

**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): December 10, 2024**

**TOURMALINE BIO, INC.**  
(Exact name of registrant as specified in its charter)

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

**27 West 24th Street, Suite 702**  
**New York, NY**  
(Address of principal executive offices)

**001-40384**  
(Commission  
File Number)

**83-2377352**  
(I.R.S. Employer  
Identification No.)

**10010**  
(Zip Code)

**Registrant's telephone number, including area code: (646) 481-9832**

**Not Applicable**  
(Former Name or Former Address, if Changed Since Last Report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions (see General Instruction A.2. below):

- 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	Name of each exchange on which registered
Common Stock, par value \$0.0001 per share	TRML	The Nasdaq Global Select 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 December 10, 2024, Tourmaline Bio, Inc. (the “Company”) made available an updated corporate presentation that may be used in connection with presentations at conferences and investor meetings, which can be found on the Company’s website (the “Corporate Presentation”). The Corporate Presentation is furnished as Exhibit 99.1 to this Current Report on Form 8-K and incorporated by reference in this Item 7.01.

The information furnished under this Item 7.01, including 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”), or subject to the liabilities of that section, nor shall it be deemed to be incorporated by reference into any of the Company’s filings with the Securities and Exchange Commission under the Exchange Act or the Securities Act of 1933, as amended, whether made before or after the date hereof, regardless of any general incorporation language in such a filing, except as otherwise expressly stated in such filing.

**Item 9.01 Financial Statements and Exhibits.**

(d) Exhibits.

Exhibit No.	Description
99.1	<a href="#">Corporate Presentation dated December 10, 2024</a>
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)

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**SIGNATURES**

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

**TOURMALINE BIO, INC.**

Date: December 10, 2024

By: /s/ Ryan Robinson

Name: Ryan Robinson

Title: Chief Financial Officer and Treasurer

# TOURMALINE

## Corporate Overview

December 2024

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## Disclaimer

The material in this presentation regarding Tourmaline Bio, Inc. ("we," "us" or the "Company") is for informational purposes only. This presentation contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995 that involve substantial risks and uncertainties. All statements, other than statements of historical facts, contained in this presentation, including statements regarding the timing of initiation, progress and results of the Company's current and future preclinical and clinical trials for its product candidates, including pacibekitug (also referred to as TOUR006); the therapeutic potential of pacibekitug; the timing and likelihood of seeking regulatory approval for the Company's product candidates, including pacibekitug; the timing of submitting investigational new drug applications and other regulatory documents; the Company's ability to achieve planned milestones; the competitive landscape for the Company's product candidates; and the Company's estimates regarding expenses, future revenue, capital requirements, cash runway and needs for additional financing. The words "may," "will," "should," "expects," "intends," "plans," "anticipates," "believes," "estimates," "predicts," "potential," "continue," and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. The Company may not actually achieve the plans, intentions, or expectations disclosed in these forward-looking statements, and you should not place undue reliance on these forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in these forward-looking statements. Many factors may cause differences between current expectations and actual results, including, but not limited to, unexpected safety or efficacy data observed during preclinical or clinical studies, clinical site activation rates or clinical trial enrollment rates that are lower than expected, changes in the regulatory environment, changes in expected or existing competition, unexpected litigation or other disputes, and other risks and uncertainties, including those described in the section titled "Risk Factors" in the Company's most recent filings with the Securities and Exchange Commission. The forward-looking statements included in this presentation represent the Company's views as of the date of this presentation. The Company undertakes no obligation to update the information contained in this presentation to reflect new events or circumstances, except as required by law.

In addition, certain information contained in this presentation relates to or is based on studies, publications, surveys and other data obtained from third-party sources and the Company's own internal estimates and research. While the Company believes these third-party sources to be reliable as of the date of this presentation, it has not independently verified, and makes no representation as to the adequacy, fairness, accuracy or completeness of any information obtained from third-party sources. In addition, all of the market data included in this presentation involves a number of assumptions and limitations, and there can be no guarantee as to the accuracy or reliability of such assumptions. Finally, while we believe our own internal research is reliable, such research has not been verified by any independent source.

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## Our mission

*We are driven by our mission to develop transformative medicines that dramatically improve the lives of patients with life-altering immune and inflammatory diseases*



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## Experienced leadership team

### Management Team

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**Sandeep Kulkarni, MD**  
Co-Founder and  
Chief Executive Officer



**Ryan Robinson, CPA**  
Chief Financial Officer



**Brad Middlekauff, JD**  
Chief Business Officer and  
General Counsel



**Susan Dana Jones, PhD**  
Chief Technology Officer



**Kevin Johnson, PhD**  
Chief Regulatory Officer



**Emil deGoma, MD**  
Senior Vice President,  
Medical Research



**Gerhard Hagn**  
Senior Vice President,  
Head of Commercial & BD



**Don Fitch**  
Senior Vice President,  
Product Development



**Dora Rau**  
Senior Vice President,  
Head of Quality

### Board of Directors

**Clay Siegall, PhD**  
*Chairman*

**Caley Castelein, MD**

**Aaron Kantoff**

**Mark McDade**

**Sapna Srivastava, PhD**

**Parvinder Thiara**

**Sandeep Kulkarni, MD**

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## Key highlights



**An IL-6 renaissance is underway:** new insights emerging about a broad range of indications where IL-6 may be clinically validated



**Pacibekitug (also referred to as TOUR006) has demonstrated best-in class potential:** long-acting, low immunogenicity, and low-volume subcutaneous administration observed in clinical trials to date



**Two paths to significant value creation:** (1) cardiovascular inflammation and (2) thyroid eye disease



**A late-stage clinical company:** Phase 2 TRANQUILITY trial in CV and pivotal Phase 2b spiriTED trial in TED ongoing



**Two potentially transformative data readouts expected in 2025:** Topline data from TRANQUILITY trial expected in Q2 2025 and topline data from spiriTED trial expected in H2 2025



**Well-financed:** cash expected to fund operations into 2027, enabling the delivery of key anticipated milestones for both paths



