Avalo Therapeutics, Inc. (AVTX)

Corporate Presentation

November 2024

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Forward-Looking Statements

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Executive Summary

AVTX-009 (anti-IL-1β mAb) has the potential for a best-in-disease profile in hidradenitis suppurativa (HS) with:

- Clinically validated and derisked MOA
- Highly potent anti-inflammatory properties with favorable half-life that may allow for improved efficacy and convenient dosing
- Favorable safety profile

Phase 2 LOTUS trial initiated

- Topline Data expected 2026

HS is anticipated to become a $10B market

AVTX-009 has the potential to treat multiple immune-mediated diseases

Expected cash runway into 2027

IL, interleukin; IND, investigational new drug application; mAB, monoclonal antibody; MOA, mechanism of action.

Avalo Management Team
175+ Years of Experience in Biotech/Pharma

A proven track record of successful leadership, product development, and commercialization in pharma and biotech

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

Mittie Doyle, MD
Chief Medical Officer

Chris Sullivan
Chief Financial Officer

Paul Varki
Chief Legal Officer

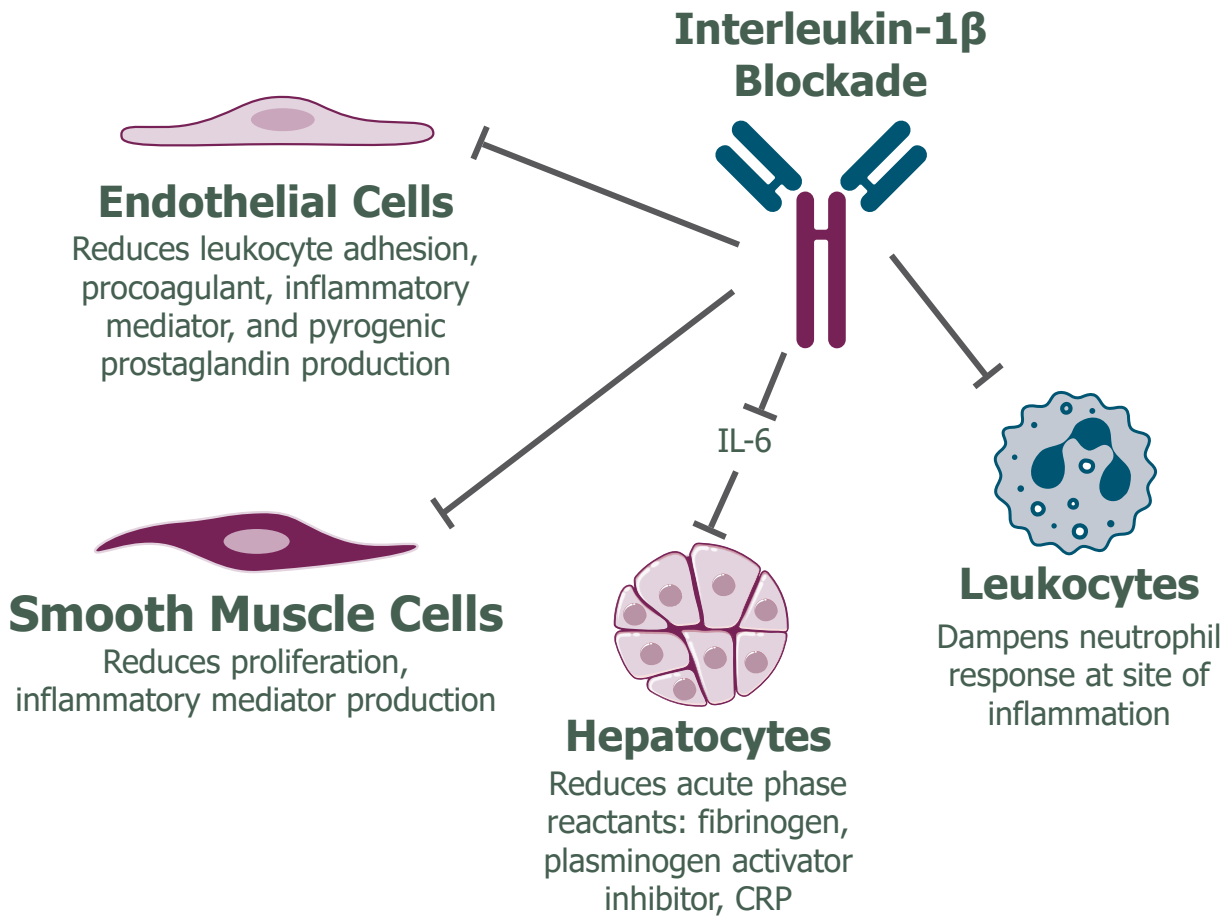
Colleen Matkowski
SVP, Global Regulatory Affairs,
Quality Assurance

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

Lisa Hegg, PhD
SVP, Program Management, Corporate
Infrastructure, Clinical Operations

IL-1β Is Increasingly Recognized as a Master Regulator of Inflammation

- IL-1β is a central driver of the inflammatory process[1] and activates immune cells that generate proinflammatory cytokines including:
  - IL-6
  - TNF-α
  - IL-17
- IL-1β is involved in the pathogenesis of many autoimmune and autoinflammatory diseases
- Inhibition of IL-1β has been shown to be effective and safe in a variety of inflammatory diseases, including hidradenitis suppurativa[1-3]



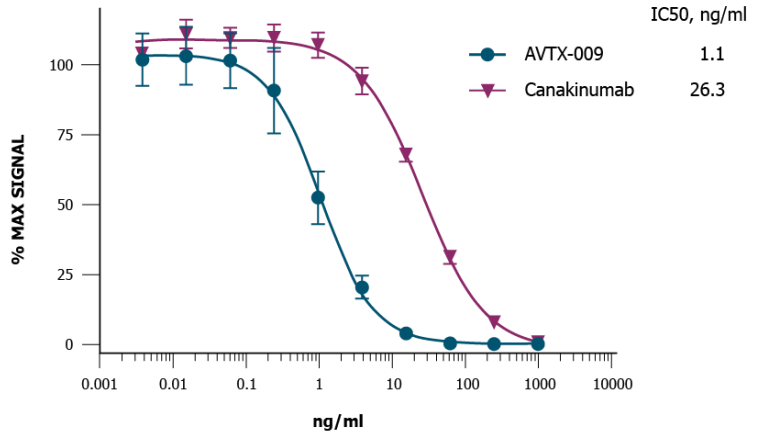
CRP, C-reactive protein; IL, interleukin; TNF, tumor necrosis factor.

1. Dinarello CA. *Immunol Rev*. 2018;281(1):8-27; 2. Kany S, et al. *Int J Mol Sci*. 2019;20(23):6008; 3. Kimball AB, Ackerman L, et al. Presented at: American Academy of Dermatology; March 8-12, 2024; San Diego, CA.

