

**Anti-LIGHT monoclonal antibody in clinical studies for Crohn's Disease and COVID-19 ARDS**

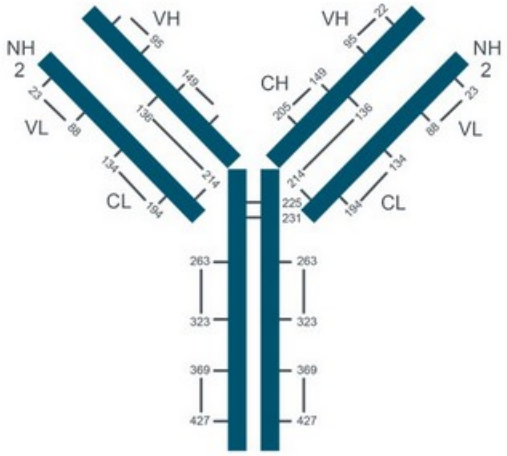
avalo THERAPEUTICS




## AVTX-002: A Novel First-in-Class Anti-LIGHT (TNFSF14) mAb

**In-licensed From Kyowa Kirin Co., Worldwide Exclusive Rights* for All Indications (2021)**

- Novel, first-in-class fully human subcutaneous (SQ) monoclonal antibody (mAb)
- Only fully human anti-LIGHT mAb
- Only anti-LIGHT mAb in clinical development




*Kyowa Kirin has an option to retain the rights in Japan.

# AVTX-002: Crohn's Disease




## Executive Summary: AVTX-002 Demonstrates Potential Proof-of-Concept in Initial Low-Dose Cohort

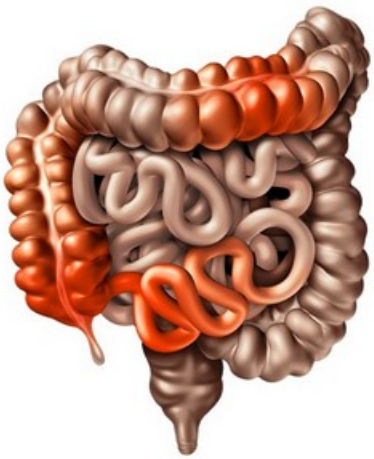
**2nd Positive Proof-of-Concept Study With AVTX-002 Further Validates the LIGHT MOA in Inflammatory Diseases**

- Open-label proof-of-concept study in patients with moderate to severe Crohn's disease who previously failed 3 or more lines of biologic therapies, including anti-TNFα*
- Clinically meaningful mucosal healing, determined by colonoscopy, in 3 of 4 patients (SES-CD)†
- Rapid response within 8 weeks
- Well-tolerated, no serious adverse events observed
- High-dose cohort fully enrolled with results expected 2H 2021

*TNFα, tumor necrosis factor alpha; †SES-CD, Simple Endoscopic Score for Crohn's Disease.

# Inflammatory Bowel Disease Overview

**Significant Unmet Need Exists in Crohn's Disease and Ulcerative Colitis**



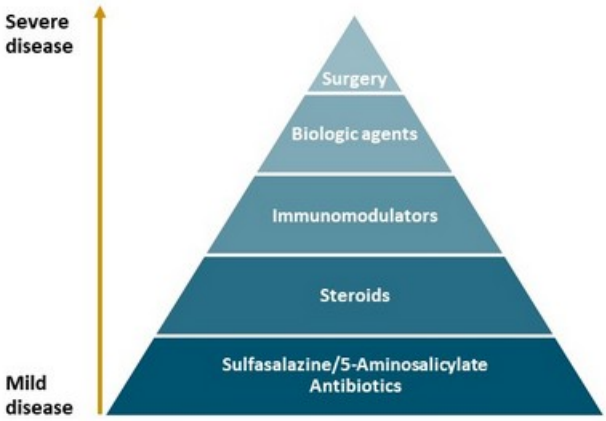
- Inflammatory bowel disease (IBD) is a broad term indicating chronic inflammation of the gastrointestinal (GI) tract and includes both Crohn's disease (CD) and ulcerative colitis (UC)[1]
  - Relapsing and remitting course characterized by intestinal inflammation and epithelial injury, causing lifelong morbidity[2] that significantly impacts quality of life[3,4]
- Standard of care relies on treating the inflammatory activity that causes strictures, fistula, and abscesses as well as heightened incidence of colitis-associated neoplasia associated with IBD[5]
- An estimated 1.6-3.1 million US adults (~1.3%) have a diagnosis of IBD[1,6]
  - Estimated US cases of CD are ~785K[7]
- Approximately $16.7B global market opportunity in 2020 with 4.5% compound annual growth rate[8]

1. Centers for Disease Control and Prevention. Inflammatory bowel disease. https://www.cdc.gov/ibd/features/IBD-more-chronic-diseases.html. Accessed July 17, 2021. 2. Atreya R et al. *Front Med (Lausanne)*. 2020;7:517. 3. Knowles SR et al. *Inflamm Bowel Dis*. 2018;24(4):742-751. 4. Byron C et al. *J Clin Nurs*. 2020;29(3-4):305-319. 5. GBD 2017 Inflammatory Bowel Disease Collaborators. *Lancet*. 2020;5:17-30. 6. Crohn's and Colitis Foundation of America. The facts about inflammatory bowel disease. https://www.crohnscolitisfoundation.org/sites/default/files/2019-02/Updated%20IBD%20Factbook.pdf. Accessed July 19, 2021. 7. Shivashankar R et al. *Clin Gastroenterol Hepatol*. 2017;15(6):857-863. 8. EMR Reports. https://www.expertmarketresearch.com/reports/inflammatory-bowel-disease-treatment-market. Accessed July 17, 2021.




avalo THERAPEUTICS

# Substantial Opportunity Remains in the Treatment of IBD




- Majority of patients are designated moderate/severe and treated with pharmacologic intervention
- Almost all patients with moderate to severe IBD will receive biologics over the course of treatment[1]
  - Approximately one-third are primary non-responders to anti-TNF therapies
  - 30-50% of initial responders become refractory
- Remission rates for advanced therapies have remained at ~20% (placebo-adjusted) for patients with moderate to severe disease[2]
- Newly developed therapies such as Janus kinase (JAK) inhibitors carry significant safety concerns
- Significant opportunity remains for new, safe, and effective treatments addressing novel targets

1. Atreya R et al. *Front Med (Lausanne)*. 2020;7:517. 2. Clearview Healthcare Partners. Crohn's disease and ulcerative colitis. Initial disease landscape overview. May 2021.

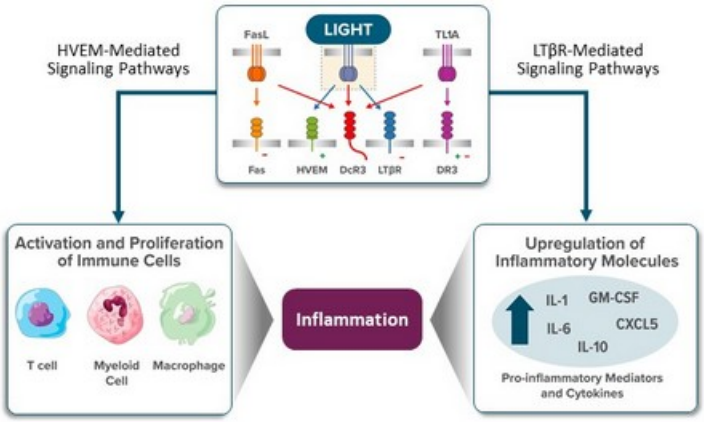



avalo THERAPEUTICS

# LIGHT Is a Key Driver of Inflammation

**Member of the TNF Superfamily (TNFSF14) of Proteins, Involved in T-Cell Activation and Inflammation**

- LIGHT (TNFSF14) is a pro-inflammatory cytokine and a co-stimulator of T cells and Th1 cytokines, including interferon (IFN)-γ[1]
- LIGHT is expressed on activated T cells, natural killer (NK) cells, monocytes, granulocytes, and immature dendritic cells[2]
- LIGHT is an important immuno-regulator in the barrier tissues: GI tract, skin, lung, and others[3-5]




LIGHT, homologous to Lymphotoxin, exhibits Inducible expression and competes with HSV Glycoprotein D for binding to herpesvirus entry mediator (HVEM), a receptor expressed on T lymphocytes.

