Avalo Therapeutics, Inc.

(AVTX)

Corporate Presentation

March 2023

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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 **I**nducible expression, and competes with HSV **G**lycoprotein D for **H**VEM, 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 **P**oorly Controlled Non-**E**osinophilic **A**sthma **K**; **BTLA**, B and T Lymphocyte Attenuator, Ig superfamily checkpoint

Pipeline

Program	Mechanism of Action	Indication	Designation	Development Stage	Anticipated Milestone
Core Programs: Immune Dysregulation Disorders					
AVTX-002	Anti-LIGHT mAb	NEA	–		Phase 2 Topline Data 2Q 2023 *(Enrollment Complete)*
		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, L**ymphotoxin-like, exhibits **I**nducible expression, and competes with HSV **G**lycoprotein D for **H**VEM, a receptor expressed by **T** lymphocytes; **mAb,** monoclonal antibody; **NEA,** non-eosinophilic asthma; **ODD,** orphan drug designation; **RPDD,** rare pediatric disease designation

AVTX-002

Anti-LIGHT mAb

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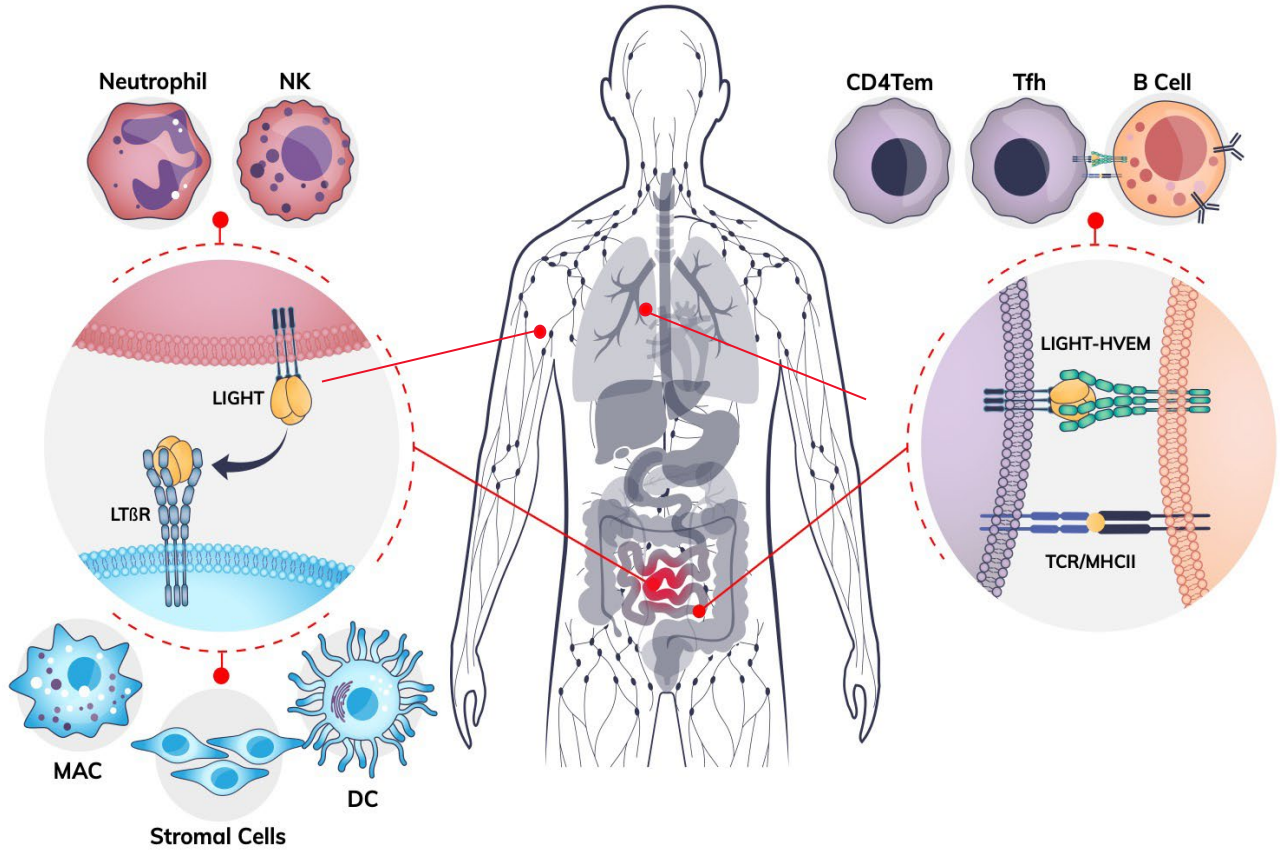
LIGHT is a Key Driver of Acute & Chronic Inflammation