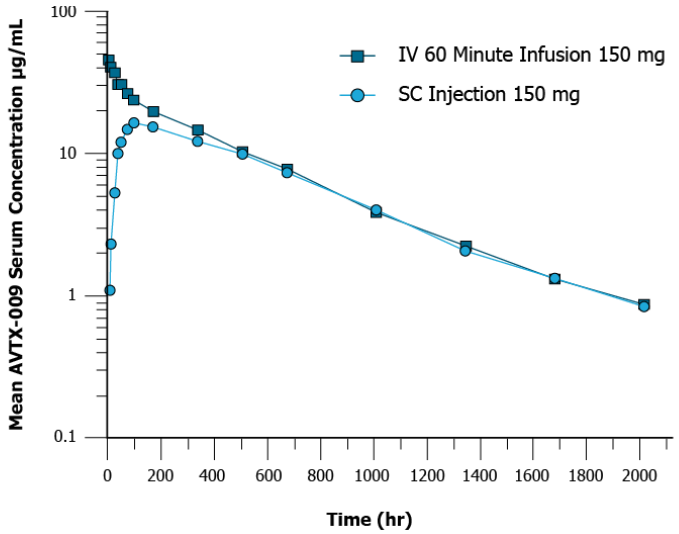
AVTX-009 Is a Highly Potent and Specific Inhibitor of IL-1β

- Originally developed by Eli Lilly[1,2]
- AVTX-009 exhibits superior potency compared to ILARIS® (canakinumab) in vitro
  - Higher affinity for IL-1β: K_D of <3 pM vs. 60 pM canakinumab[3]
- Stable 150 mg/mL dosage formulation[4]
  - Suitable for subcutaneous and intravenous administration
  - Initial presentation will be a prefilled syringe, post-approval plan to provide as an autoinjector
- Clinical experience: 245 patients studied in phase 1 and phase 2 trials[2,4-7]
  - Significant and rapid lowering of inflammatory biomarkers after a single dose in clinical trials
  - Excellent tolerability and safety at all doses up to 180 mg weekly
- Potency and half-life expected to support Q4W or less frequent dosing

AVTX-009 Has Higher Potency than Canakinumab



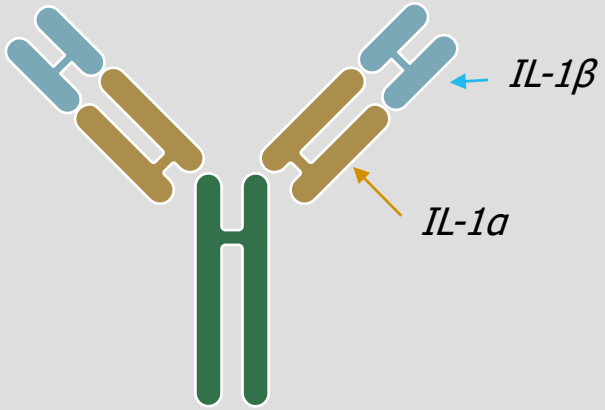
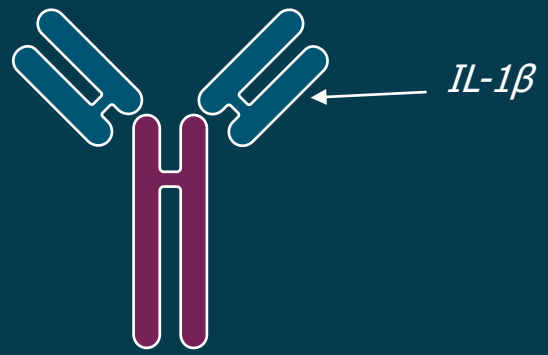
AVTX-009 Has a Strong Pharmacokinetic Profile



IL, interleukin; IV, intravenous; K_D, dissociation constant; Q4W, every 4 weeks; SC, subcutaneous.

1. Bihorel S, et al. *AAPS J.* 2014;16(5):1009-1017; 2. Sloan-Lancaster J, et al. *Diabetes Care.* 2013;36(8):2239-2246; 3. Chakraborty A, et al. *Clin Pharmacokinet.* 2012;51(6):e1-e18; 4. Data on file; 5. NCT04983732. Clinicaltrials.gov. Accessed September 5, 2024. https://clinicaltrials.gov/study/NCT04983732; 6. NCT00942188. Clinicaltrials.gov. Accessed September 5, 2024. https://clinicaltrials.gov/study/NCT00942188; 7. NCT00380744. Clinicaltrials.gov. Accessed September 5, 2024. https://clinicaltrials.gov/study/NCT00380744.

AVTX-009 Has High Affinity, High Bioavailability, and Long Half-Life

	Lutikizumab[1,2]	AVTX-009[3]
		
IL-1β K_D (pM)	21	**<3**
Subcutaneous bioavailability	46%	**73%**
Half-life	10-14 days	**19 days**

K_D, dissociation constant; pM, picomolar.

1. Lacy SE, et al. *mAbs.* 2015;7(3):605-619.
2. Wang SX, et al. *Osteoarthritis Cartilage.* 2017;25(12):1952-1961.
3. Bihorel S, et al. *AAPS J.* 2014;16(5):1009-1017.

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Hidradenitis Suppurativa (HS)