1. Ware CF. *Annu Rev Immunol*. 2005;23:787-819. 2. Wang J, Fu YX. *Immunol Res*. 2004;30(2):201-214. 3. Herro R et al. *J Invest Dermatol*. 2015;135(8):2109-2118. 4. Herro R et al. *J Allergy Clin Immunol*. 2015;136(3):757-768. 5. Gilles DA et al. *Front Immunol*. 2018;9:2585.




avalo THERAPEUTICS

# Multiple Lines of Evidence Support Importance of LIGHT in IBD

- Patient data
  - Elevated levels of LIGHT in patients with CD[1] and UC[2]
  - High LIGHT mRNA levels detected in human inflamed intestinal tissue compared with normal tissue[1,3]
  - LIGHT gene upregulation is observed in CD and UC[4]
- Animal models of IBD
  - LIGHT overexpression increases intestinal inflammation in rodents[5]
  - Anti-LIGHT monoclonal antibody (mAb) treatment ameliorates inflammation in the dextrate sulfate sodium (DSS)–induced colitis model[6]
  - Knockout of the LIGHT (or its ligand, HVEM) gene results in reduced intestinal inflammation (in some models)[7]

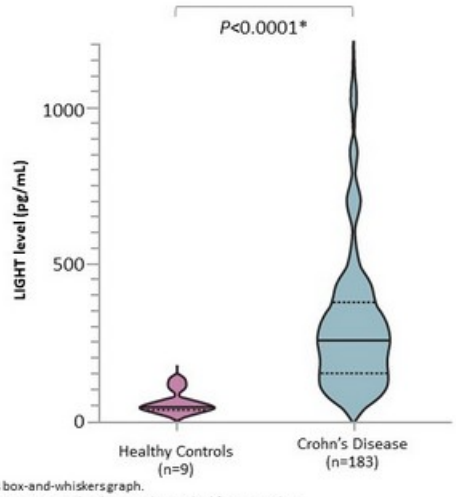
1. Data on file, Avalo Therapeutics, Inc. 2. Moraes L et al. *Inflamm Bowel Dis*. 2020;26(6):874-884. 3. Cohavy O et al. *J Immunol*. 2005;174(2):646-653. 4. Wang J et al. *J Immunol*. 2005;174(12):8173-8182. 5. Shaikh RB et al. *J Immunol*. 2001;167(11):6330-6337. 6. Jungbeck M et al. *Immunology*. 2009;128(3):451-458. 7. Schaer C et al. *PLoS One*. 2011;6(4):e18495.




avalo THERAPEUTICS

# Elevated LIGHT Levels Detected in Pediatric Crohn's Disease

**Plasma LIGHT levels Were Significantly Elevated in Patients With CD vs Healthy Individuals**




Data displayed as box-and-whiskers graph.
Plasma samples from CHOP Biobank; controls matched for age and sex.
*Determined by Mann-Whitney U test.
*Source*: Cardinale C et al. Manuscript in preparation.

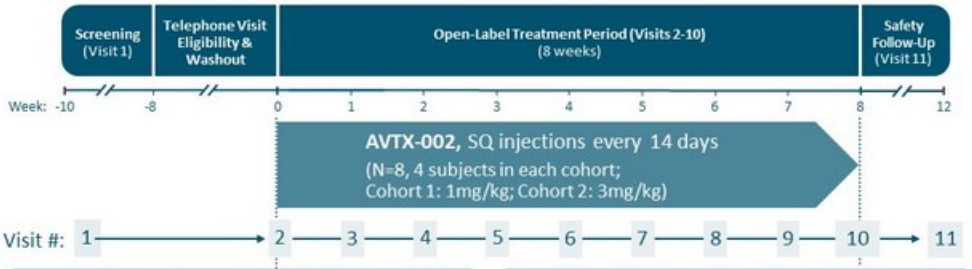
- Approximately 83% of pediatric patients with CD had significantly elevated LIGHT levels
  - Cross-sectional study of pediatric patients with CD from Center for Applied Genomics at CHOP
  - Studied pediatric patients with CD (n=183) versus healthy age-matched controls (n=9)




# AVTX-002 Crohn's Disease Proof-of-Concept

**Proof-of-Concept Trial Design**

Open-Label Proof-of-Concept Clinical Trial of AVTX-002 in adults with moderate to severe, active Crohn's disease who have previously failed anti-tumor necrosis factor alpha (anti-TNFα) treatment




**Primary Endpoint**

- Safety
- Tolerability

**Key Secondary / Exploratory Endpoints**

- Pharmacokinetics
- Short-term efficacy – as measured by SES-CD, CDAI, and IBDQ scores

- Moderate to severe disease
- Anti-TNFα failure
- Heavily pre-treated patients
- Dose escalation starting at 1mg/kg every 2 weeks
- Short duration (8 weeks)

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

# Clinical Trials in CD Consistently Suggest More Severe Patients Are Less Likely to Achieve Spontaneous Remission

## Key Takeaways from KOL interviews - Placebo Response and Remission in CD

- **Gastroenterology KOLs (N=6) noted that they expect low PBO rates in heavily pre-treated patient populations (as low as single-digits in 4L+ patients)**
- **Patients with more severe disease are less likely to have spontaneous remission**
- **Studies using endoscopic healing as a primary endpoint have lower PBO response and remission rates vs. those that use symptomatic endpoints (e.g., CDAI)**
- **Studies with shorter treatment duration have lower PBO response rates vs. those with longer treatment duration**

PBO, placebo; KOL, key opinion leader.

Source: Su. Gastroenterology. 2004; Su. Gastroenterology. 2007; Physician Interviews; ClearView Analysis.




avalo THERAPEUTICS

# AVTX-002 Crohn's Disease Proof-of-Concept:
## Phase 1b Initial Data (Cohort 1)

**Patient-Level Data**

| Subject # | Age (yrs) | Prior Therapy / # of Prior Lines | SES-CD | | LIGHT (pg/mL) | | Response |
|---|---|---|---|---|---|---|---|
| | | | Baseline | 8 Weeks | Baseline | 8 Weeks | |
| Subject 1 | 42 | Remicade, Entyvio, Stelara | 11 | 4 | 455 | 24 | Significant mucosal healing:<br>• 64% reduction in SES-CD score (moderate to mild)<br>• Patient relapsed post treatment and needed surgery |
| Subject 2 | 63 | Remicade, Humira, Entyvio, Stelara | 18 | 19 | 193 | 29 | No evidence of improvement |
| Subject 3 | 28 | Remicade, Humira, Stelara, Methotrexate | 21 | 15 | 75 | 27 | Significant mucosal healing:<br>• 29% reduction in SES-CD score (severe to moderate)<br>• Exploring single-patient IND |
| Subject 4 | 49 | Remicade, Stelara, Humira, Entyvio, Methotrexate, Mercaptopurine | 12 | 3 | 162 | 45 | Significant mucosal healing:<br>• 75% reduction in SES-CD score (moderate to mild)<br>• Exploring single-patient IND |