- 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

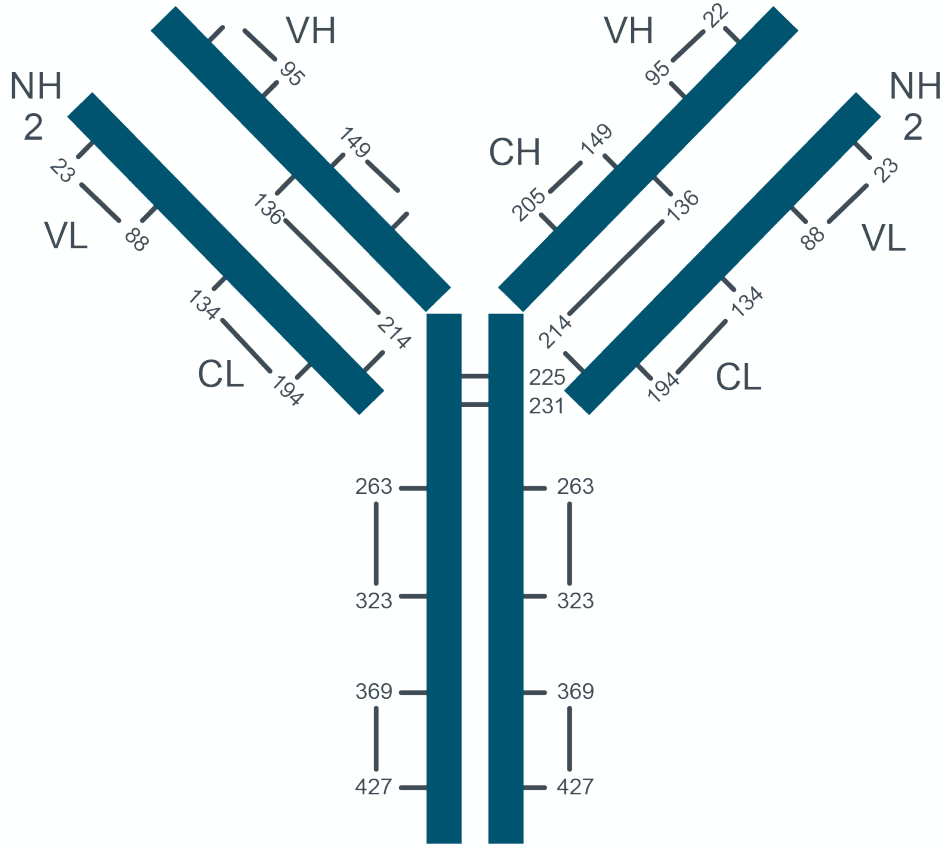


Ware, C., Croft, M., and Neil, G. *J.Exp Med.* 2022 Jul 4;219(7):e20220236. 10.1084/jem.20220236.

CD4Tem, CD4 effector-memory T cells; **DC,** dendritic cell; **HVEM,** herpes virus entry mediator; **LTβR,** 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

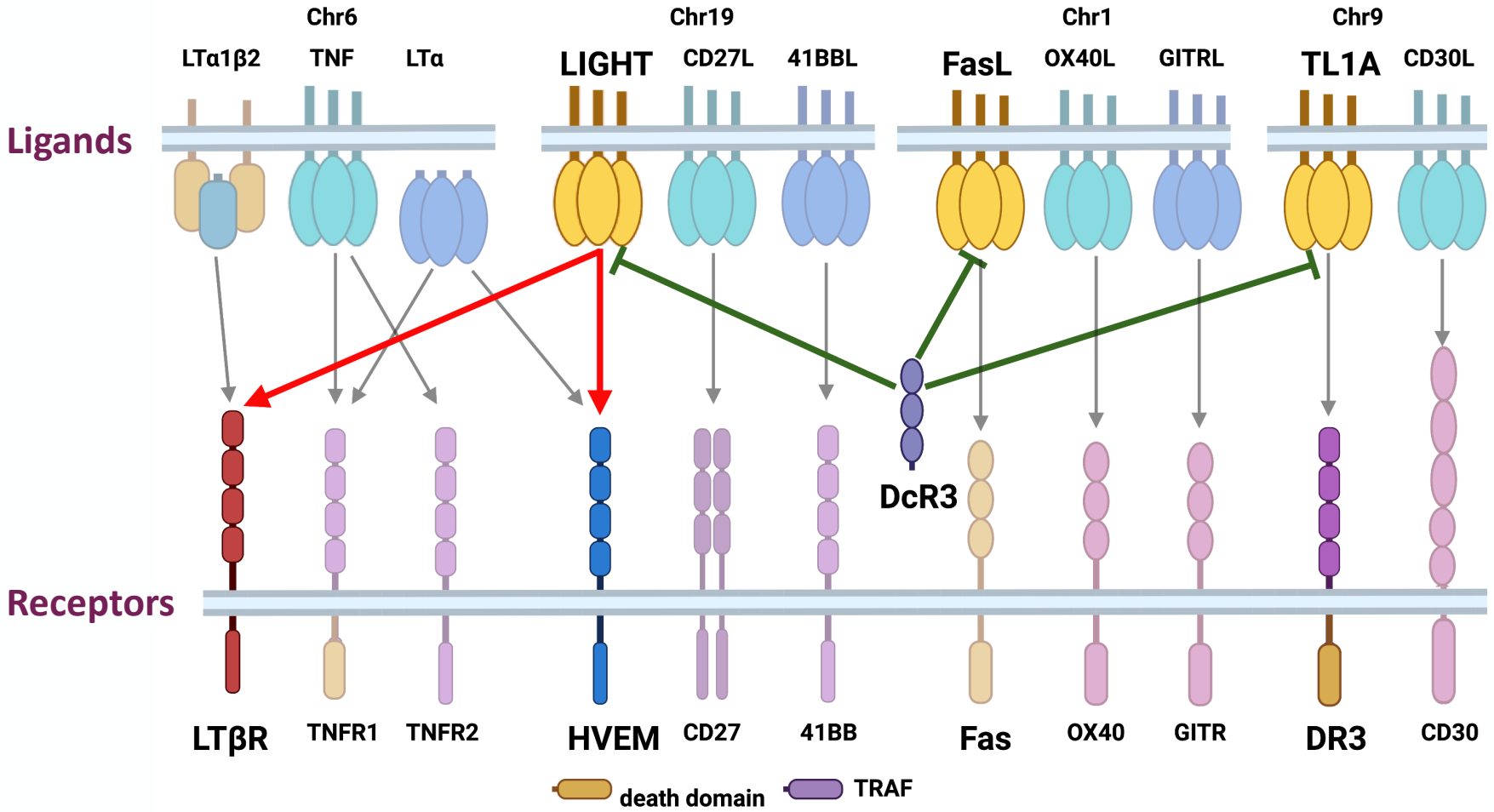
- Fully human monoclonal antibody to LIGHT
- CMC at 2,000 L scale; 6-month toxicology study near completion
- POC in two indications:
  - COVID-19 ARDS
  - Crohn's Disease
- Currently in Phase 2 (POC) for NEA
- Additional indications in immune dysregulation under consideration