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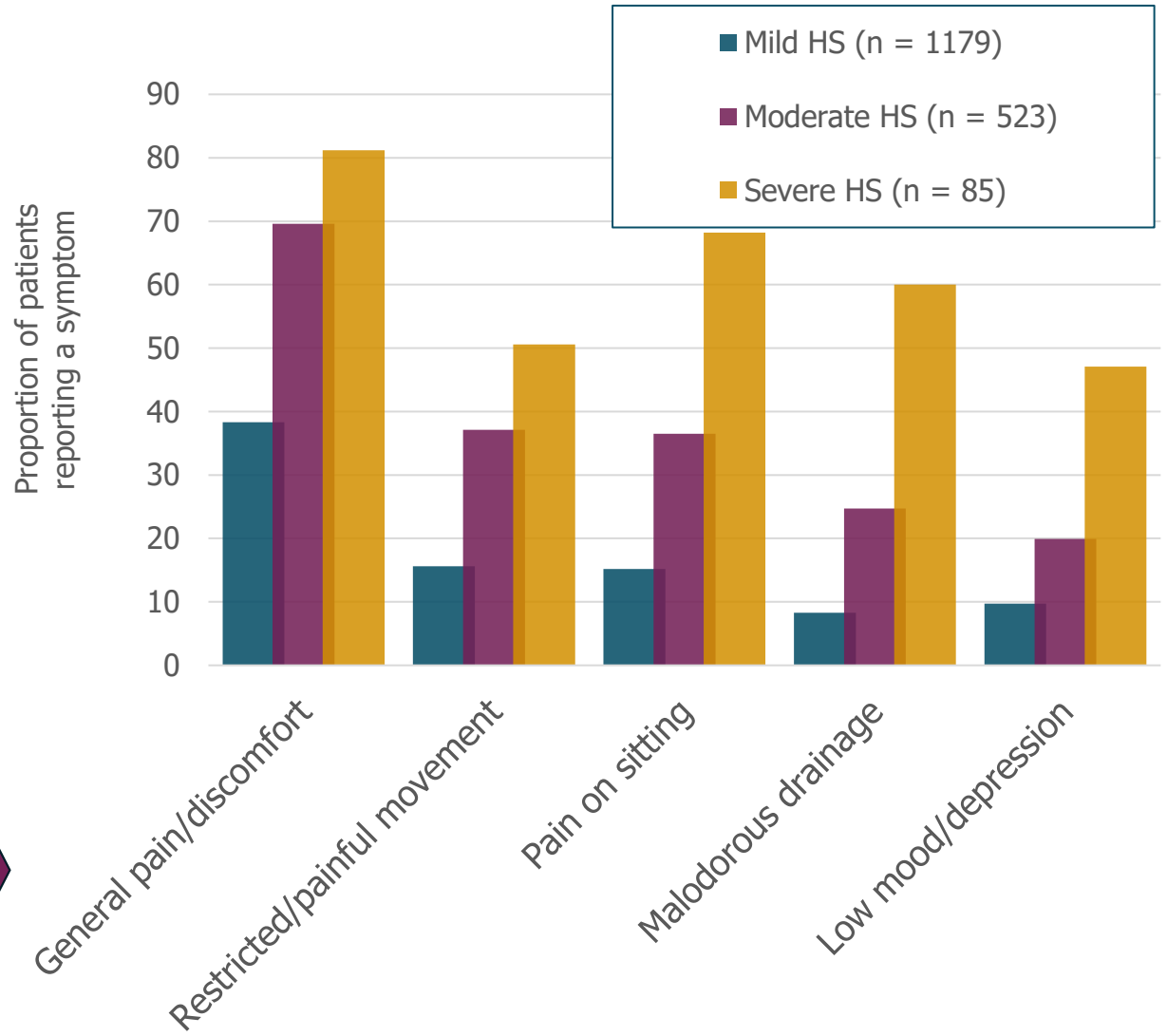
Hidradenitis Suppurativa: a Chronic Disease with a High Unmet Need

- Hidradenitis suppurativa is a chronic, often debilitating inflammatory skin disease that causes painful lumps, abscesses, and tunnels to form under the skin
- **Current treatments include:**
  - Antibiotics
  - Retinoids
  - Steroids
  - Cosentyx, Humira

Despite treatment, a large proportion of patients still report significant and life-disrupting symptoms[1]



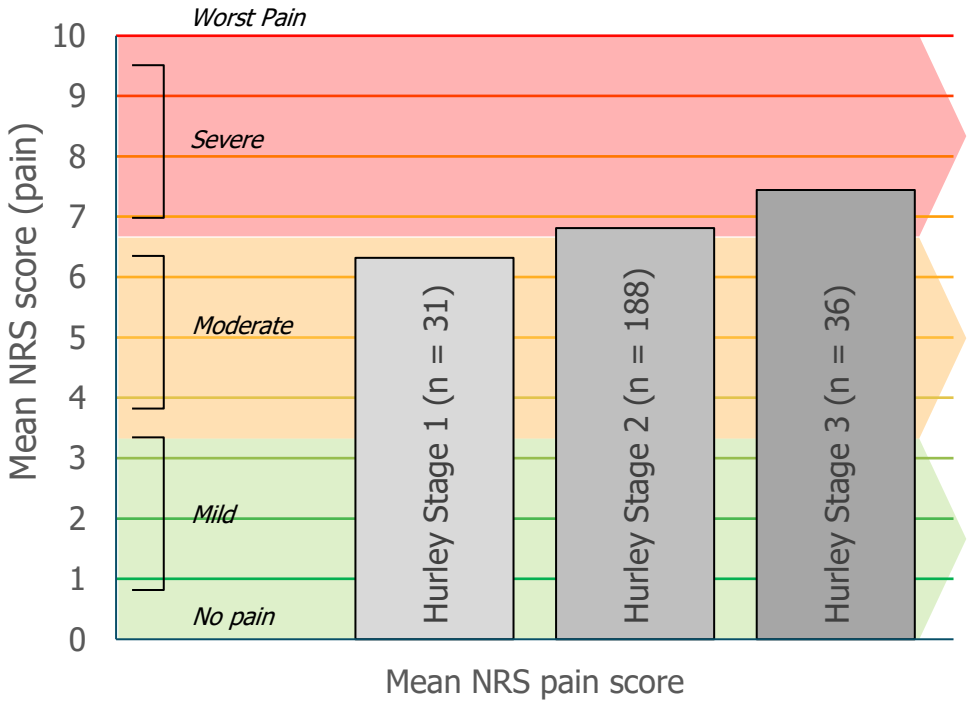
HS, hidradenitis suppurativa.

1. Ingram JR, et al. *J Eur Acad Dermatol Venereol.* 2022;36(9):1597-1605.

HS Causes Severe Pain and High Patient Burden

- Pain is a frequently overlooked aspect of HS[1,2]
- Even patients with "mild" disease report high levels of pain[3,4]
- This pain interferes with everyday life, sleep, and even movement[2]
- IL-1β blockade has been shown to reduce pain in multiple inflammatory conditions[5]

Mean Pain Scores by Disease Stage[3,4]



Areas commonly affected by HS include[2]:

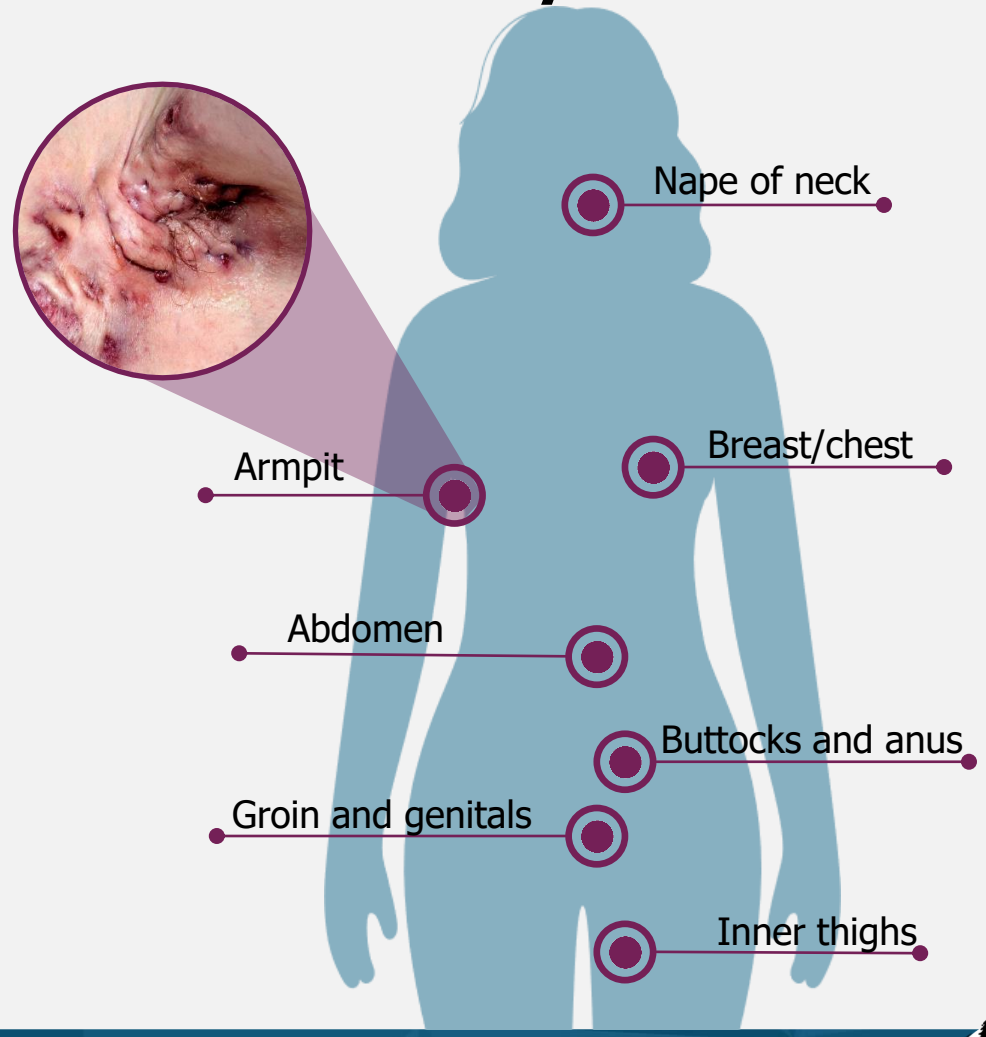
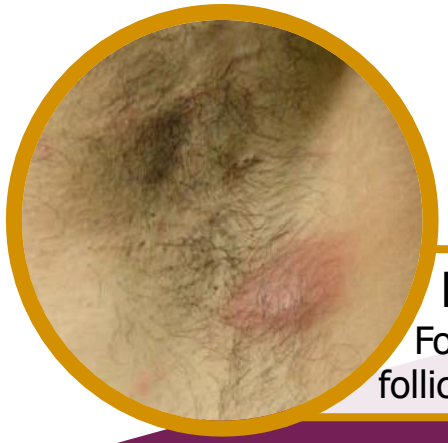


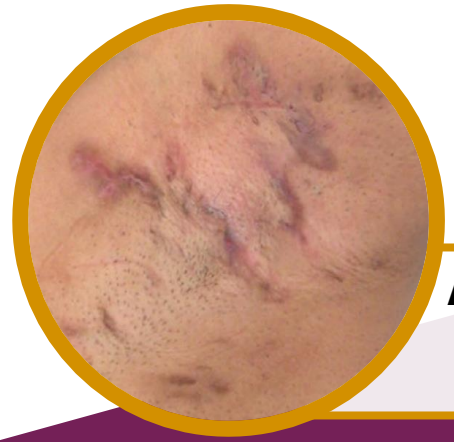
Photo from Cotter C, Walsh S. *Skin Health and Disease.* 2021;1(1):e7. CC-BY-4.0 License.
HS, hidradenitis suppurativa; IL, interleukin.

1. Johnston L, et al. *J Cutaneous Med Surg.* 2023;27(5):487-492; 2. Ingram JR, et al. *J Eur Acad Dermatol Venereol.* 2022;36(9):1597-1605; 3. Kimball AB, et al. *Dermatol Ther.* 2024;14:83-98; 4. Grimstad Ø, et al. *J Eur Acad Dermatol Venereol.* 2019;33(6):1164-1171; 5. Ren K, Torres R. *Brain Res Rev.* 2009;60(1):57-64.

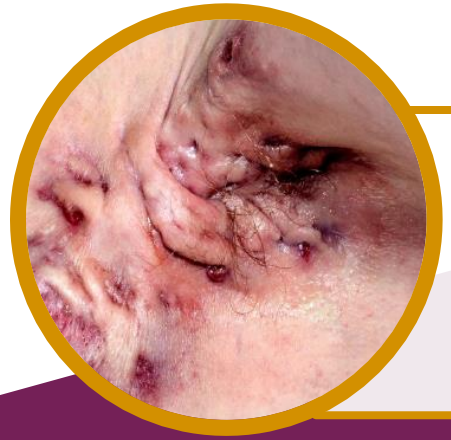
Chronic Inflammation in Hidradenitis Suppurativa Progresses to Tissue Destruction



Nodule
Formed from follicular blockage



Abscess
Follicular rupture



Tunnels
- Formed from progressing abscesses
- Infection and malodorous discharge
- Scarring

Long-term inflammatory dysregulation
Continued extracellular matrix breakdown and remodeling

Disease progression

Hidradenitis suppurativa patients need a potent and targeted anti-inflammatory treatment

Photos from Mendes-Bastos P, et al. *Front Med (Lausanne).* 2024;11:1403455; Ovadja ZN, et al. *Brit J Dermatol.* 2019;181:243-244; Cotter C, Walsh S. *Skin Health and Disease.* 2021;1(1):e7.

1. Diaz MJ, et al. *Curr Iss Mol Bio.* 2023;45:4400-4415; 2. Agnese ER, et al. *Cureus.* 2023;15(11):e49390; 3. de Oliveira ASLE, et al. *Biomolecules.* 2022;12(10):1371.