Disease severity according to SES-CD score[1]:
Remission: 0-2
Mild: 3-6
Moderate: 7-15
Severe: >15

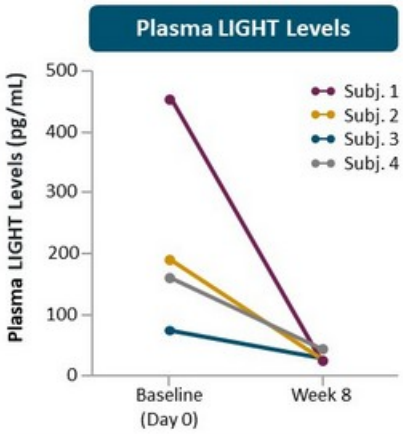
1. Italian Group for the Study of Inflammatory Bowel Disease. https://www.igibdscores.it/en/info-sescd.html. Accessed July 19, 2021.

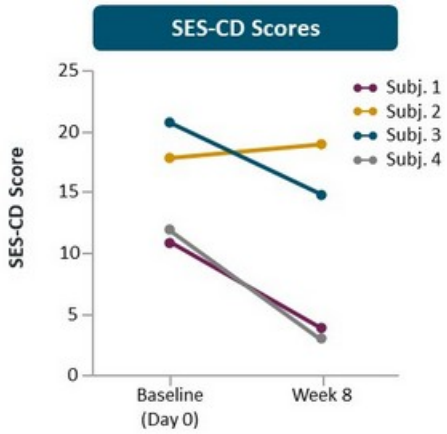



avalo THERAPEUTICS

# AVTX-002 Crohn's Disease Proof-of-Concept:
## Phase 1b Initial Data (Cohort 1)

**Preliminary Efficacy Results (Patient-Level Data)**




**Clinically meaningful mucosal healing, determined by colonoscopy, in 3 of 4 patients (SES-CD)**




# AVTX-002 Crohn's Disease Proof-of-Concept:
## Phase 1b Initial Data (Cohort 1)

**Independent Preliminary Safety Data Results – AVTX-002, SQ Injection (1mg/kg)**

- No serious adverse events attributable to study drug
  - Consistent with 83-patient COVID-19 ARDS clinical trial[1]
- Adverse events were mild to moderate in nature
  - Most common: GI symptoms consistent with CD
- No evidence of increased infections or adverse events related to immunosuppression
- Recommended by independent safety review committee to continue to next cohort (3mg/kg) without changes to protocol (currently fully enrolled)

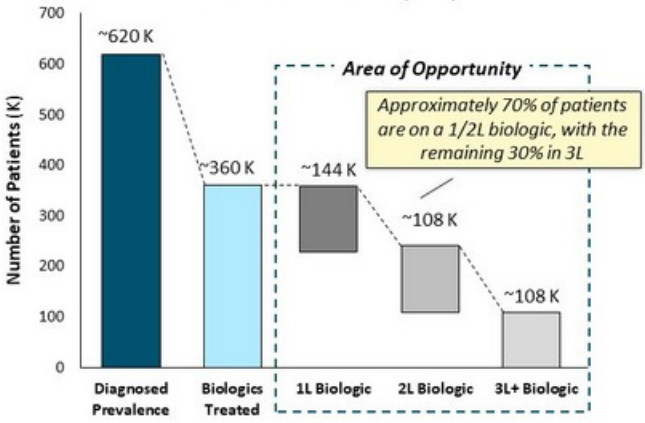
1. Perlin DS et al. AVTX-002, a human anti-LIGHT mAb reduces respiratory failure and death in hospitalized COVID-19 ARDS patients (https://medrxiv.org/cgi/content/short/2021.04.03.21254748v1).

# Despite the Number of Agents Available, There Remains Significant Opportunity Among Later Line CD Patients

DIRECTIONAL

## Crohn's Disease Opportunity

**U.S. Crohn's Disease Cases** (2021)




**Key Takeaways**

According to claims data, **~60% of the CD population is likely to be treated with a biologic agent**

Based on physician insights and published scientific literature, **~60% of biologics-treated CD patients will fail a 1L biologic and ~50% of those patients will fail a 2L biologic**

*"About 30% of CD patients may require a 3L intervention, but the options are limited." – KOL*

Source: Cohen. Digestive Disease Week. 2021. Fine. Gastroenterol Hepatol. 2019. Yu. Aliment Pharmacol Ther. 2018. Physician Interviews; ClearView Analysis.




avalo THERAPEUTICS

# AVTX-002: COVID-19 ARDS

avalo THERAPEUTICS

# Executive Summary: Final Data Analysis

**Phase 2 Clinical Trial Met Primary Endpoint in Patients Hospitalized With COVID-19 ARDS**

- AVTX-002 significantly reduced respiratory failure and mortality in a Phase 2 clinical trial in patients hospitalized with COVID-19 acute respiratory distress syndrome (ARDS)
  - This analysis updates the preliminary top-line data reported on January 5, 2021, and is inclusive of 60-day safety data
  - Hospitalized COVID-19 patients treated with a single dose of AVTX-002 demonstrated statistically significant improvement in the primary endpoint (proportion of patients alive and free of respiratory failure over the 28-day study period) compared with placebo (n=62, *P*=0.044)
  - Efficacy was highest in a prespecified subpopulation of patients aged ≥60 years (n=34, *P*=0.042), the population most vulnerable to severe complications and death with COVID-19 infection
  - At both the 28-day and 60-day final timepoints, an approximate 50% trend in mortality reduction (22.5% vs 10.8%) was observed
  - AVTX-002 showed statistically significant efficacy on top of corticosteroids and standard of care in COVID-19 ARDS (~88% of patients in the trial received corticosteroids and ~58% received remdesivir)
- AVTX-002 was well tolerated, with no appreciable differences in immunosuppression or other serious adverse events between AVTX-002 and placebo
- AVTX-002 dramatically and rapidly reduced serum free-LIGHT levels
  - ~85% reduction in free LIGHT achieved in 1 day
- AVTX-002 recently granted Fast Track designation for the treatment of hospitalized patients with COVID-19
- Additionally, the Company is exploring the applicability of AVTX-002 in non-COVID-19 ARDS

*Source:* Data on file, Avalo Therapeutics, Inc.