CMC, Chemistry, manufacturing and control

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

Inflammation, Immunoregulation and Homeostasis



- LIGHT is a member of a select group of key immunomodulator cytokines (TL1A, FasL) that are "regulated" by Decoy Receptor 3 (DcR3)
- DcR3 loss of function has been associated with autoimmune diseases including Crohn's disease

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.

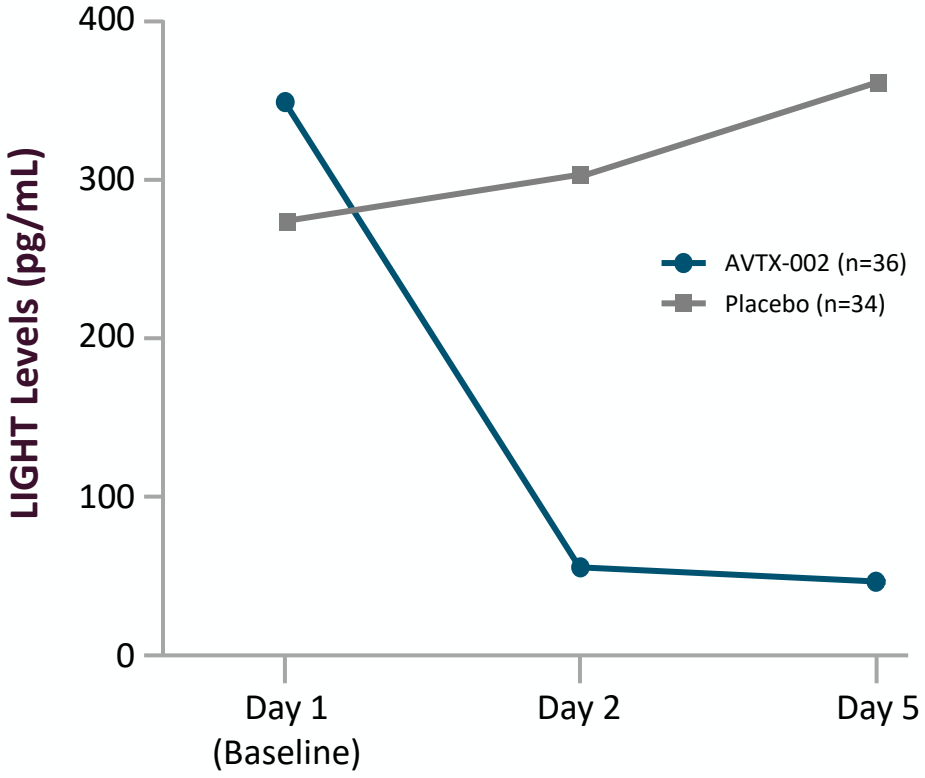
POC Demonstrated in Phase 2 COVID-19 ARDS Trial

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

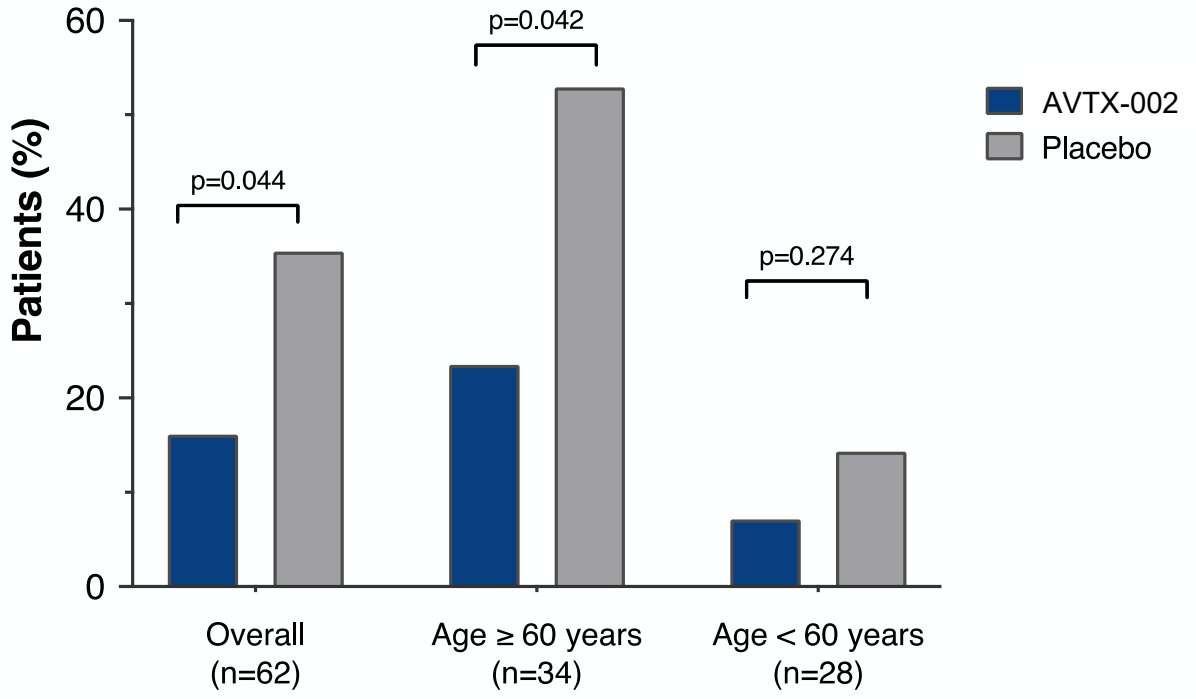
1. Perlin DS et al., Randomized, double-blind, controlled trial of human anti-LIGHT monoclonal antibody in COVID-19 acute respiratory distress syndrome. J. Clin. Invest. 2022