# Pacibekitug: a long-acting anti-IL-6 monoclonal antibody with best-in-class potential



## Attributes observed to date

Long-acting with terminal half-life of ~7 weeks<sup>1</sup>

>90% pathway inhibition after single 10mg dose<sup>2</sup>

Fully human with ADAs in only 0.5% of patients<sup>3</sup>

High affinity to IL-6<sup>4</sup>

Existing data from approximately 450 study participants<sup>1</sup>



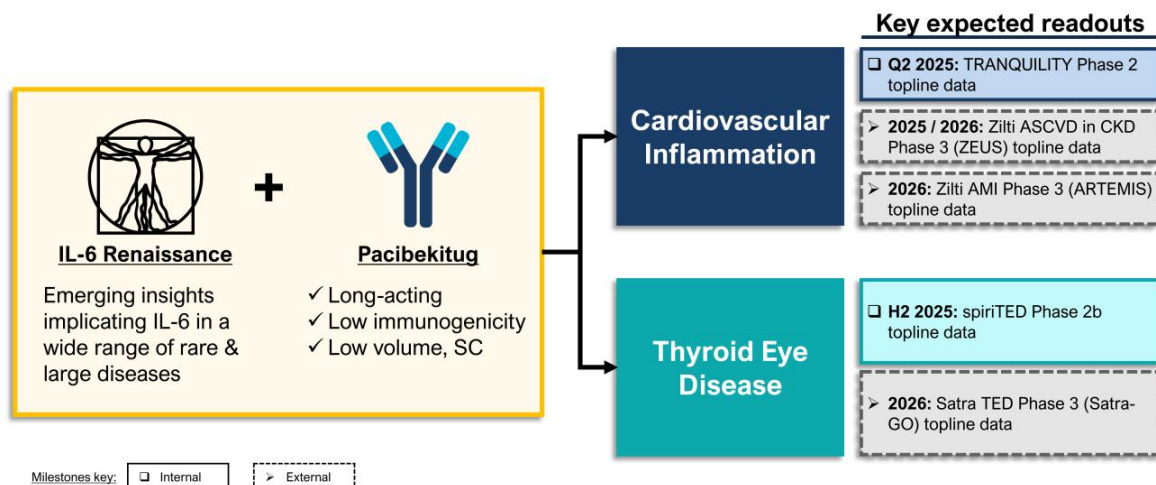
## Potential value to patients

- Dosing quarterly<sup>5</sup> (CV) or every 8 weeks<sup>6</sup> (TED)
- Rapid and robust impact across diseases
- Durable benefit **without need to increase dose**
- Volume of ≤1ml for **SC injection**<sup>5,6</sup>
- Generally **well-tolerated safety profile** observed to date

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<sup>1</sup>Across six clinical trials in healthy volunteers and RA, SLE, and CD patients. <sup>2</sup>Data on file; single intravenous 10mg dose in Ph1 MAD study in RA patients, as measured by C-reactive protein (CRP), a pharmacodynamic marker of IL-6 signaling. <sup>3</sup>Generated from Medarex transgenic mouse platform; across approximately 450 subjects dosed with pacibekitug, only 2 subjects generated anti-drug antibodies (ADAs) following treatment. <sup>4</sup>Data on file. <sup>5</sup>To be evaluated in CV Phase 2 trial. <sup>6</sup>To be evaluated in TED Phase 2 trial. Every 8week dosing was achieved in prior Phase 2 trials. CD: Crohn's Disease. CV: cardiovascular. SC: subcutaneous. RA: rheumatoid arthritis. SLE: systemic lupus erythematosus. TED: thyroid eye disease.

## Two paths to unlock major value creation



# Clinical development plan for pacibekitug

Disease Focus	Indication	Preclinical	Phase 1	Phase 2	Phase 3	Expected key milestones
Cardiovascular inflammation	Atherosclerotic Cardiovascular Disease (ASCVD)					TRANQUILITY Phase 2 topline data expected in Q2 2025
	Abdominal aortic aneurysm (AAA)					Phase 2 PoC trial initiation expected after TRANQUILITY topline data
Autoimmune disease	Thyroid Eye Disease (TED)					spiriTED Phase 2b topline data expected in H2 2025

Note: Hatched bars represent trials that have not yet commenced  
The timing of regulatory submissions and clinical trial milestones are subject to change and additional discussion with the FDA

# Cardiovascular Inflammation

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## Reducing inflammation: the next frontier in CV diseases



Increasing validation for IL-6 driven inflammation as a critical and modifiable risk factor driving residual cardiovascular risk

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Potential of IL-6 inhibition spans a broad range of cardiovascular indications, affecting tens of millions of patients globally

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Converging lines of human evidence across multiple settings support the transformative potential of IL-6 inhibition

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IL-6 inhibition is being evaluated in multiple cardiovascular outcomes trials with external readouts expected over the next 12 to 24 months

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Pacibekitug's potentially best-in-class profile, including quarterly SC administration, is being evaluated in the Phase 2 TRANQUILITY trial – over-enrollment completed, topline data expected in Q2 2025

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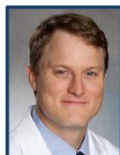
## World-class Cardiovascular Scientific Advisory Board providing insight on our development strategy for pacibekitug



**Deepak L. Bhatt, MD, MPH, MBA**  
*SAB Chair*  
Mount Sinai Fuster Heart Hospital



**Joshua A. Beckman, MD, MSc**  
University of Texas Southwestern



**Marc P. Bonaca, MD, MPH**  
University of Colorado  
CPC Clinical Research



**Robin Choudhury, MA, DM**  
University of Oxford



**Dipender Gill, MD, PhD**  
Sequoia Genetics



**Douglas L. Mann, MD**  
Washington University  
School of Medicine



**James Min, MD**  
Cleerly, Inc.



**Pradeep Natarajan, MD, MMSC**  
Massachusetts General Hospital  
Harvard Medical School



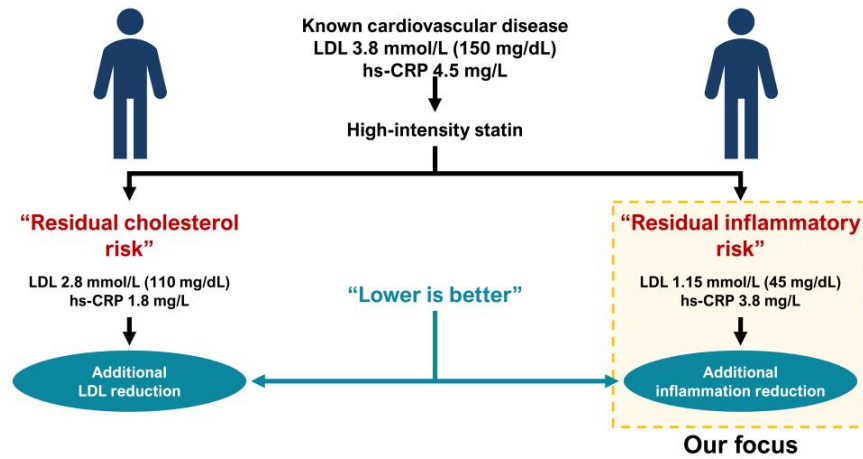
**Michael D. Shapiro, DO, MCR**  
Wake Forest University



**Michael Szarek, PhD**  
University of Colorado  
CPC Clinical Research

# Many CV disease patients have residual inflammatory risk

## Differential secondary prevention treatment options for statin-treated patients<sup>1</sup>



# Research increasingly highlights inflammation as a driver of CV risk and supports therapeutic potential of IL-6 inhibition



## RESEARCH LETTER

**Genetically Downregulated Interleukin-6 Signaling Is Associated With a Favorable Cardiometabolic Profile**  
A Phenome-Wide Association Study

## Association of Interleukin 6 Receptor Variant With Cardiovascular Disease Effects of Interleukin 6 Receptor Blocking Therapy