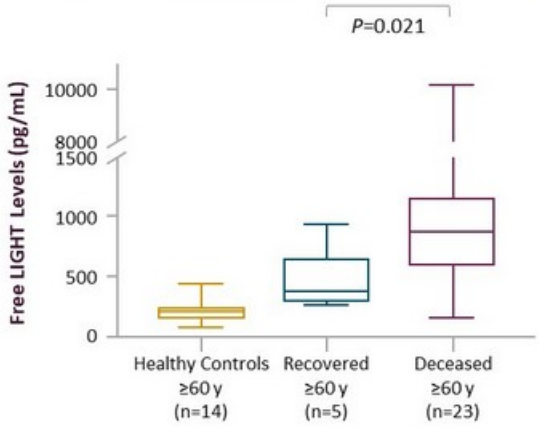



avalo THERAPEUTICS

# LIGHT Is a Central Driver of COVID-19–Related Cytokine Storm

**Clinical Trial Initiated After Compelling Biomarker Study Completed June 2020**

**Association Between Elevated LIGHT and Mortality Strongest in Patients >60 Years**




**Key Implications**

- In patients ≥60 years, LIGHT levels were significantly higher in those who eventually died than in those who recovered (*P*=0.021)
- Observed mortality rate was higher for patients ≥60 years (82%) compared with patients <60 years (32%)

**Elevated LIGHT levels in hospitalized COVID-19 patients were most strongly associated with mortality in patients ≥60 years**

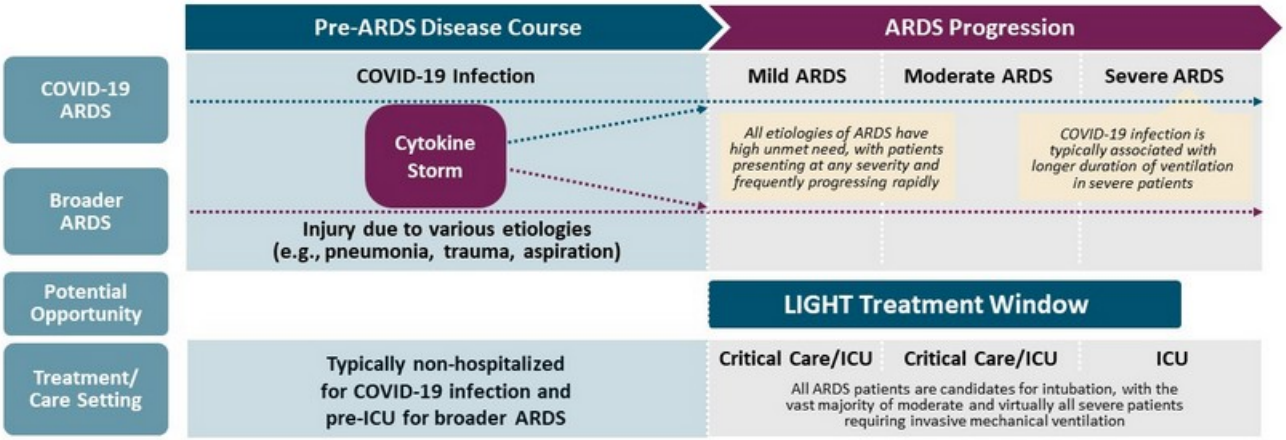
1. Perlin DS et al. *mSphere*. 2020;5(4):e00699-20. 2. Arunachalam PS et al. *Science*. 2020;369(6508):1210-1220.




avalo THERAPEUTICS

# Cytokine Storm Drives ARDS Across Etiologies

**Patients May Progress Rapidly and Often Require Invasive Mechanical Ventilation**




**Reducing LIGHT levels may limit the proportion of patients requiring invasive mechanical ventilation, which drives high cost of treatment and low quality of life in ARDS**

*Source:* Physician Interviews; Papazian L et al. *Ann Intensive Care* 2019;9(1):69; Bhatraju PK et al. *N Engl J Med*. 2020;382(21):2012-2022.




---

# AVTX-002 Treatment of Cytokine Storm-Induced COVID-19 ARDS

**Primary Endpoint: Respiratory Failure and Mortality Over 28 Days**

## Proof-of-Concept Trial Design

Randomized, Double-Blind, Placebo-Controlled, Multicenter, Proof-of-Concept Clinical Trial of AVTX-002 in Adults With COVID-19 ARDS

### Inclusion Criteria

Hospitalized patients with documented COVID-19 infection and clinical evidence of pneumonia with mild to moderate ARDS

**Enrollment (N=83)**

**1:1 Randomization**

- AVTX-002 (16 mg/kg [max. 1200 mg]) on Day 1 by SQ injection + Standard of Care at the site
- Placebo-matched SQ injection + Standard of Care at the site

### Primary Endpoint

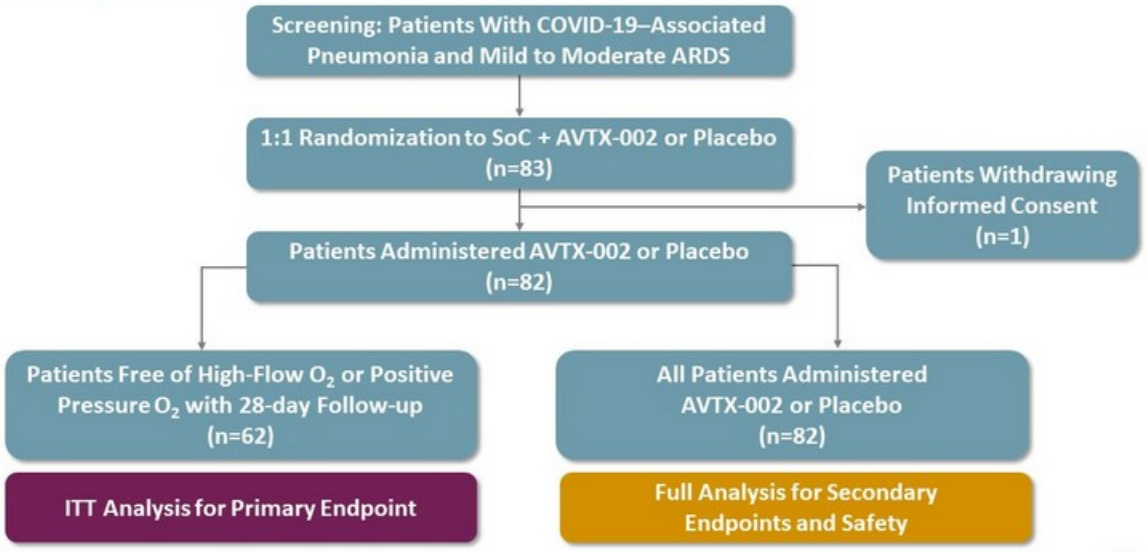
- Proportion of patients treated with AVTX-002 compared with placebo in addition to standard of care at site, alive and free of respiratory failure over 28 days
- 80% power to show an absolute difference of 25% between cohorts

### Key Secondary / Exploratory Endpoints

- 1-month mortality
- Change in $PaO_2/FiO_2$ ratio
- Time to and duration of invasive ventilation
- LIGHT levels and other biomarkers of inflammation
- Viral load

$PaO_2$, partial pressure of oxygen, $FiO_2$, fraction of inspired oxygen.

# Patient Disposition




ITT, intent-to-treat; SoC, standard of care.

*Source:* Data on file, Avalo Therapeutics, Inc.