Significant Reduction in COVID-19 Induced Respiratory Failure and Mortality

LIGHT Levels (pg/mL) Over Treatment Period



Percentage of Patients with Respiratory Failure and/or Death by Day 28



Perlin, D. S. *et al.,* Randomized, double-blind, controlled trial of human anti-LIGHT monoclonal antibody in COVID-19 acute respiratory distress syndrome. *J Clin Invest* (2021) doi:10.1172/jci153173.

AVTX-002

Non-Eosinophilic Asthma

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Non-Eosinophilic Asthma

Patient Population

- US prevalence of asthma ≃ 25M[1]
- NEA accounts for ≃ 47% of asthma[2,3]
- Majority of patients with asthma remain uncontrolled[4]
- Higher need in underserved populations[1]

Signs and Symptoms[4]

- Asthma symptoms often more severe/resistant to treatment[5]
- Associated with smoking, pollution, infections, obesity[5]

Treatment Approach[4]

- Standard therapies for asthma; many NEA patients remain uncontrolled[6,7]
- Currently no approved targeted therapies for NEA

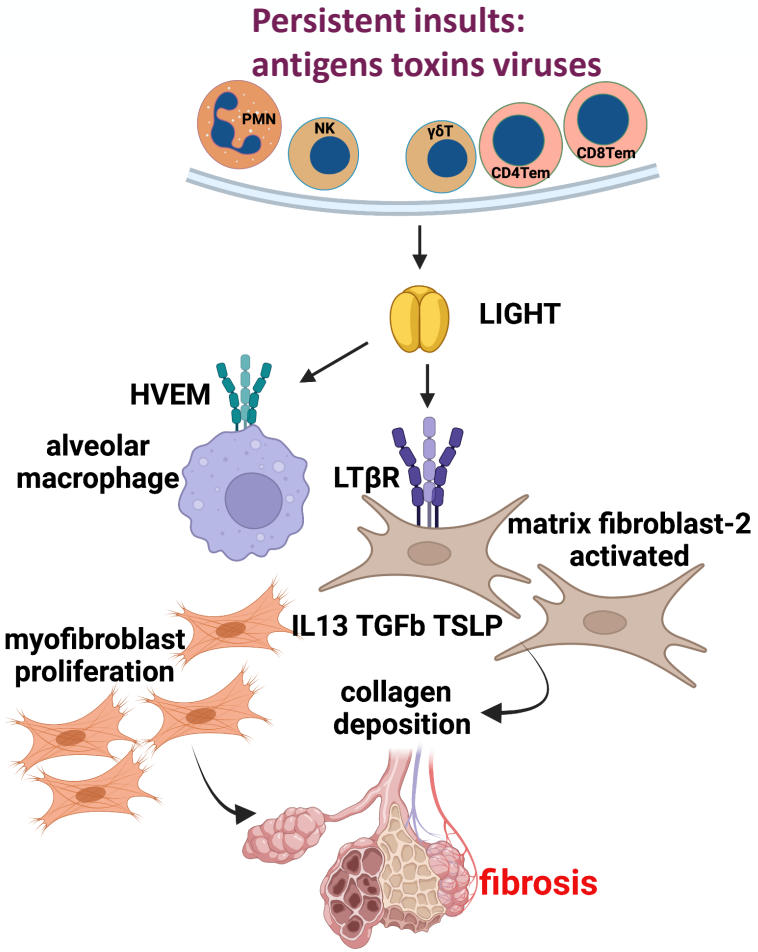
Rationale for AVTX-002

- Sputum LIGHT levels negatively associated with lung function (FEV and FVC) in asthma[8,9]
- Higher LIGHT levels in sputum in asthma patients with neutrophilia[8]
- Neutrophils have high, pre-formed LIGHT levels[10]

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 LTβR 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
  - LTβR 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 LTβR