A Phenome-Wide Association Study

Tapani Caia, Sidi, Yun-Zhang, PhD, Yik-Lam Yu, MPH, Nicholas Loh, BA, Jiahuan Sun, PhD, Jie Huang, MS, Tamara A. Caia, MD, Scott Dimsdale, MD, Kaitiaki D. Sackey, PhD, Richard A. Anderson, PhD, PhD, MPH, Jie Huang, PhD, Lauren Collins, MPH, Heidi Schuber, MPH, Chuan-Feng, PhD, David Gagnon, MD, MPH, PhD, Yan-Yi, Sus, PhD, J. Michael Gaziano, MD, MPH, Peter Wilson, MD, Kelly Chu, PhD, MPH, Philip Tsai, PhD, Christopher J. O'Donnell, MD, MPH, Katherine F. Lau, MD, MPH, for the VA Million Veteran Program

## RESEARCH LETTER

## A Missense Variant in the IL-6 Receptor and Protection From Peripheral Artery Disease

Michael G. Laven, Derek Klarn, Marco K. Georgakopoulos, Julie Lynch, Katherine F. Lau, Benjamin F. Voight, Christopher J. O'Donnell, Kyong-Mi Chang, Theodoros L. Assimes, Philipp S. Tsao, Scott M. Denman, on behalf of the VA Million Veteran Program

## Interleukin-6 in Patients With Heart Failure and Preserved Ejection Fraction

Alejo Alagna, MD, PhD, Kathryn E. Koerpp, PhD, Michael Sabbah, MD, Fair M. Ezzamel Netto, PhD, Michael D. Jensen, MD, James L. Kirkland, MD, PhD, Carolyn S.P. Lam, MBBS, Masaru Obokata, MD, PhD, Mark C. Petrek, MD, Paul M. Burke, MD, MPH, Siddharth Kotturachi, MD, PhD, Tamara Tchkonia, PhD, Adnan Vozni, MD, Margaret M. Redfield, MD, Barry A. Borlag, MD

## Research Letter

## Genetically Proxied IL-6 Receptor Inhibition and Coronary Artery Disease Risk in a Japanese Population

Sizheng Steven Zhao<sup>1,2</sup>, Dipender Gill<sup>2</sup>

<sup>1</sup>Center for Macrobiochemical Research, Division of Macrobiochemical and Dermatoimmunological Science, School of Biological Science, Faculty of Biological Medicine and Health, The University of Manchester, Manchester Academic Health Science Centre, Manchester, UK  
<sup>2</sup>Department of Epidemiology and Biostatistics, Imperial College London, London, UK

## RESEARCH LETTER

## Circulating Interleukin-6 Levels and Incident Ischemic Stroke

A Systematic Review and Meta-analysis of Prospective Studies

Andreas Panagiotou, MD, Konstantinos Papatheodorou, MD, Harry Birkbak, PhD, Annette Peters, PhD, James A. de Lencastre, MD, Sushil Kishore, MD, Martin O'Donoghue, MD, and Marco K. Georgakopoulos, MD, PhD  
doi:10.1161/STROKEAHA.118.049313

Correspondence  
Dr. Georgakopoulos  
mkg@georgakopoulos.com

## Quantifying inflammation using interleukin-6 for improved phenotyping and risk stratification in acute heart failure

Eleni Michou, Desiree Wustler, Maria Belkin, Cornelia Simmen, Ivo Stroh, Albina Nowak, Nikola Kozhuharov, Samyut Shrestha, Pedro Lopez-Ayala, Zaid Sabit, Constantinos Papanicolaou, Matthias Diebold, Tiffany Pequignot, Katharina Rentsch, Arnold von Eckardstein, Danielle M. Gualandri, Tobias Breithardt, and Christian Mueller

## ORIGINAL RESEARCH

## Elevated Interleukin-6 Levels Are Associated With an Increased Risk of QTc Interval Prolongation in a Large Cohort of US Veterans

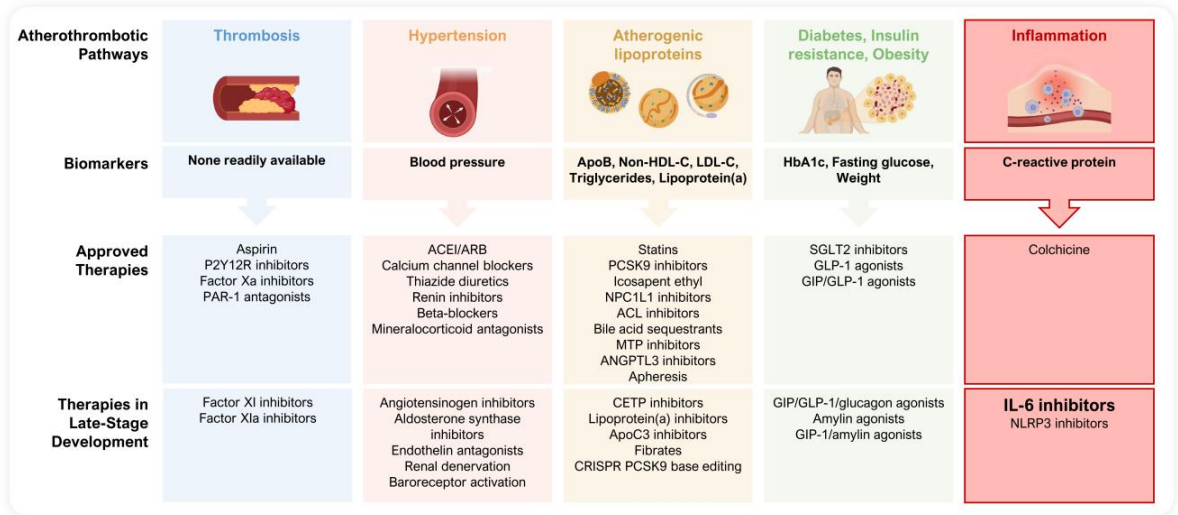
Harshdeep Singh, MD, Michael L. Cleveland, PhD, Alexander C. Foy, MD, Ingrid Isaksson, MD, Yehuda Shoenberger, MD, David S. Siscovick, MD, Robert M. L. Johnson, MD, James H. Brown, MD, Michael A. Jensen, MD, Michael J. Blaha, MD, and Scott D. Cook, MD, PhD, for the VA Million Veteran Program

## Associations of genetically predicted IL-6 signaling with cardiovascular disease risk across population subgroups

Marika K. Georgakopoulos, Rainer Malik, Tom G. Richardson, Rainer M. M. Hoes, Christopher D. Anderson, Stephen Burgess, Guo-Kun Hoque, Martin Dichgans, and Dipender Gill