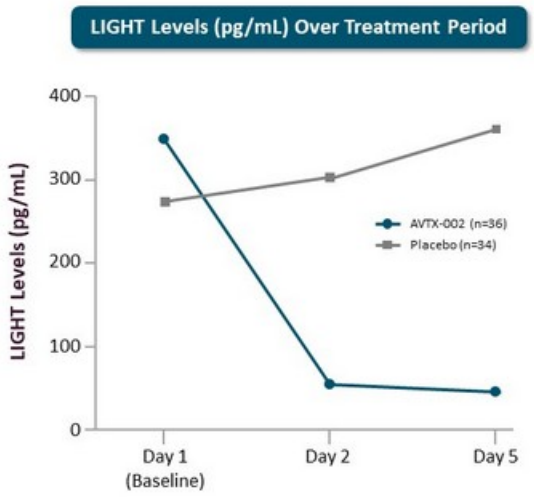



# Patient Demographics

| Characteristic | AVTX-002 (n=41) | Placebo (n=42) |
|---|---|---|
| Age (yrs), mean (SD) | 59.2 (14.5) | 58.1 (14.2) |
| Age Group, n (%) | | |
| <60 yrs | 20 (48.8) | 21 (50.0) |
| ≥60 yrs | 21 (51.2) | 21 (50.0) |
| Gender, n (%) | | |
| Male | 25 (61) | 32 (76.2) |
| Female | 16 (39) | 10 (23.8) |
| Race, n (%) | | |
| White | 31 (75.1) | 37 (88.1) |
| Black or African American | 7 (17.1) | 3 (7.1) |
| Asian | 2 (4.9) | 0 (0) |
| Other | 1 (2.4) | 2 (4.8) |
| Free LIGHT Level at Baseline (pg/mL), mean (range) | 329 (22–1050) | 276 (37–843) |
| Concomitant Medication Use at Baseline, n (%) | | |
| Systemic corticosteroids | 37 (90.2) | 36 (85.7) |
| Remdesivir | 21 (51.2) | 27 (64.3) |

*Source:* Data on file, Avalo Therapeutics, Inc.

# A Single Dose of AVTX-002 Reduced LIGHT Levels Dramatically and Rapidly




- Mean LIGHT levels were comparable at baseline across cohorts
- Mean LIGHT levels were ~100 pg/mL higher in patients aged ≥60 years
- LIGHT levels declined rapidly in the active cohort and increased in the placebo cohort
- Pharmacodynamic effect was in addition to standard of care
  - Approximately 90% of patients received systemic corticosteroids

**Rapid and significant reduction in LIGHT levels after a single SQ dose (16 mg/kg)**

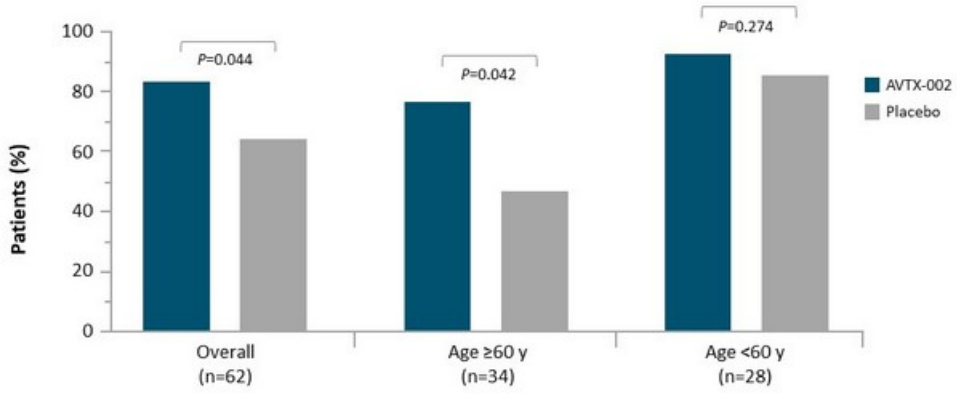
*Source:* Perlin DS et al. CERC-002, a human anti-LIGHT mAb reduces respiratory failure and death in hospitalized COVID-19 ARDS patients (https://medrxiv.org/cgi/content/short/2021.04.08.21254748v1).




avalo THERAPEUTICS

# AVTX-002 Significantly Reduced Respiratory Failure and Mortality

**Primary Endpoint: Percentage of Patients Alive and Free of Respiratory Failure at Day 28**




**Efficacy was highest in patients aged ≥60 years* (n=34, *P*=0.042), the population most vulnerable to severe complications and death with COVID-19 infection**

*Prespecified analysis.

*Source:* Data on file, Avalo Therapeutics, Inc.




avalo THERAPEUTICS

# A Single Dose of AVTX-002 Reduced Mortality by ~50%

| | AVTX-002 | Placebo |
|---|---|---|
| 28-day Mortality | 7.7% | 14.3% |
| 60-day Mortality | 10.8% | 22.5% |

- A trend in ~50% reduction in mortality was observed at both the 28-day and 60-day timepoints
- Efficacy observed is on top of corticosteroids and standard of care
  - ~88% of patients in the trial received corticosteroids and ~58% received remdesivir

*Source:* Data on file, Avalo Therapeutics, Inc.




# Safety and Tolerability

- AVTX-002 was well-tolerated at a single dose of 16 mg/kg
- No serious adverse events (SAEs) attributable to AVTX-002
- Majority of adverse events (AEs) judged to be mild or moderate
- No evidence of increased infections or AEs related to immunosuppression

| | AVTX-002 (n=40) | Placebo (n=42) |
|---|---|---|
| Subjects with ≥1 AE, n (%) | 16 (40) | 21 (50) |
| Subjects with ≥1 drug-related AE, n (%) | 8 (20) | 6 (14.3) |
| AEs >5%, n (%) | | |
| Leukocytosis | 6 (15) | 4 (9.5) |
| Anemia | 4 (10) | 3 (7.1) |
| Hepatic enzyme increase | 4 (10) | 2 (4.8) |
| Acute kidney injury | 3 (7.5) | 2 (4.8) |
| Respiratory failure | 3 (7.5) | 3 (7.1) |

*Source:* Data on file, Avalo Therapeutics, Inc.

# Broader ARDS Target Populations

**COVID-19 ARDS Provides Potential Path to Treat a Larger Patient Population in Broader ARDS**

**Annual US ARDS Incidence (non-COVID)**


Historically, ARDS has been underdiagnosed due to lack of physician awareness of the wide range of underlying causes – particularly for mild to moderate disease

Prior to the pandemic, it is estimated that the number of diagnosed ARDS cases may have only represented about half of the true incidence due to limited physician experience triaging patients with acute respiratory failure

Looking forward, the COVID-19 pandemic experience will likely significantly increase physician awareness and ability to accurately diagnosis less severe forms of ARDS

**There is a high unmet need for effective therapy in cytokine storm–induced ARDS beyond COVID-19**

CAGR, compound annual growth rate.

*Sources:* Eworuke E et al. *J Crit Care*. 2018;47:192-197; Bellani G et al. *JAMA*. 2016;315(8):788-800; Rubenfeld GD et al. *N Engl J Med*. 2005;353(16):1685-1693; UpToDate; Physician Interviews; ClearView Analysis 2021.




# AVTX-002 Clinical Program

**Next Steps**

- **Crohn's Disease**
  - Further evaluation of cohort data, including tissue LIGHT levels
  - Cohort 2 (3 mg/kg dose) fully enrolled; complete data anticipated in 2H 2021
- **Ulcerative Colitis**
  - Expand clinical study to patients with moderate to severe UC refractory to anti-TNFα*
- **ARDS Program**
  - Continuing dialogue with FDA to determine registration trial design and timing, including potential expansion to broader ARDS patient population
- **Exploring additional indications for disease in which LIGHT is a driver of inflammation**

*TNFα, tumor necrosis factor alpha.