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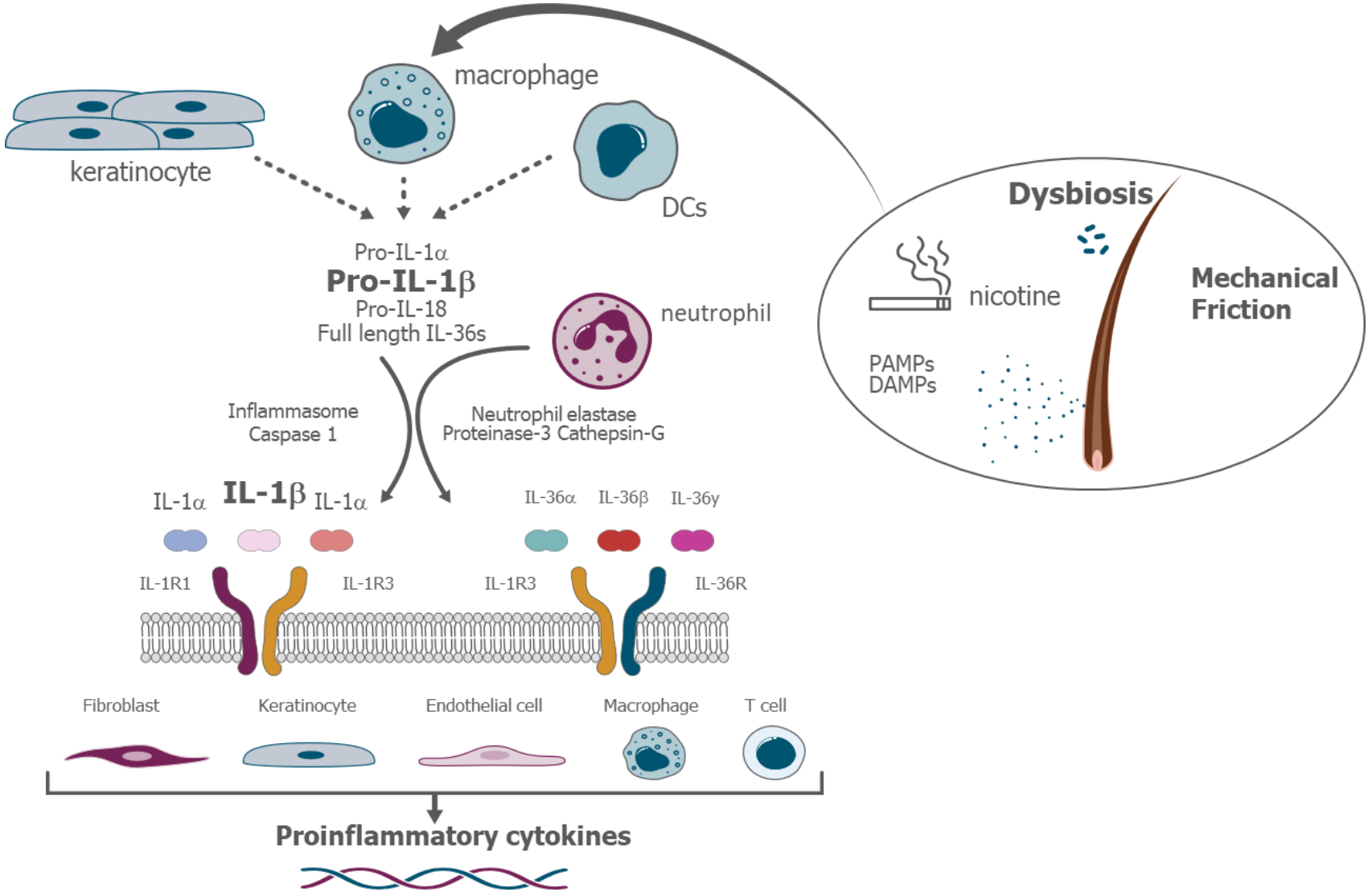
Diagnosed and Treated HS Population is Projected to Grow Substantially into a $9.5B+ Market by 2035[1]

	2023 *US Base Data*	2035 *US Projected*	MARKET DRIVERS
Overall HS prevalence[2]	**3.3 million**	**3.5 million** *(0.5% US population CAGR)*	**Potential Market Opportunity** Overall prevalence of HS of 3.3M expected to grow to 3.5M
HS diagnosed and treated[3]	**1.0 million**	**1.6 million** *(4% HS diagnosis CAGR)[a]*	**Total Addressable Market** Number of patients with HS diagnosed and treated will grow significantly from 30% to 45% of the total population, driven by new development and visibility with HCPs and patients
Moderate-to-severe HS[4]	**320,000**	**513,000**	**Segment Addressable Market** Increased recognition of disease leads to 60% growth of identified moderate to severe HS
Receiving biologics[5]	**105,000** *(33% on biologics in 2023)*	**205,000** *(40% on biologics in 2030)[a]*	**Treated Addressable Market** New approvals will lead to more patients being given biologics, increasing from 30% to 40% share of segment, evidenced by the recent quickly growing use of Cosentyx in HS post-approval

[a]HS diagnosis and treatment rates and biologic treatment rates are expected to increase over time.
CAGR, compound annual growth rate; HCP, healthcare provider; HS, hidradenitis suppurativa; US, United States.
1. HS Market Research 2024. Avalo Therapeutics Data on File; 2. Garg A, et al. *Am J Clin Dermatol.* 2023;24:977-990; 3. Garg AX, et al. *Dermatol Ther.* 2022;3:581-594; 4. Ingram JR, et al. *J Eur Acad Dermatol Venereol.* 2022;36(9):1597-1605; 5. Rinderknecht FB, Naik HB. *Int J Womens Dermatol.* 2024;10(1):e130.

IL-1β is Strongly Implicated in the Pathophysiology of HS[1]

- The inflammatory cascade in HS is triggered by various external stimuli including:
  - Smoking
  - Dysbiosis
  - Mechanical stress
- IL-1β is a key driver of the inflammatory cascade that leads to the destruction of the pilosebaceous unit
- HS patients exhibit increased IL-1β levels in lesional skin[2,3]
- Clinical benefit for HS has been observed with anti-IL-1 drugs[4]



DAMP, damage-associated molecular pattern molecule; DC, dendritic cell; HS, hidradenitis suppurativa; IL, interleukin; R, receptor; PAMP, pathogen-associated molecular pattern molecule.

1. Calabrese L, et al. *Biomolecules*. 2024;14(2):175; 2. Vossen ARJV, et al. *J Invest Dermatol*. 2020;140(7):1463-1466.e2; 3. Kelly G, et al. *Br J Dermatol*. 2015;173(6):1431-1439; 4. Kimball AB, et al. Presented at: American Academy of Dermatology; March 8-12, 2024; San Diego, CA.

Hidradenitis Suppurativa Patients Often Have Other Comorbidities That Could Impact Treatment

Patients have a **~2-6x** increased risk of inflammatory bowel disease[1]

Patients have a **~2x** increased risk of myocardial infarction, acute embolism, or deep vein thrombosis[2]

Patients have a **~1.5x** increased risk of cancer (overall) and a **~2.6x** increased risk of cutaneous squamous cell carcinoma[3]

22-50%

of patients are obese and nearly

1 in 3

have diabetes[2,3]

1. Chen WT, Chi CC. *JAMA Dermatol.* 2019;155(9):1022-1027; 2. Krajewski PK, et al. *Int J Dermatol.* 2024;63(6):799-805; 3. Abu Rached N, et al. *Ann Med.* 2024;56(1):2382372; 4. Garg A et al. *Am J Clin Dermatol.* 2023; 24: 977–990; 5. Rinderknecht F-AB, Naik HB. *Int J Womens Dermatol.* 2024;10(1): e130.