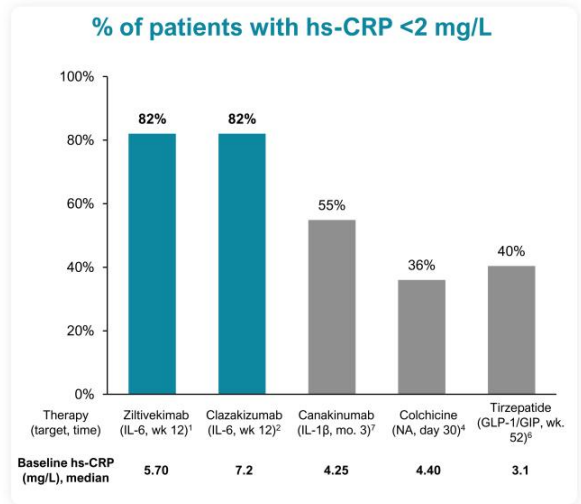
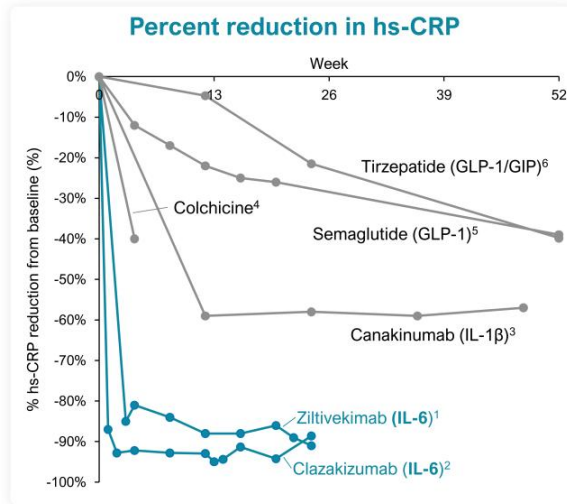
# Cardiovascular inflammation largely unaddressed by existing treatments



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List of therapies not exhaustive. ACEI: angiotensin-converting enzyme inhibitor. ACL: adenosine triphosphate-citrate lyase. ANGPTL3: angiotensin-like protein 3. ApoB: apolipoprotein B. ApoC3: apolipoprotein C3. ARB: angiotensin receptor blocker. CETP: Cholesteryl ester transfer protein. CRISPR: clustered regularly interspaced short palindromic repeats. GIP: gastric inhibitory polypeptide. GLP-1: glucagon-like peptide-1. IL-6: Interleukin-6. MTP: microsomal triglyceride transfer protein. NLRP3: nucleotide-binding domain, leucine-rich-containing family, pyrin domain-containing-3. NPC1L1: Niemann-Pick C1-Like 1. PAR: protease-activated receptors. PCSK9: proprotein convertase subtilisin/ kexin type 9. P2Y12R: purinergic 2Y type 12 receptor. SGLT2: sodium-glucose cotransporter 2.

# IL-6 inhibition has produced rapid and robust hs-CRP reductions in patients with established or at high-risk of CVD



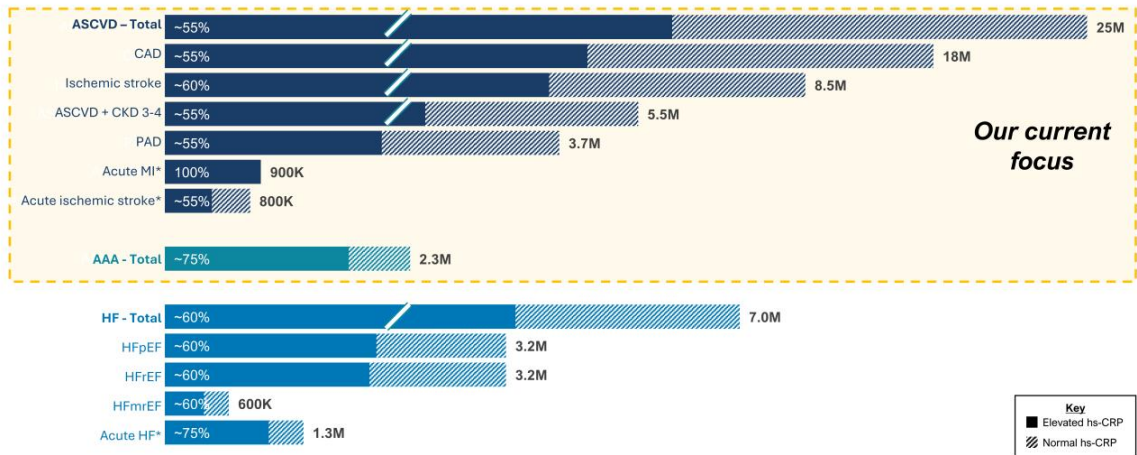
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<sup>1</sup>RESOLVE: Ridker et al., Lancet (2021). Ziltivekimab 15mg q4w arm. <sup>2</sup>Chertow et al., Nat Med (2024). Clazakizumab 5mg q4w arm. <sup>3</sup>CANTOS: Ridker et al., N Eng J Med (2017). 100mg q3m arm. <sup>4</sup>Fiolet et al., PLOS ONE (2020). Colchicine 0.5mg QD. <sup>5</sup>SELECT1: Plutzky et al., EAS Congress (2024). Semaglutide 2.4mg QW maintenance. <sup>6</sup>Borbaug et al., Nat Med (2024). Tirzepatide up to 15mg QW. <sup>7</sup>Ridker et al., Lancet (2017). Time course values obtained by webplotdigitizer. Values are not placebo adjusted. CVD: cardiovascular disease. GIP: gastric inhibitory polypeptide. GLP-1: glucagon-like peptide-1. hs-CRP: high sensitivity C-reactive protein. Certain data in this presentation are based on a cross-trial comparison and are not based on head-to-head clinical trials. Cross trial comparisons are inherently limited and may suggest misleading similarities or differences in outcomes. Results of head-to-head comparisons may differ significantly from those set forth herein.

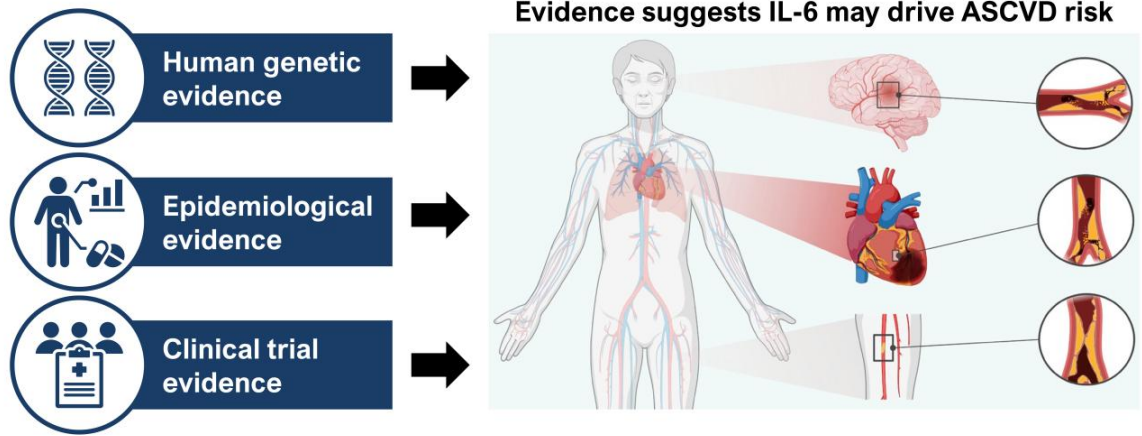
# IL-6 inhibition has the potential to address millions of patients across a wide range of inflammation mediated CV conditions