# AVTX-007

## Phase 1b anti-IL-18 monoclonal antibody for Multiple Myeloma and Still's Disease (AOSD and sJIA)

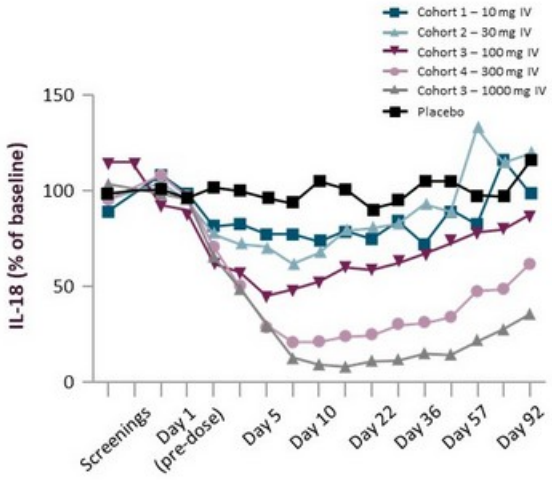
avalo THERAPEUTICS




# First-in-Class Anti-IL-18 High-Affinity Monoclonal Antibody

**Data From Phase 1 Study Demonstrated Favorable PK and Safety Profile**

- In-licensed from Medimmune/AstraZeneca
- Potent and durable IL-18 inhibition
  - Evaluated in Phase 1 SAD* for COPD* (n=31)
  - IV* doses of 10, 30, 100, 300 or 1000 mg
  - Well tolerated
- Phase 1b asset
  - 13-week monkey toxicity completed
  - Frozen, unformulated bulk material available to support clinical proof-of-concept in patients and nonclinical 6-month chronic toxicity studies




*COPD, chronic obstructive pulmonary disease; IV, intravenous; PK, pharmacokinetic; SAD, single ascending dose.

*Source:* Data on file, AstraZeneca.

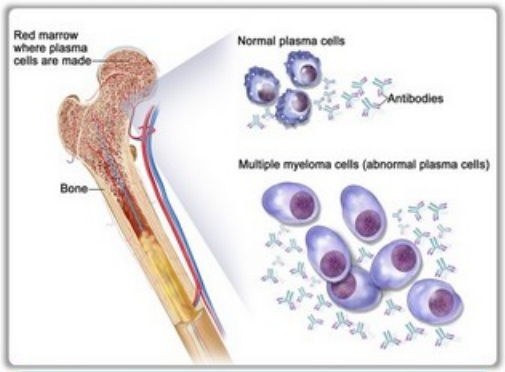



avalo THERAPEUTICS

# Multiple Myeloma: Second Most Common Blood Cancer Globally

**Characterized by Neoplastic Proliferation of Plasma Cells With Overproduction of Monoclonal Proteins (M-proteins)**

## Multiple Myeloma (MM) Pathophysiology




**Progressive disease with both cell-autonomous genetic abnormalities and microenvironmental changes contributing to growth of the malignant neoplasm[2]**

## Disease Overview

| | |
|---|---|
| **Patient Population** | • Prevalence in US ~140,000[1]<br>• Occurs in older people (median age at diagnosis, 69)[1]<br>• 35% of patients are younger than 65[1] |
| **Signs and Symptoms** | • Majority may present with anemia, bone pain, or elevated creatinine, while fatigue, hypercalcemia, and weight loss observed in a minority of patients[2] |
| **Treatment Approach** | • Treated with at least one of three main classes of agents, utilized in combination across all lines of therapy[3]:<br>– Immunomodulators – Revlimid®, Pomalyst®<br>– Protease inhibitors – Velcade®, Kyprolis®<br>– Anti-CD38 – Darzalex®, Sarclisa® |
| **Prognosis** | • Estimated 5-year survival is ~50% in the US, though specific genetic deletions such as 17p may be associated with shorter survival[1] |

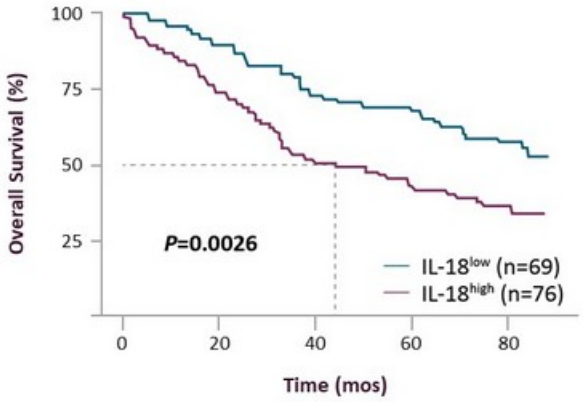
1. NCI SEER. Cancer statfacts: myeloma. https://seer.cancer.gov/statfacts/html/mulmy.html. Accessed July 22, 2021. 2. Palumbo A et al. *N Engl J Med*. 2011;364(11):1046-1060. 3. ClearView Analysis 2020.




avalo THERAPEUTICS

# Strong Potential in Multiple Myeloma

**IL-18 Levels Are Elevated in Many Multiple Myeloma Patients and Correlate With Poor Survival**




- Patients with high IL-18 have significantly worse median survival (42 mo vs >84 mo; *P*=0.0026; HR*, 1.84)
- Reducing IL-18† levels prolongs survival in rodent models of multiple myeloma

*HR, hazard ratio; †IL, interleukin.

*Source*: Nakamura K et al. *Cancer Cell*. 2018;33(4):634-648.e5.




avalo THERAPEUTICS

# AVTX-007 Treatment of Resistant and Refractory Multiple Myeloma

**Initiating Trial in Multiple Myeloma as a Single Agent With Plans for Combination**

**Dose Escalation and Expansion Trial Design**

Multicenter, Open-Label, Dose-Escalation Phase 1b Study of AVTX-007 in Subjects With Relapsed or Refractory Multiple Myeloma

**Inclusion Criteria**

Treatment-resistant and refractory multiple myeloma with exposures to IMiDs*, proteasome inhibitors, and anti-CD38 mAb

No more than 4-6 lines of therapy

**Estimated Enrollment**

Dose Escalation Phase ~14

Expansion Phase = 14

AVTX-007: Dose Escalation Phase 3 + 3 Design → AVTX-007: Expansion Phase at RP2D N = 14

**Primary Endpoint**

- Establishment of RP2D† in Dose Escalation Phase
- Response rate by International Myeloma Working Group criteria at 8 weeks in Expansion Phase

**Key Secondary / Exploratory Endpoints**

- Change in SPEP‡ from baseline
- Safety and tolerability
- Change in IL-18§ levels in blood and bone marrow
- Change in myeloid-derived suppressor cells in bone marrow from baseline to 8 weeks

**Initial cohort successfully completed 1Q 2021**
**Proof-of-concept top line data anticipated 2H 2021**

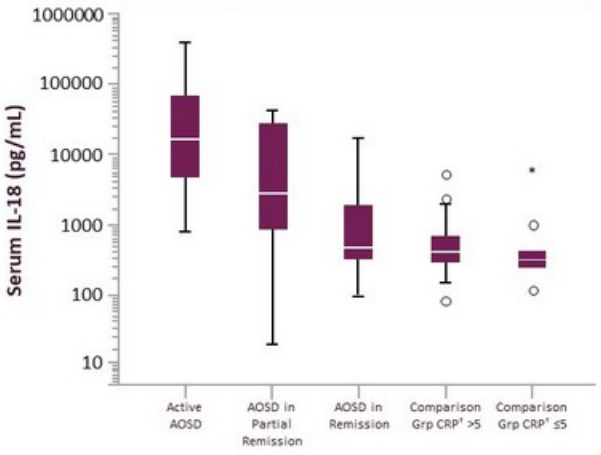
*IMiD, immunomodulatory drug; †RP2D, recommended phase 2 dose; ‡SPEP, serum protein electrophoresis; §IL, interleukin.