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Warnings and Precautions in Commonly Used Immunologic Drugs

RINVOQ® upadacitinib

JAK1 Inhibitor[1]

- Serious infection
- Opportunistic infection
- Risk of malignancy
- Thrombosis
- Blackbox warning: All-cause mortality

HUMIRA® adalimumab

Anti-TNF1[2]

- Serious infection
- Opportunistic infection
- Risk of malignancy
- Thrombosis

Cosentyx® (secukinumab) Bimzelx® (bimekizumab-bkzx)

Anti-IL-17[3,4]

- Serious infection
- IBD exacerbation
- Suicidal ideation (Bimzelx)

ILARIS (canakinumab) 150 mg subcutaneous injection Arcalyst® (rilonacept) For Injection Kineret® (anakinra)

Anti-IL-1β[5]/IL-1[6,7]

- Serious infection
- Opportunistic infection (isolated cases with Ilaris)

HS, hidradenitis suppurativa; IBD, inflammatory bowel disease; IL, interleukin; JAK1, janus kinase 1; MOA, mechanism of action; TNF, tumor necrosis factor.

1. Rinvoq. Package insert. AbbVie Inc.; 2024; 2. Humira. Package insert. AbbVie Inc.; 2024; 3. Cosentyx. Package insert. Novartis Pharmaceuticals Corporation; 2024; 4. Bimzelx. Package insert. UCB Inc.; 2023; 5. Ilaris. Package insert. Novartis Pharmaceuticals Corporation; 2023; 6. Arcalyst. Package insert. Kiniksa Pharmaceuticals (UK), Ltd.; 2021; 7. Kineret. Package insert. Swedish Orphan Biovitrum AB; 2000.

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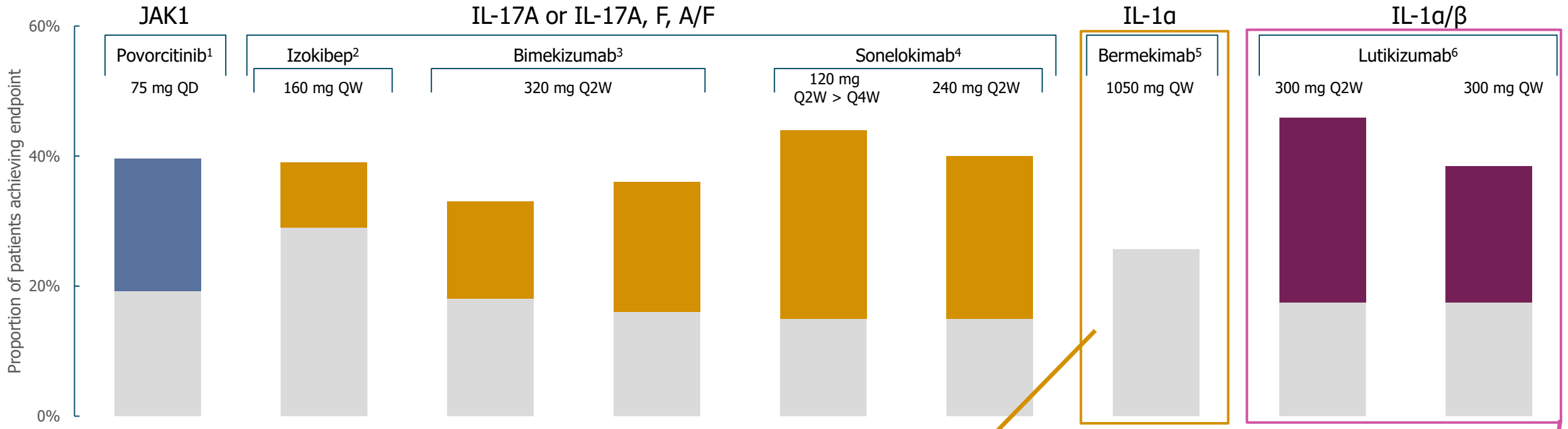
Previous Clinical Trials Validate and Derisk Our MOA

HiSCR75



Trial	Phase 2	Phase 2B/3	BE HEARD II	BE HEARD I	Phase 2	Phase 2	Phase 2 interim analysis	Phase 2	Phase 2
n/N	52/52	57/175	291/509	289/505	67/234	66/234	35/70	37/153	39/153
Time	12 wk	16 wk	16 wk	16 wk	12 wk	12 wk	16 wk	16 wk	16 wk

Placebo
Investigational drug (placebo adjusted)

Failure in phase 2 validates focusing on IL-1β

Comparable efficacy in a sicker population (65%-74% Hurley stage III) that had already failed anti-TNF therapy

HiSCR, hidradenitis suppurativa clinical response; IL, interleukin; JAK1, janus kinase 1; MOA, mechanism of action, TNF, tumor necrosis factor; wk, week; QD, daily; QW, weekly, Q2W, every other week; Q4W, ever 4 weeks.
1. Kirby JS, et al. *JAAD*. 2024;90(3):P521-529; 2. Acelyrin Press Release. September 11, 2023. Accessed September 10, 2024. https://investors.acelyrin.com/news-releases/news-release-details/acelyrin-inc-announces-top-line-results-placebo-controlled; 3. Kimball AB, et al. *Lancet*. 2024;403(10443):2504-2519; 4. Kimball AB, Kirby B, et al. Presented at: American Academy of Dermatology; March 8-12, 2024; San Diego, CA; 5. ClinicalTrials.gov identifier: NCT04988308. Accessed September 5, 2024. https://clinicaltrials.gov/study/NCT04988308; 6. Kimball AB, Ackerman L, et al. Presented at: American Academy of Dermatology; March 8-12, 2024; San Diego, CA.

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Phase 2 LOTUS Trial in Hidradenitis Suppurativa (AVTX-009-HS-201, NCT06603077)