*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

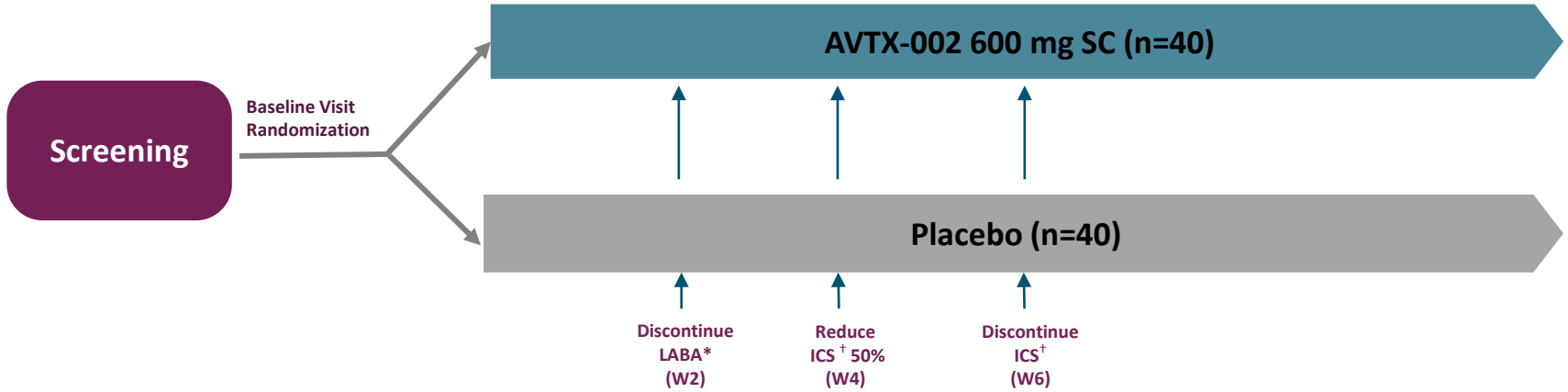
PEAK Trial

Phase 2, Randomized, Double-Blind, Placebo-Controlled, Parallel Group Trial of AVTX-002 in patients with NEA

Key Inclusion Criteria

- Poorly controlled asthma on LABA* and ICS †
- Exacerbation in the last 24 months
- Blood eosinophil count <300 cells/µL

Final Enrollment (n=91)



Primary Endpoint

- Proportion of patients who experience an asthma related event defined as:
  - ≥6 additional reliever puffs of SABA‡ (compared to baseline) in a 24-hour period on 2 consecutive days, or
  - Increase in ICS† dose ≥4 times than the dose at baseline or,
  - A decrease in peak flow of 30% or more (compared to baseline) on 2 consecutive days of treatment, or
  - An asthma exacerbation requiring the use of systemic corticosteroids (tablets, suspension, or injection) for at least 3 days, or
  - A hospitalization or emergency room visit because of an asthma exacerbation

Key Secondary/Exploratory Endpoints

- Change in FEV_1‡ from baseline
- Time to asthma related event
- Change in FeNO# from baseline
- Change in ACQ§ from baseline

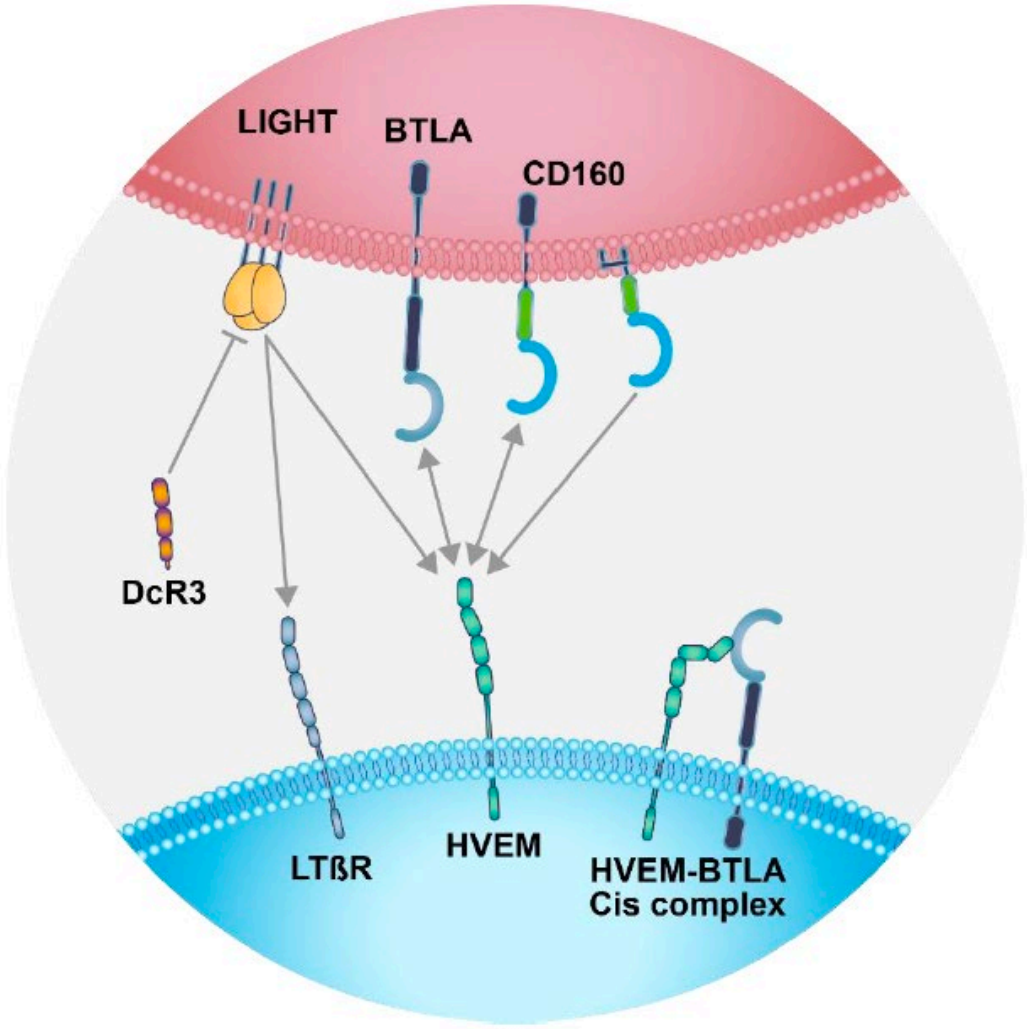
Enrollment Complete with Phase 2 Topline Data Expected 2Q 2023

***LABA,** long-acting beta-agonist; **†ICS,** inhaled corticosteroid; **‡SABA,** short-acting beta agonist; **‡FEV_1,** forced expiratory volume in 1 second; **#FeNO,** fractional exhaled nitric oxide; **§ACQ,** asthma control questionnaire.