# Adult-Onset Still's Disease (AOSD) Overview

- Rare disease with estimated US diagnosed prevalence of 3,500 to 7,000[1]
- Symptoms include fever, rash, pharyngitis, arthritis, liver disease, increased ferritin
- No definitive genetic or infectious cause
- ~40% have severe chronic disease[2]
- Treatment: NSAIDs‡, steroids, immunosuppressants and anti-IL-1

**Serum IL-18* Levels Significantly Elevated in AOSD Patients[3]**



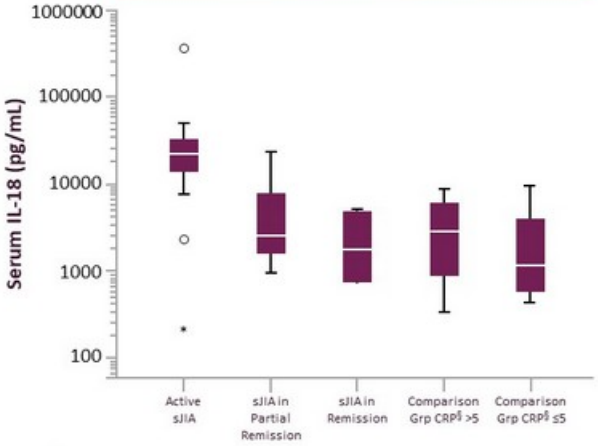

*IL, interleukin; †CRP, C-reactive protein; ‡NSAID, nonsteroidal anti-inflammatory drug.

1. ClearView Healthcare Partners Analysis, May 2017. 2. Gerfaud-Valentin M et al. *Autoimmun Rev*. 2014;13(7):708-722. 3. Kudela H et al. *BMC Rheumatol*. 2019;3:4.

# Systemic Juvenile Idiopathic Arthritis (sJIA) Overview

- Rare childhood-onset disease with estimated US diagnosed prevalence of 4,500 to 6,500[1]
- Intermittent fever, rash, and arthritis; often splenomegaly, lymph nodes
- Autoinflammatory disease – not autoimmune
  - *IL-1, IL-6, IL-18 other cytokines important in the pathogenesis
- Treatment: NSAIDs†, DMARDs‡, and targeted therapies (anti-IL-1 and anti-IL-6)
  - Significant number of refractory patients

**Serum IL-18 Levels Significantly Elevated in sJIA Patients[2]**




*IL, interleukin; †NSAID, nonsteroidal anti-inflammatory drug; ‡DMARD, disease-modifying anti-rheumatic drug; §CRP, C-reactive protein.

1. ClearView Healthcare Partners Analysis, May 2017. 2. Kudela H et al. *BMC Rheumatol*. 2019;3:4.



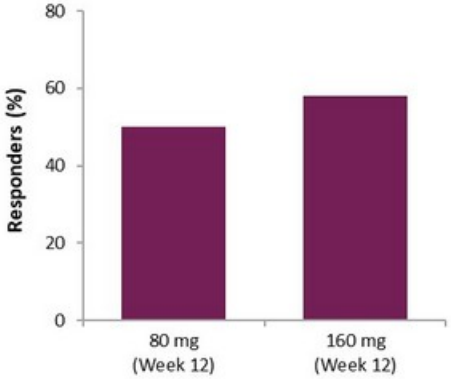

avalo THERAPEUTICS

# Proof-of-Concept Clinical Data

**IL-18* Binding Protein Demonstrates Response in Over 50% Treated Patients With AOSD**

- AB2 Bio clinical proof-of-concept in AOSD (n=23) using IL-18 binding protein ($t_{½}$† = 40 h)
  - >50% of AOSD patients treated with IL-18 binding protein achieved response
- Serum IL-18 correlates with disease severity
  - 4/4 patients with undetectable serum IL-18 had a clinical response

**IL-18 Binding Protein Response Rates**




Subcutaneous administration of 80 mg or 160 mg 3 times weekly.

Response defined as an improvement of joint count (both Swollen Joint Count [SJC] and Tender Joint Count [TJC] according to a 44-joint assessment) by ≥20% from baseline values, and a 70% decrease of CRP levels compared with baseline values (or reduction to normal levels) or normalization of ferritin.

*IL, interleukin; †$t_{½}$, elimination half-life.

Gabay C et al. *Ann Rheum Dis*. 2018;77(6):840-847.




avalo THERAPEUTICS

# AVTX-007 Treatment of Adult-Onset Still's Disease

**Potential Best-in-Class and First-in-Class Anti-IL-18* mAb**

## Proof-of-Concept Trial Design

Multicenter, Phase 1b Study of AVTX-007 in patients with active adult-onset Still's disease

### Inclusion Criteria

- Active AOSD as measured by high fever, elevated CRP and ferritin
- Failed on NSAIDS and corticosteroids

**Estimated Enrollment: N=12**

**12 weeks**

AVTX-007 7 mg/kg (max 500 mg) q4wks (n=6)

**12 weeks**

AVTX-007 14 mg/kg (max 500 mg) q4wks (n=6)

### Primary Endpoint

- Reduction in CRP† by ≥50% and elimination of fever for >48 hours

### Key Secondary / Exploratory Endpoints

- Change from baseline DAS‡ score, modified Pouchet score, and DAS-CRP
- Change in CRP, ferritin, and ESR§
- Change in IL-18 levels
- Safety and tolerability

**AOSD initial data anticipated 4Q 2021**

*IL, interleukin; †CRP, C-Reactive Protein; ‡DAS, Disease Activity Score; §ESR erythrocyte sedimentation rate.




avalo THERAPEUTICS

# AVTX-006

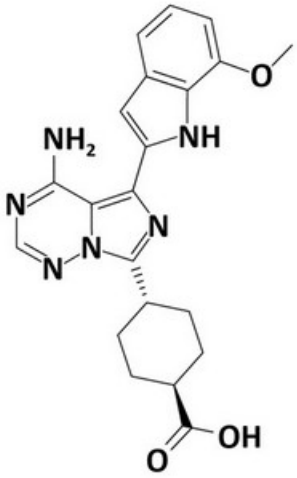
## Phase 2-ready, dual mTORC 1/2 small-molecule inhibitor for Complex Lymphatic Malformations

avalo THERAPEUTICS

# High-Potency, Second-Generation, Dual Inhibitor of mTORC1/2

**Potential for Improved Efficacy and Tolerability**

- In-licensed from Astellas
- Phase 2–ready asset
  - 4-week nonclinical tox studies completed
  - Previously studied in Phase 1 MAD* (n=128)
  - Development discontinued upon determination that target efficacious doses were above MTD† (30mg QD)[1]
  - Significantly lower doses than MTD likely required to treat complex lymphatic malformations
- Dual mTOR‡ inhibitor maximizes impact of mTOR blockade, as mTORC2 is insensitive to rapalogs
  - Orally available, ATP-competitive kinase inhibitor§
  - $IC_{50}$¶ = 22 nM and 65 nM for mTORC1 and mTORC2, respectively[2]




*MAD, multiple ascending dose; †MTD, maximum tolerated dose; ‡mTOR, mammalian target of rapamycin; §ATP, adenosine triphosphate; ¶IC, half maximal inhibitory concentration.

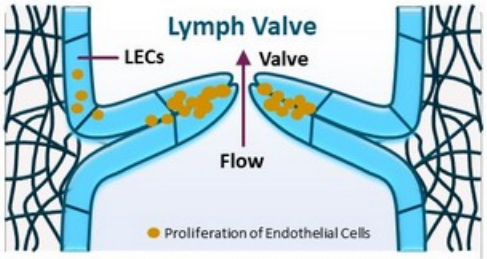
1. Mateo J et al. *Br J Cancer*. 2016;114(8):889-896. 2. Bhagwat SV et al. *Mol Cancer Ther*. 2011; 10(8):1394-1406.