## Estimated US prevalence (2024)<sup>1</sup>

Populations are not mutually exclusive



# Convergence of human evidence supports therapeutic potential of IL-6 inhibition for ASCVD



# Human genetic studies provide initial support for IL-6 pathway inhibition to lower ASCVD risk



## Concordance between results of human genetic studies and randomized clinical trials

Therapeutic target	Genetic Result	RCT Result
Lowering LDL-C to lower ASCVD risk <sup>1,2</sup>	Positive	Positive
Inhibiting IL-6 to treat polymyalgia rheumatica <sup>3,4</sup>	Positive	Positive
Lowering blood pressure to lower ASCVD risk <sup>5,6</sup>	Positive	Positive
Raising HDL-C to lower ASCVD risk <sup>7,8</sup>	Negative	Negative
Inhibiting LpPLA2 to lower ASCVD risk <sup>9,10</sup>	Negative	Negative
Inhibiting TNF $\alpha$ to treat multiple sclerosis <sup>11,12</sup>	Negative (harm)	Negative (harm)
Inhibiting IL-6 to lower ASCVD risk <sup>13-17</sup>	Positive	Trials Ongoing

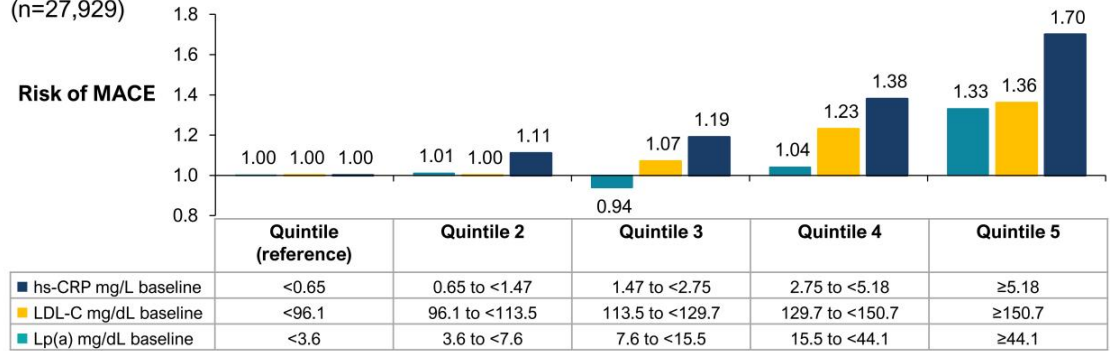
“Probability of success for drug mechanisms with genetic support is 2.6 times greater than those without.”<sup>18</sup>

# Emerging evidence suggests that hs-CRP is more strongly associated with MACE than both LDL and Lp(a)



Late breaking data presented at European Society of Cardiology 2024 Congress and simultaneously published in the New England Journal of Medicine

30-year longitudinal data from the Women's Health Study<sup>1</sup>  
(n=27,929)



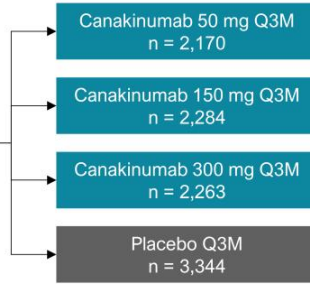
# Landmark CANTOS study validated therapeutic potential of addressing inflammation in ASCVD