LIGHT-Signaling Network & AVTX-008

BTLA agonist fusion protein

The LIGHT-Signaling Network: A Key Immunoregulatory System



Arrow heads refer to mono and bidirectional signaling

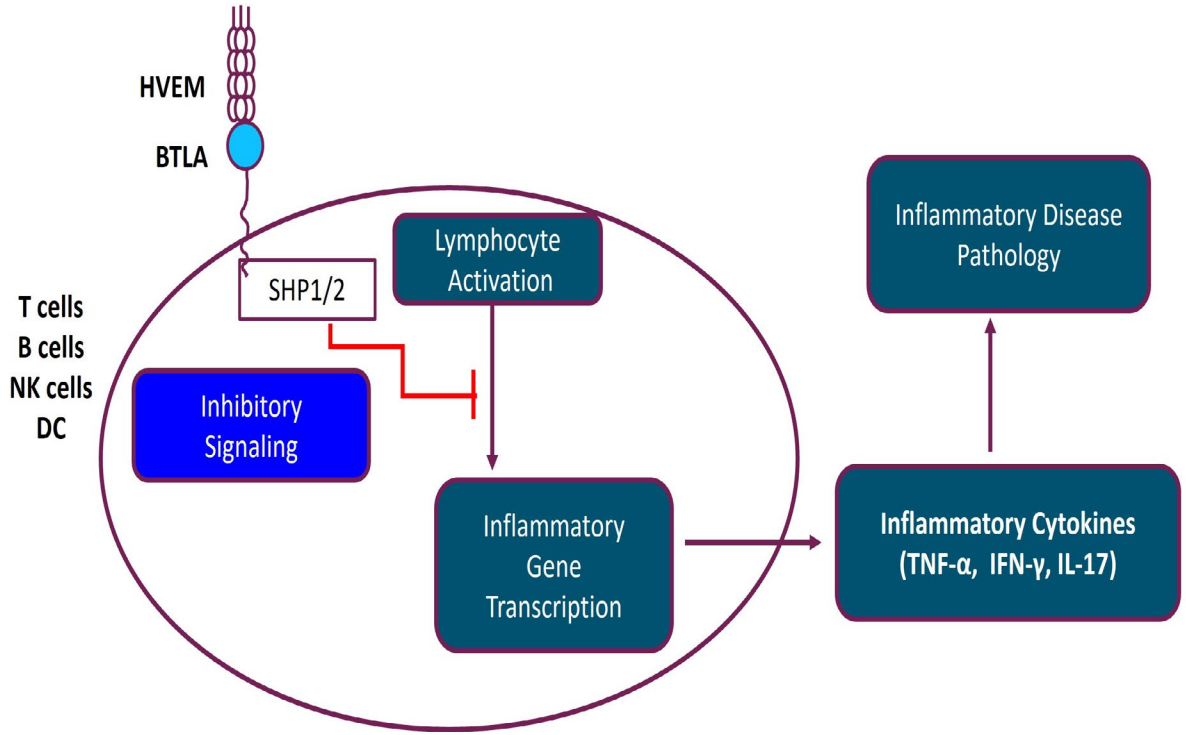
- BTLA - B and T lymphocyte attenuator (Ig superfamily checkpoint)
  - Co-expressed with HVEM in T and B cells
  - "Dampens" the immune response
- LIGHT activates HVEM
  - Inhibits BTLA signaling, allowing immune stimulation
- LIGHT activates LTβR
  - Activates dendritic cells, macrophages, stromal cells
  - 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

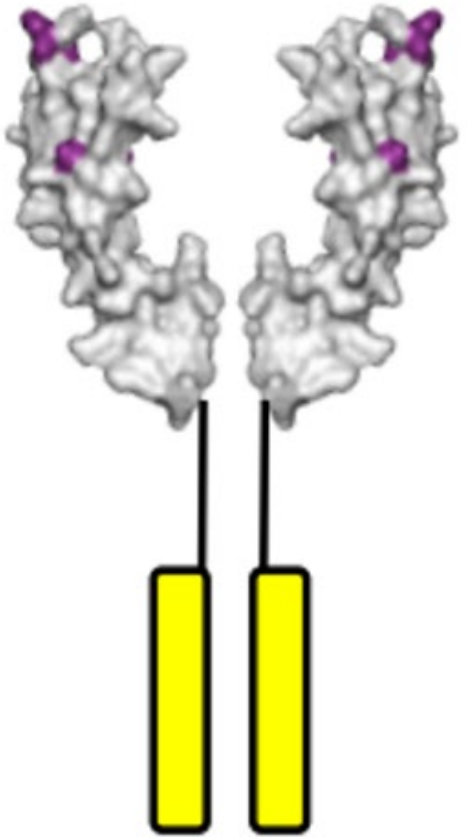
*Includes SHP-1 and SHP-2: **SHP-1,** sarcoma (SRC) homology 2 domain-containing protein tyrosine phosphatase 1; **SHP-2,** SRC homology 2 domain-containing protein tyrosine phosphatase 2

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

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

Sanford™ Burnham Prebys

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Finance Update

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 shares[3] – 11.3M[1, 2]
- Average daily trading volume – 17K

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

[2]On 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.