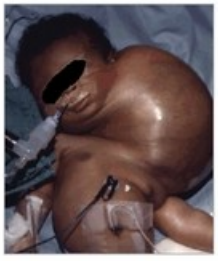

# Complex Lymphatic Malformations:

## Family of Potentially Life-Threatening Congenital Diseases

- Neoplastic lesions caused by mutations in PI3K/AKT/mTOR pathway
- Leads to local proliferation of lymphatic endothelial cells and perturbation of lymph flow




- Fluid accumulation in limbs, abdomen, and chest which can lead to major disability and death
- Complex lymphatic malformations are not readily treatable by sclerosing agents or surgery many times due to their complexity and location



*Source*: Figure adapted from Brouillard P et al. *J Clin Invest*. 2014;124(3):898-904.

# Off-Label Use of mTOR Inhibitor Sirolimus in Lymphatic Malformations

**Open-Label Clinical Studies Support Efficacy; Use Is Limited by Tolerability Issues and Lack of FDA Approval**

- Phase II trial enrolled patients with complicated vascular anomalies
  - Enrolled patients with different subtypes of lymphatic malformations not controlled by previous medication, sclerotherapy, and/or surgery
  - Sirolimus was administered orally for 12 courses of 28 days each
  - 57 patients were evaluable for efficacy at the end of course 6, and 53 were evaluable at the end of course 12
- Safety and tolerability profile leads to low compliance, requires frequent monitoring
  - Physicians reported that sirolimus caused high rates of stomatitis (~60%)
  - Sirolimus bears black box warning for immunosuppression and malignancies

| Overall Response | 6-month (n=57) | 12-month (n=53) | Grade 2 or >AEs |
|---|---|---|---|
| Complete response | 0 | 0 | • Blood/bone marrow (50%)<br>• Gastrointestinal (55%)<br>• Metabolic/laboratory (20%)<br>• Infection (15%) |
| Partial response | 47 (83%) | 45 (85%) | |
| Progressive disease | 7 (12%) | 8 (15%) | |
| Stable disease | 3 (5%) | 0 | |

*Source:* Adams DM et al. *Pediatrics*. 2016;137(2):e20153257.




# AVTX-006 Treatment of Complex Lymphatic Malformations

**Dual mTOR Inhibitor to Modulate PI3K* and AKT† Activity**

**Proposed Phase 1b Study**

Multicenter, Phase 1b Study of AVTX-006 in patients with complex lymphatic malformations

**Inclusion Criteria**

Adults 18-31 years with moderate to severe complex lymphatic malformations

**Estimated Enrollment: N=10**

**AVTX-006 two dose groups:**
**0.5 mg and 1mg twice daily**
**4-week treatment**

**Primary Endpoint**

- Safety and tolerability of AVTX-006

**Key Secondary / Exploratory Endpoints**

- PK and PD characteristics of AVTX-006
- Evidence of clinical signals utilizing quality of life and radiologic evaluation
- Clinical and laboratory safety assessments
- Selected biomarkers

**Initial data anticipated 4Q 2021**

*PI3K, phosphatidylinositol 3-kinase; †AKT, protein kinase B.

# AVTX-800s

## Monosaccharide therapy for Congenital Disorders of Glycosylation (CDGs)

avalo THERAPEUTICS




## Congenital Disorders of Glycosylation (CDGs):
### Life-Threatening, Ultra-Rare Disease

**Impaired Glycoprotein Production and Function Restored With Therapeutic Dose of Monosaccharide Therapies**

- Glycosylation is essential for protein structure & function, particularly for circulating proteins and enzymes such as hormones and coagulation factors
- Currently approximately 150 CDGs identified
- Due to a genetic mutation, CDG patients lack the ability to synthesize functioning glycoproteins
- Life-threatening multi-system diseases: failure to thrive, developmental delay, hypotonia, neurologic abnormalities, hepatic disease, and coagulopathy
- Administration of therapeutic doses of specific monosaccharides targeted to specific CDGs can partially restore impaired glycoprotein production resulting in a meaningful clinical benefit
  - PGM1-CDG: D-galactose supplementation[1]
  - MPI-CDG: D-mannose supplementation[2]
  - LAD-II (SLC35C1-CDG): L-fucose supplementation[3]

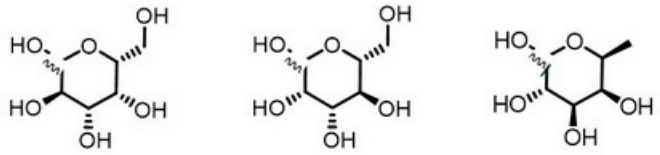
1. Wong et al. *Genet Med*. 2017;19(11):1226-1235. 2. Harms et al. *Acta Paediatr*. 2002;91(10):1065-1072. 3. Marquardt et al. *Blood*. 1991;94(12):3976-3985.

avalo THERAPEUTICS

# Pharmaceutical Grade Treatments for CDGs

**Opportunity to Be the First FDA-Approved Drugs for CDGs**

- Established therapeutic proof-of-concept
- GMP‡ manufacturing and FDA approval will ensure quality and consistency
- Potential for reimbursement



● D-Galactose ● D-Mannose ◄ L-Fucose

| | AVTX-801 | AVTX-802 | AVTX-803 |
|---|---|---|---|
| Accelerated pathway | ✓ | ✓ | ✓ |
| FDA ODD*§ | ✓ | ✓ | ✓ |
| Priority Review Voucher† | ✓ | ✓ | ✓ |
| Pivotal data anticipated | 2022 | 2022 | 1H 2022 |

*Designation makes AVTX-800 compound's respective CDG indication eligible for 7-year orphan exclusivity upon approval.
†All three AVTX-800 compounds granted Rare Pediatric Disease Designation prior to September 30, 2020; eligible for Priority Review Voucher upon approval.
‡GMP, Good Manufacturing Practices; §ODD, Orphan Drug Designation; RPDD; Rare Pediatric Disease Designation.




avalo THERAPEUTICS

# Key Financial Information

avalo THERAPEUTICS

# Financial & Investor Information

## Key Financial Highlights

**NASDAQ: AVTX**

**The following data is as of June 30, 2021**

- Outstanding common shares – ~96M
- Fully diluted shares – 114.8M
- Average daily trading volume – ~2M
- Cash – $40.4M*

**Preliminary unaudited cash balance as of August 31, 2021 is approximately $42M.*




avalo THERAPEUTICS

# Select Management Team Members

## Proven Track Record in Drug Development and Commercialization

**Michael Cola | Chief Executive Officer, Chairman of the Board**

- Former President of Specialty Pharmaceuticals, Shire plc
- Senior Management, AstraMerck and AstraZeneca plc

Shire
AstraZeneca

**Garry Neil, MD | Chief Scientific Officer**

- Former Corporate VP of Science & Technology, Johnson & Johnson
- Former Group President, Johnson & Johnson Pharmaceutical Research and Development
- Former VP of Clinical Research, AstraZeneca plc and Merck KGaA

Johnson & Johnson
MERCK

**H. Jeffrey Wilkins, MD | Chief Medical Officer**

- Former VP, Worldwide Clinical Research, Inflammation/Oncology at Cephalon and SVP of Clinical Development with Ception Therapeutics
- Former VP of Discovery Medicine for GSK's Center of Excellence in External Drug Discovery

Cephalon
CEPTION
gsk




avalo THERAPEUTICS


NASDAQ:AVTX
www.avalotherapeutics.com
avalo
THERAPEUTICS