## Canakinumab Anti-inflammatory Thrombosis Outcomes Study (CANTOS) Trial Design<sup>1</sup>

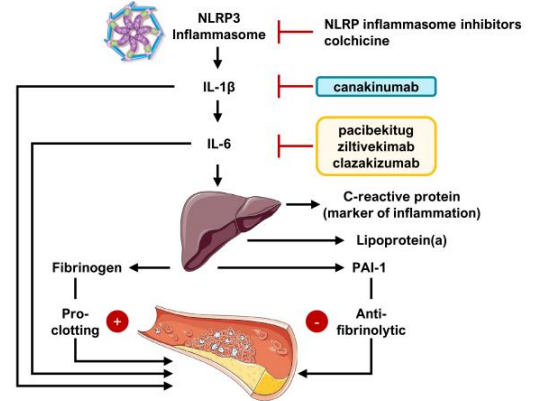
**10,061 patients**

- Stable CAD (post MI)
- On Statin, ACE/ARB, BB, ASA
- hs-CRP  $\geq 2$  mg/L

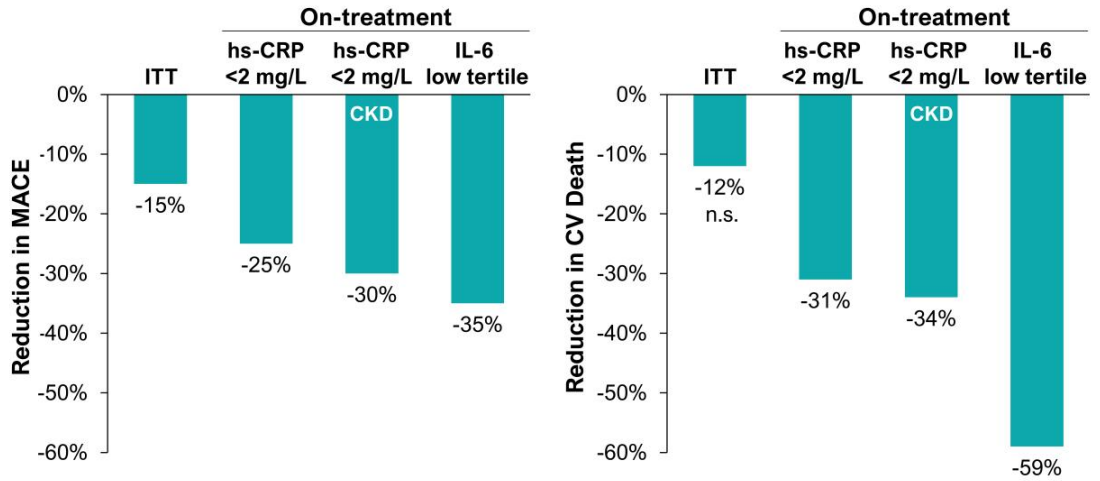


**Primary endpoint:**  
Time to the first occurrence of MACE (CV death, non-fatal MI, or non-fatal stroke)

## IL-1 $\beta$ is upstream of IL-6<sup>2</sup>

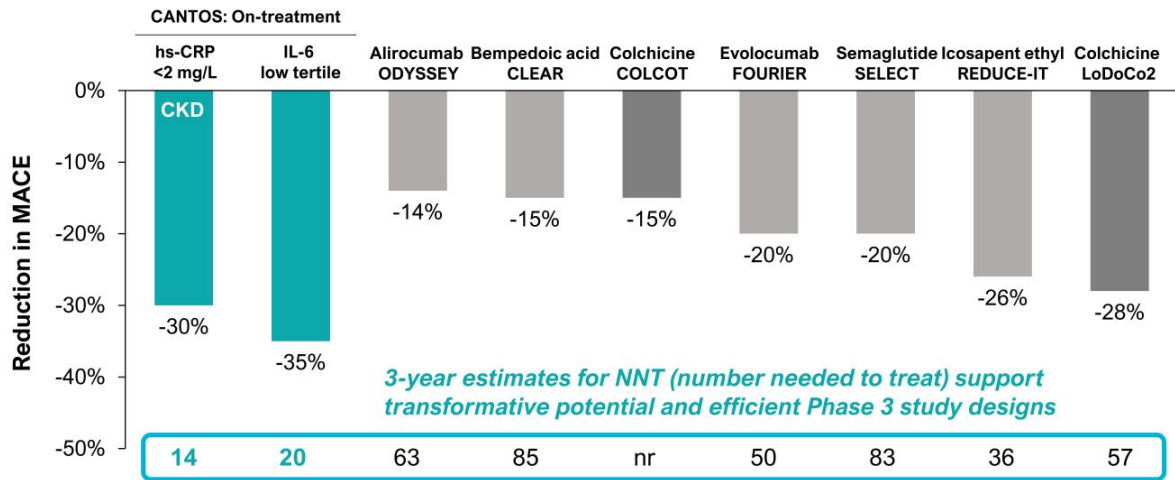


# Lessons from canakinumab (anti-IL-1 $\beta$ mAb): “Lower is better” for downstream biomarkers of IL-6 activity





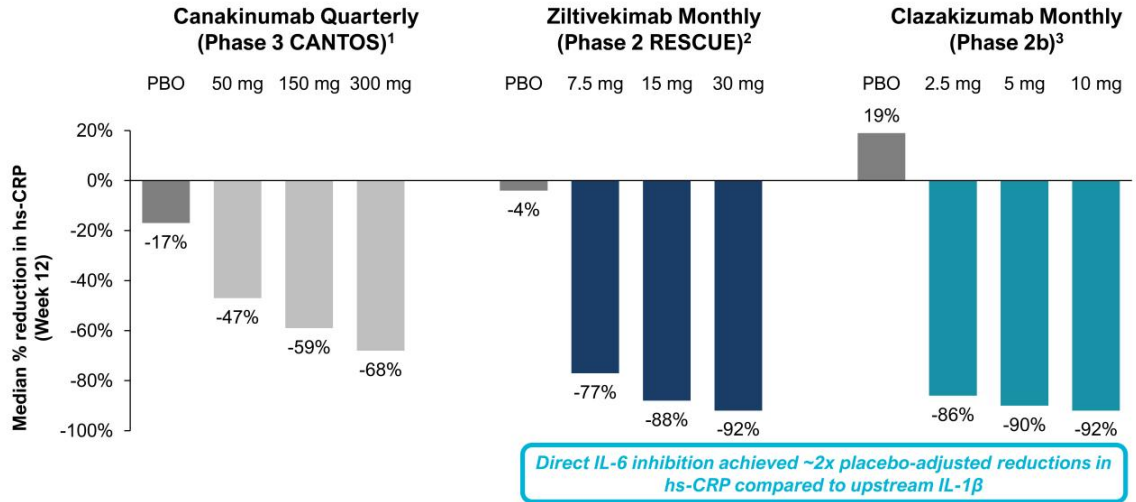
# Lessons from canakinumab (anti-IL-1 $\beta$ mAb): Robust inhibition of IL-6 pathway has transformative potential in ASCVD



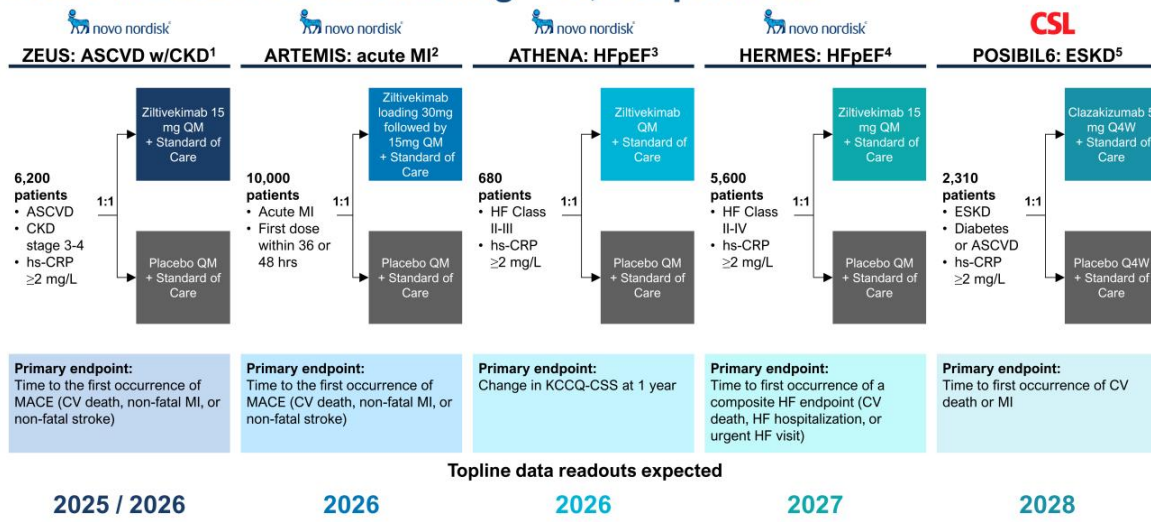
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Reduction in MACE shown as 1-Hazard Ratio. MACE: major adverse cardiovascular events including CV death, myocardial infarction (MI), stroke except for: ODYSSEY OUTCOMES (all death, MI, ischemic stroke); COLCOT (CV death, MI, stroke, revascularized cardiac arrest); LoDoCo2 (CV death, MI, ischemic stroke); main CANTOS analysis presents data for 150mg dose group; values for CANTOS subanalyses combine all doses (50, 150, 300mg); control arms were placebo + background Svc. Certain data in this slide are based on a cross-trial comparison and are not based on head-to-head clinical trials. Cross-trial comparisons are inherently limited and may suggest misleading similarities or differences in outcomes. Results of head-to-head comparisons may differ significantly from those set forth herein. NNT (number needed to treat) values obtained from absolute risk extracted from Kaplan-Meier figures via webplotdigitizer, unless directly reported. NNT for IL-6 < median shown; not reported for IL-6 low tertile. The information on this slide is based on Tourmaline-generated analysis of third-party data and is being presented for hypothesis generating purposes only. As a result, the actual MACE risk reduction hypothesized may be more or less than the data presented in this slide. Publications available upon request.