[3]Based 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

Chris Sullivan
Chief Financial Officer

Lisa Hegg, PhD
SVP, Program Management,
Corporate Infrastructure

Colleen Matkowski
SVP, Global Regulatory Affairs,
Quality Assurance

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

AstraZeneca

SUCAMPO
The Science of Innovation

aclaris
THERAPEUTICS

Takeda

ALEXION

Johnson & Johnson

OpGen

gsk
GlaxoSmithKline

BIOMARIN

ARENA
PHARMACEUTICALS

EY

FDA

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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)

Appendix

AVTX-803

Leukocyte Adhesion Deficiency Type II (LAD II, also known as SLC35C1-CDG)

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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

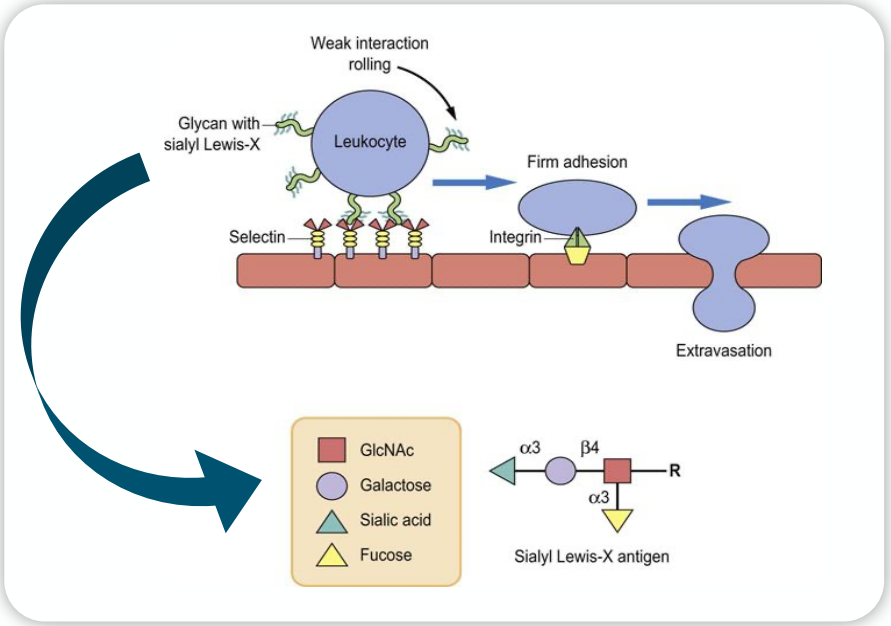
Diagnosis/ Evaluation

- 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

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

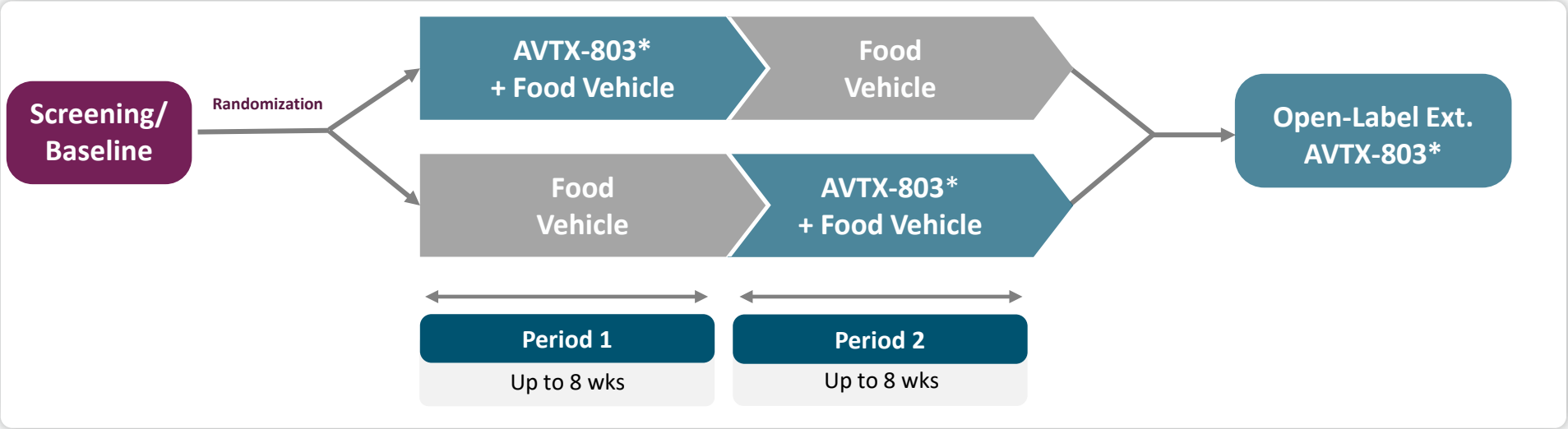
LADDER Trial Design

Single-Center (US), Double-Blind (plus Open-Label Extension) Pivotal Trial of AVTX-803 in patients with LAD II (SLC35C1-CDG)

Key Inclusion Criteria

- Known *SLC35C1* mutation
- Previous known response to fucose

Estimated Enrollment (n=2)



Primary Endpoint

- Restoration of sialyl Lewis X biomarker

Key Secondary/Exploratory Endpoints

- Leukocyte function assay
- Neutrophil counts

Pivotal Trial Data
Timing under evaluation

*100-340 mg/kg up to 5x/d based on clinical response

AVTX-002

TNF SuperFamily

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TNF SuperFamily: Proven Target-rich Opportunities