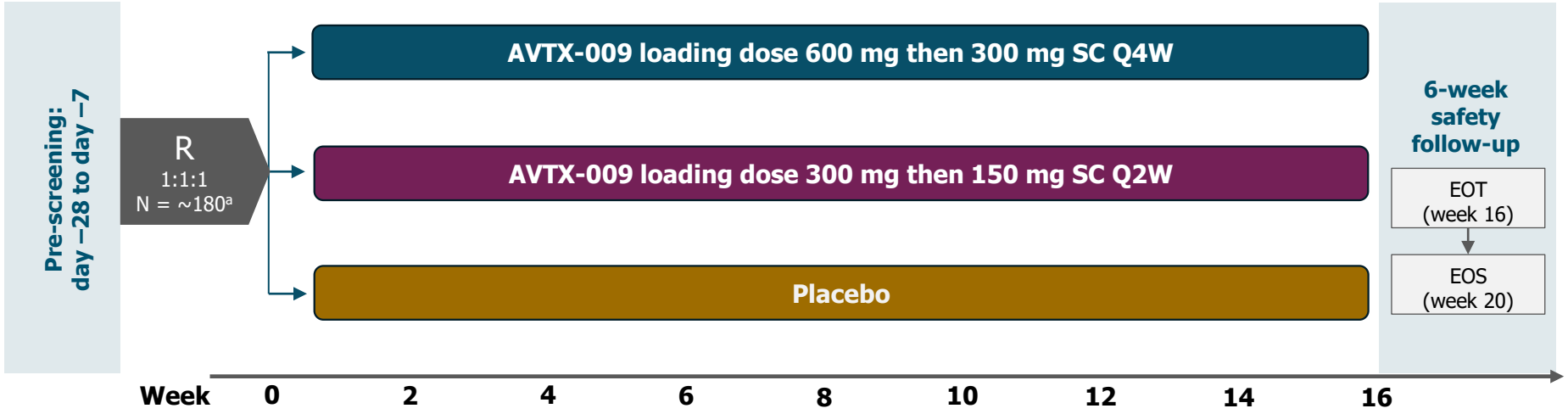
Efficacy and Safety of AVTX-009 Treatment in Participants With Hidradenitis Suppurativa

Primary Study Endpoint

Primary Endpoint: Percentage of participants achieving HiSCR75 at 16 weeks

Key Inclusion Criteria

- HS for at least 6 months prior to baseline
- Total AN count of ≥5 at baseline
- HS lesions must be present in at least 2 distinct anatomic areas
- At least one HS lesion that is Hurley stage II or III
- Enrollment of patients who have not failed anti-TNF therapy (naive or exposed) will be capped at 40%



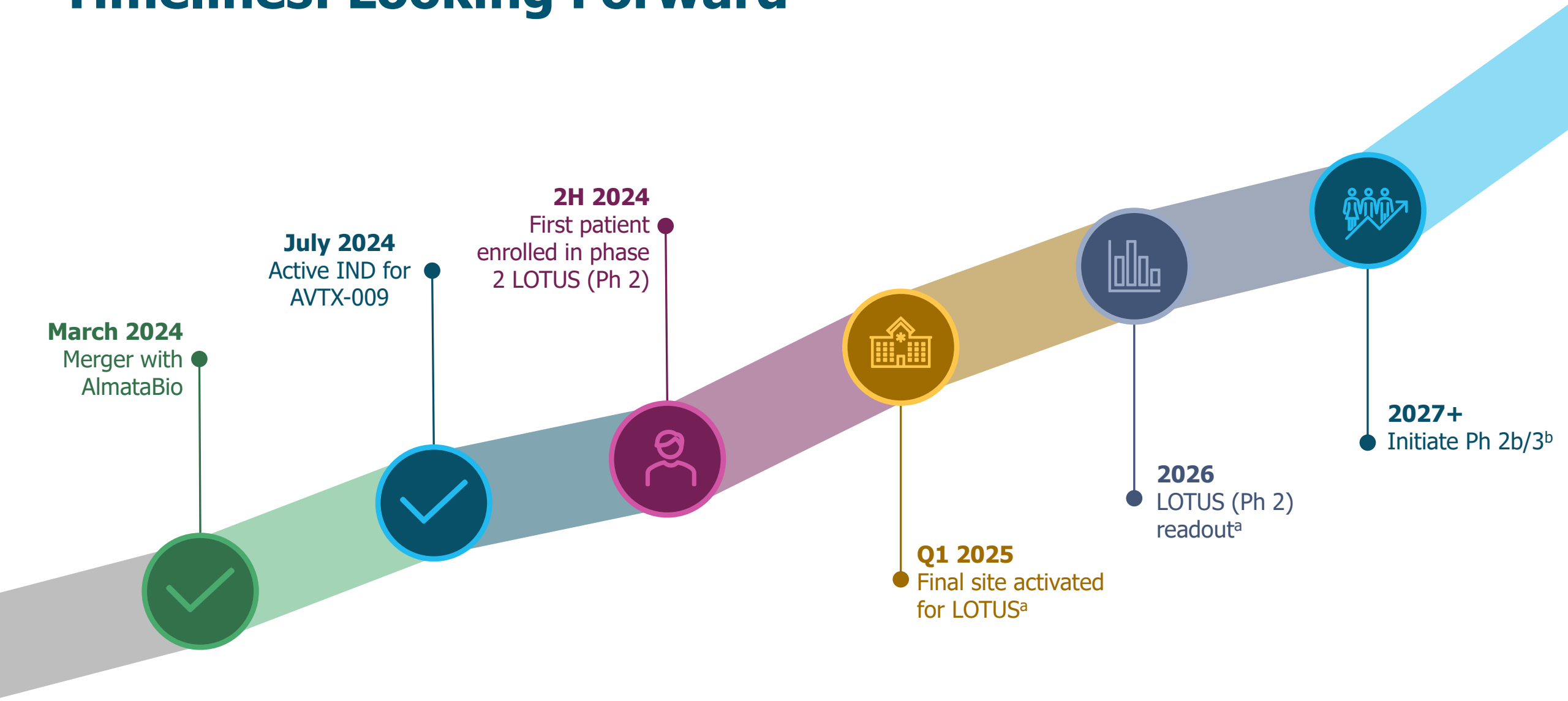
Key Secondary/Exploratory Endpoints

Key Secondary Endpoints:
- TEAEs
- HiSCR50, HiSCR90
- International HS Severity Score System (IHS4)
- AN count, draining fistula count
- Patient's Global Assessment of Skin Pain (PGA Skin Pain) (NRS30)
- Percentage of subjects with flares
- ADA

Exploratory Endpoints:
- PK
- HiSQOL, DLQI, PHQ-9
- Biomarkers:
  - CRP
  - IL-6
  - Potentially other biomarkers

[a]Trial has 80% power to show a HiSCR75 response for each individual arm (based on lutikizumab phase 2 HiSCR75).
ADA, antidrug antibody; AN, abscess and inflammatory nodule; CRP, C-reactive protein; DLQI, dermatology life quality index; EOS, end of study; EOT, end of treatment; HiSCR, Hidradenitis Suppurativa Clinical Response; HiSQOL, hidradenitis suppurativa quality of life; HS, hidradenitis suppurativa; NRS30, numerical rating scale 30; PHQ-9, patient health questionnaire-9; PK, pharmacokinetics; Q2W, every 2 weeks; Q4W, every 4 weeks; R, randomize; SC, subcutaneous; TEAE, treatment emergent adverse event; TNF, tumor necrosis factor.