# In independent studies, direct IL-6 inhibition lowered hs-CRP more than upstream IL-1 $\beta$ blockade




# Five Phase 3 CVOTs enrolling >24,000 patients



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The timing of clinical trial milestones are subject to change.  
 ASCVD: atherosclerotic cardiovascular disease. CKD: chronic kidney disease. CVOT: cardiovascular outcome trial. ESKD: End Stage Kidney Disease. HFpEF: heart failure with preserved ejection fraction. MACE: major adverse cardiovascular event. MI: myocardial infarction.  
<sup>1</sup>Clinicaltrials.gov: NCT05021835. <sup>2</sup>Clinicaltrials.gov: NCT06118281. <sup>3</sup>Clinicaltrials.gov: NCT06200207 <sup>4</sup>Clinicaltrials.gov: NCT05636176 <sup>5</sup>Clinicaltrials.gov: NCT05485961 (Phase 3 portion only)

## Pacibekitug designed to offer best-in-class potential profile in cardiovascular diseases

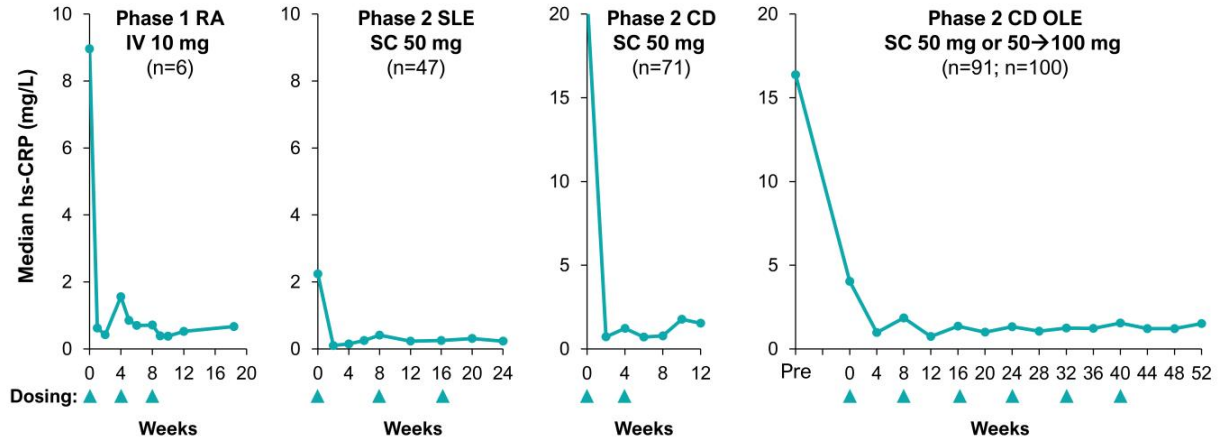
	Pacibekitug	Ziltivekimab	Clazakizumab
Company	<b>TOURMALINE</b>	 novo nordisk®	<b>CSL</b>
Monoclonal antibody	<b>fully human (IgG2)</b>	fully human (IgG1k, YTE mutation)	humanized rabbit (IgG1k)
Anti-drug antibodies <sup>1</sup>	<b>0-1%</b>	6-13% <sup>3,4</sup>	0-10% <sup>7-9</sup>
Route of administration <sup>2</sup>	<b>SC 0.6 mL</b>	SC <sup>5,6</sup> 1.0 mL	IV <sup>10</sup>
Longest dosing intervals in completed studies	<b>Q8W (SLE, CD)</b>	Q4W (NDD-CKD) <sup>5,6</sup>	Q4W <sup>10</sup> (HD-CKD)
Targeted dosing intervals	<b>Quarterly</b>	Monthly	Monthly

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CD: Crohn's disease, CKD: chronic kidney disease, HD: hemodialysis, NDD: non-dialysis dependent, SLE: systemic lupus erythematosus. <sup>1</sup>Incidence of ADAs in repeat-dose studies calculated as reported per dosing arm. <sup>2</sup>Route of administration in planned or ongoing studies in patients with or at high-risk of ASCVD. <sup>3</sup>Clinicaltrials.gov NCT03925117, <sup>4</sup>Pergola et al., JASN (2021), <sup>5</sup>Ridker et al., Lancet (2021), <sup>6</sup>Wada et al., J Cardiol (2023), <sup>7</sup>Clinicaltrials.gov NCT01490450, <sup>8</sup>Clinicaltrials.gov NCT01545290, <sup>9</sup>Wassilari et al., Arthritis Rheum (2015), <sup>10</sup>Clinicaltrials.gov NCT05482661. Data reported in publications or on clinicaltrials.gov as detailed above. No head-to-head studies have been conducted between the mAbs shown here, which have each been evaluated in different populations.

25

# Pacibekitug achieved robust and durable suppression of CRP in patients with high-grade inflammatory autoimmune disorders

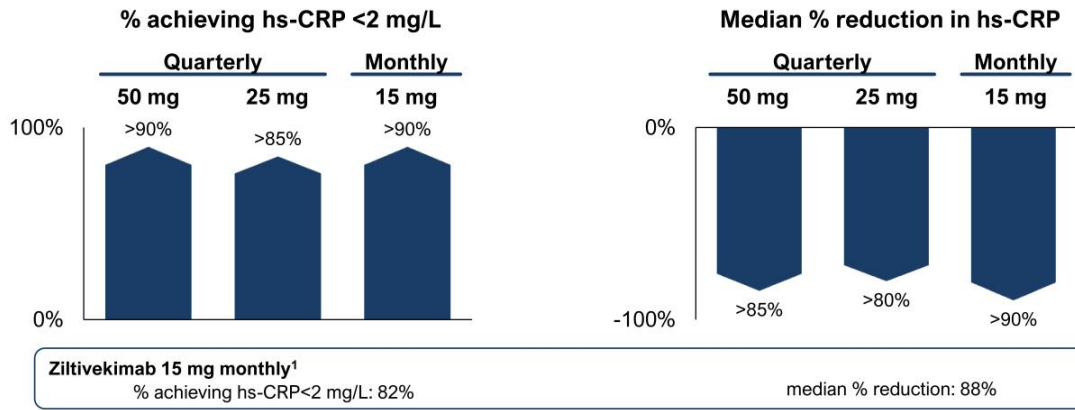


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CD: Crohn's disease, OLE: open-label extension, RA: rheumatoid arthritis, SLE: systemic lupus erythematosus. Rheumatoid arthritis: B0151002 study report, Table 14.4.7.1.1. Median baseline CRP 9.0 mg/L. Key eligibility: active disease, background methotrexate. Crohn's disease: B0151003 study report, Table 14.2.4.1.3. Median baseline hs-CRP 21.1 mg/L. Key eligibility: active disease, failed/intolerant to anti-TNF $\alpha$ . CD OLE B0151005 study report, Table 14.2.4.1. Median pre-baseline hs-CRP 16.4 mg/L, baseline hs-CRP 4.0 mg/L. Systemic lupus erythematosus: B0151006 study report, Table 14.3.4.1.3. Median baseline hs-CRP 2.2 mg/L.