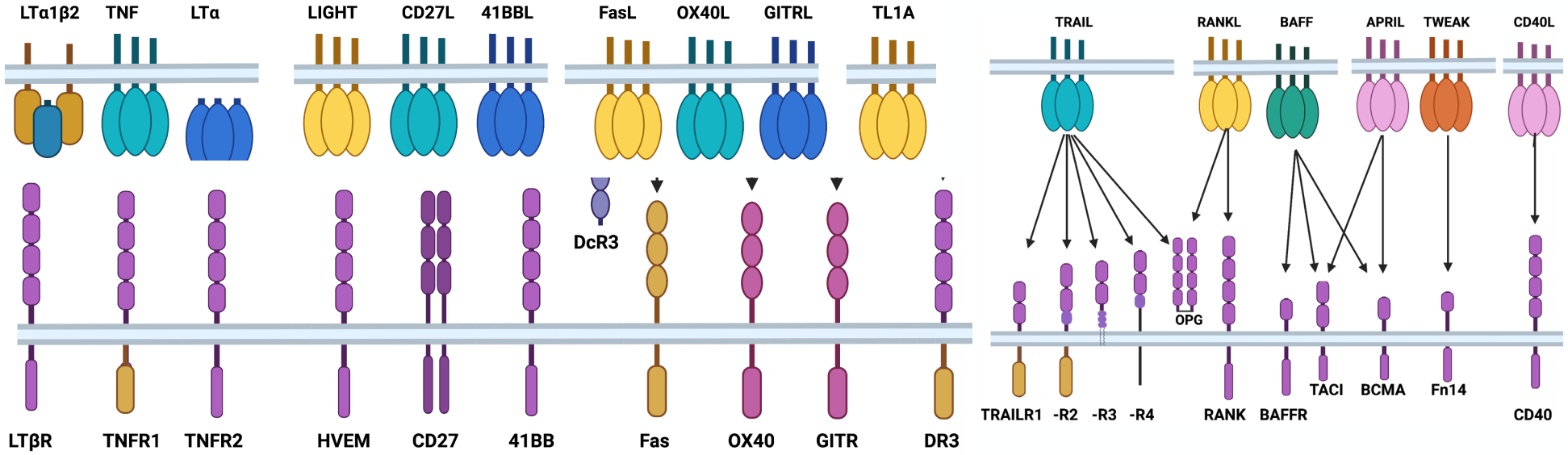
TNF inhibitors (Autoimmune)
Humira Cimzia Remicade
Simponi ENBREL

LIGHT inhibitor
AVTX-002

TL1A inhibitors
PRA023
PF-06480605

RANKL inhibitor
Prolia
osteoporosis

BAFF inhibitor
Benlysta



HVEM mimetics - BTLA agonists:
AVTX-008, LY3361237, MB272, ANB032

41BB signaling
CAR-T Cancer

OX40 agonists
Cancer

GITR antagonist
Treg modulation

TRAILR agonists
Cancer

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.

AVTX-002

Crohn’s Disease Phase 1b Proof of Concept Trial

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

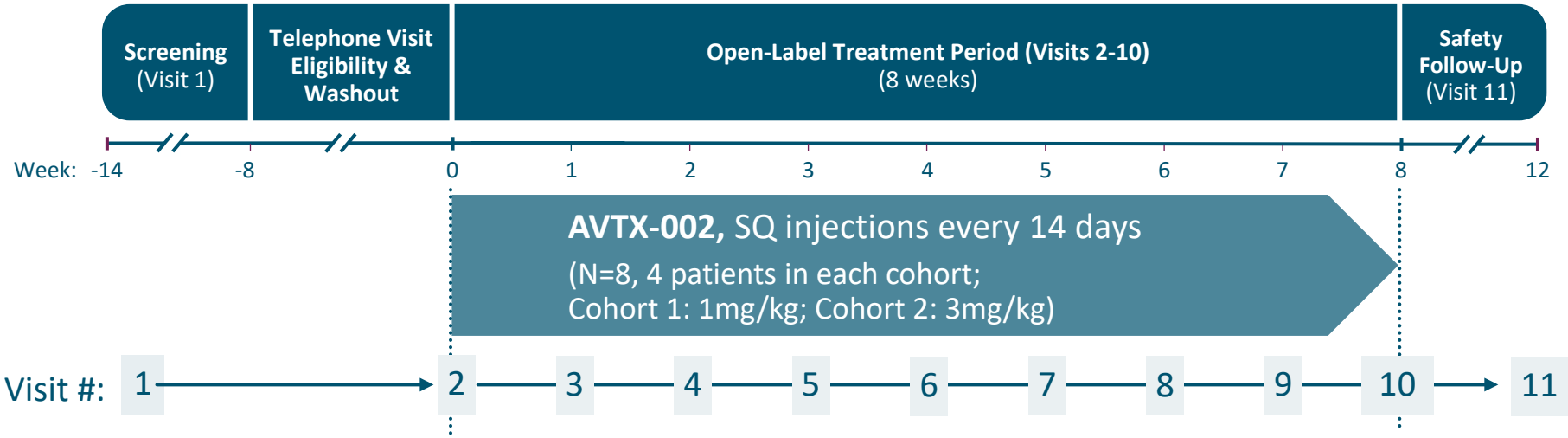
- Phase 1b Escalating Dose, Open-Label, Signal-Finding Trial to Evaluate the Safety, Tolerability, and Short-Term Efficacy of the Anti-Light Monoclonal Antibody AVTX-002 in Adults with Moderate to Severe Active Crohn's Disease (CD) who have Failed Prior Treatment with an Anti-TNFα Agent
- Rapid reduction 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]**TNFα**, tumor necrosis factor alpha; [†]**SES-CD**, Simple Endoscopic Score for Crohn's Disease

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

Phase 1b Proof of Concept Trial Design

Open-Label, Phase 1b POC 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 Objectives/Endpoints

- Safety
- Tolerability

Key Secondary/Exploratory Objectives/Endpoints

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

Inclusion Criteria

- Moderate-to-severe disease
- Anti-TNFα failure
- Heavily pre-treated patients
- Dose escalation starting at 1mg/kg every 2 weeks
- Short duration (8 weeks)
- SES-CD* score ≥7

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