Timelines: Looking Forward

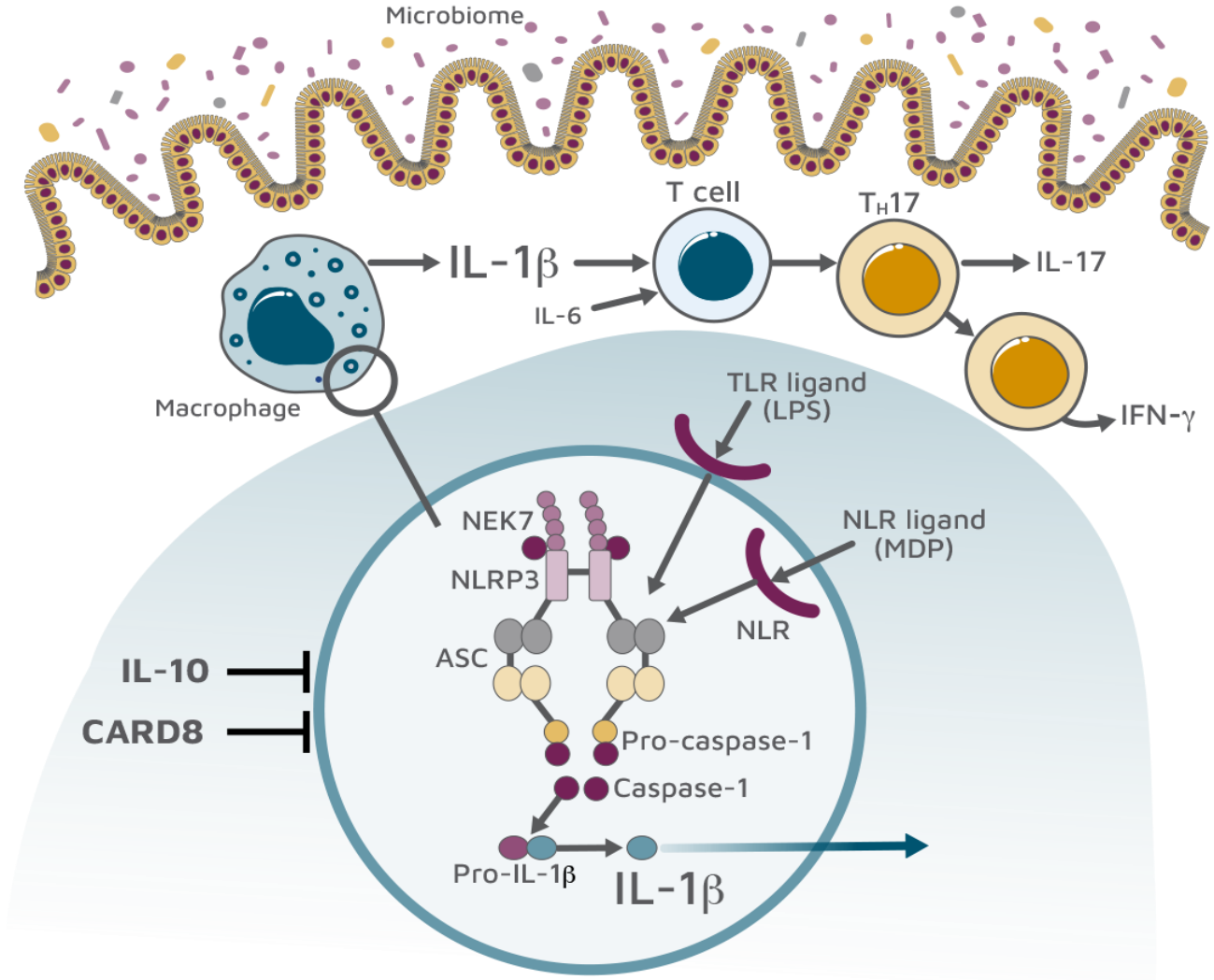


[a]Projected; [b]Pending readout from phase 2.
IND, investigational new drug application.

Potential Additional Indications

Role of IL-1β in IBD

- IL-1β plays a central role in inflammation in IBD[1]
  - IL-1β is a key cytokine produced upon inflammasome activation
  - Dysregulated inflammasome activation has been implicated in the pathogenesis of Crohn's disease
- IL-1–driven stromal–neutrophil interactions define a subset of patients who do not respond to current therapies[2,3]
- There is an observed overlap of patients that have IBD and HS[4,5]



HS, hidradenitis suppurativa; IBD, inflammatory bowel disease.

1. Mao L, et al. *Front Immunol*. 2018;9:2566; 2. Friedrich M, et al. *Nat Med*. 2021;27(11):1970-1981; 3. Cader MZ, Kaser A. *Nat Med*. 2021;27(11):1870-1871; 4. Chen WT, Chi CC. *JAMA Dermatol*. 2019;155(9):1022-1027; 5. Zhang M, et al. *World J Clin Cases*. 2021;9(15):3506-3516.

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Recent IL-1 Trial Initiations in IBD

- The goal of IBD therapeutics is remission, yet only a minority of IBD patients obtain remission with current therapies
- AbbVie is currently conducting studies to evaluate lutikizumab, a dual variable domain IL-1α/1β antagonist as monotherapy in ulcerative colitis and in combination with Skyrizi in Crohn's Disease

> "…we believe lutikizumab has the potential to be used in combinations to provide transformational levels of efficacy in IBD. We plan to evaluate combo approaches with lutikizumab and Skyrizi…in Crohn's. Our Phase 2 studies in IBD are expected to begin later this year."
>
> – Roopal Thakkar, MD
> SVP, Global Therapeutics
> Chief Medical Officer
> *AbbVie 4Q23 Earnings Call Transcript*

There is an opportunity for greater efficacy for patients with IBD with AVTX-009 as a monotherapy and in combination with anti-IL-23

IBD, inflammatory bowel disease; UC, ulcerative colitis.

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NASDAQ: AVTX

www.avalotx.com

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Appendix

Avalo Capitalization

As of September 30, 2024		Number of shares
Common Stock	• Common shares outstanding[1]	9.7M
Assuming Conversion of Preferred Stock and Exercise of Warrants	• Preferred stock[1]	13.7M
	• Warrants issued on March 28, 2024[1,2]	12.0M
Adjusted Share Count[3]	• Adjusted common shares outstanding[3]	35.4M
Adjusted Market Capitalization	• Stock price[4]	$9.50
	• **Adjusted market capitalization**	**$335.9M**

[1] Subsequent to September 30, 2024 and through November 6, 2024, 10,026,847 warrants have been exercised for gross proceeds of $58.1M which resulted in the issuance of 711,580 shares of common stock and 9,315.267 shares of series C preferred stock. Each share of series C preferred stock is convertible into 1,000 shares of common stock, subject to certain beneficial ownership limitations; [2]The warrants are exercisable for ~$5.80 per underlying share of common stock and expire on November 8, 2024; [3]Does not include 2.6M stock options and restricted stock units outstanding resulting in a fully dilutive share count of ~38M; [4]Reported closing price of our common stock on September 30, 2024