# PK/PD modeling supports potential for quarterly dosing of pacibekitug SC in ASCVD

**Results of PK/PD model developed from five studies in patients with RA, SLE, CD and healthy volunteers**



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ASCVD: atherosclerotic cardiovascular disease, RA: rheumatoid arthritis, SLE: systemic lupus erythematosus, CD: Crohn's disease. The PK and PK/PD models for pacibekitug were developed based on the data from 5 clinical studies (two phase 1 studies in healthy volunteers, one phase 1 study in RA, one phase 2 study in SLE, and one phase 2 study in CD). A two-compartment model with first-order absorption and linear elimination and a mechanism-based indirect response model (in a relationship on CRP) adequately described the PK and PK/PD relationships, respectively. Simulations were performed assuming an RA-like population with baseline CRP 2 mg/L to 10 mg/L. Results at Day 50 are shown. <sup>1</sup>Tridder et al., Lancet (2021). Results after 12 weeks of treatment are shown. Certain data in this slide are based on a cross-trial comparison and are not based on head-to-head clinical trials. Cross-trial comparisons are inherently limited and may suggest misleading similarities or differences in outcomes. Results of head-to-head comparisons may differ significantly from those set forth herein.

# TRANQUILITY Phase 2 trial supporting development in ASCVD

Double-blinded, placebo-controlled Phase 2 trial (NCT06362759) | Status: **over-enrollment completed**



#### Study population:

- CKD stage 3-4 (eGFR 15-59 ml/min/1.73m<sup>2</sup>) or UPCR>200 mg/g
- hs-CRP ≥2 mg/L and <15 mg/L
- Exclude patients at higher risk for safety complications (e.g., immunocompromised patients)

#### Primary pharmacodynamic endpoint:

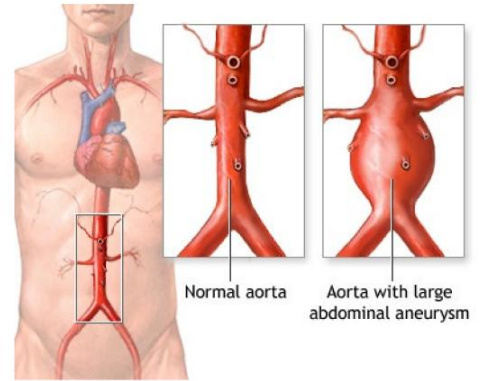
- Change from baseline in hs-CRP through Day 90

#### Additional endpoints:

- Percent of participants who achieve hs-CRP <2 mg/L
- Other pharmacodynamic markers, including lipoprotein (a)
- Safety and tolerability

## Abdominal aortic aneurysm: a high-mortality, first-in-disease opportunity for pacibekitug

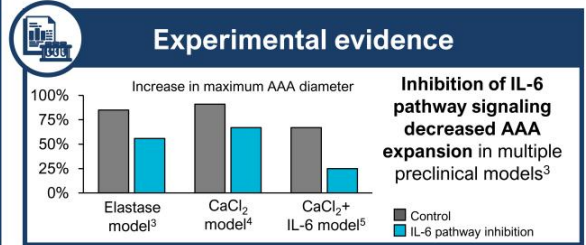
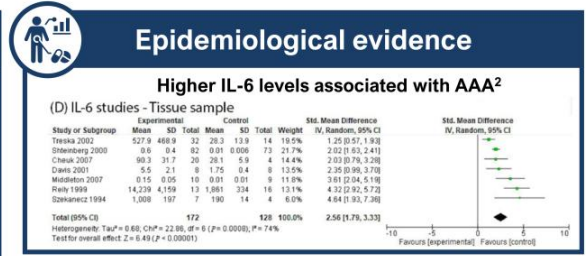
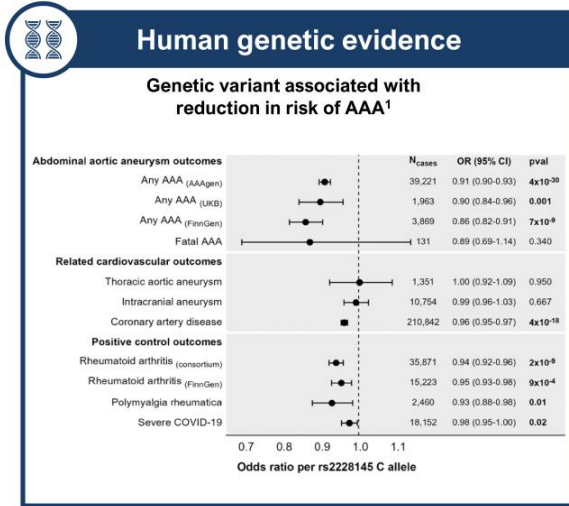
- High-risk vascular disease with **significant unmet need in approximately 2M people in US<sup>1</sup>**
- **Strong strategic fit** with ASCVD due to overlapping prescribers
- Progressive disease with increasing risk of **rupture, usually a fatal event<sup>2</sup>**
- **In less than 5 years**, majority of medium-sized AAA grow to threshold for surgical repair<sup>3,4</sup>
- Surgical repair, recommended for large AAA to prevent rupture, is **associated with complications<sup>5-9</sup>**



**No FDA approved treatment**



# Compelling evidence supports IL-6 inhibition to slow AAA growth

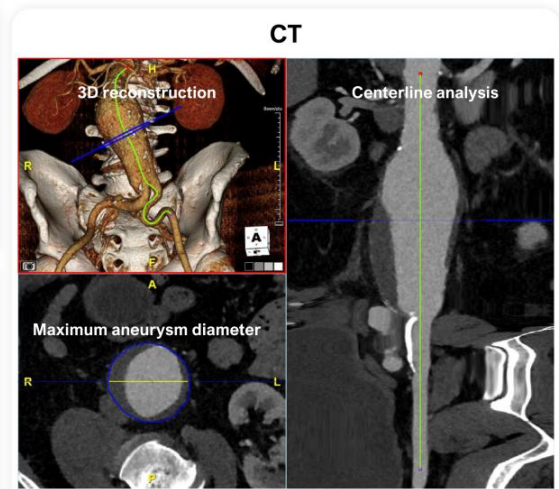


## Phase 2 PoC study expected to use imaging to evaluate the ability of pacibekitug to inhibit AAA growth

- Serial imaging is the foundation of clinical care<sup>1</sup>
- Phase 2 PoC expected to use multimodality imaging to efficiently characterize pacibekitug

### Next steps:

- TRANQUILITY topline data in Q2 2025
- Alignment with FDA on Phase 2 PoC design
- Details to be shared prior to study start



# Thyroid Eye Disease

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## TED: our beachhead indication designed to validate pacibekitug's potential in autoantibody-driven diseases

### 1 High unmet medical need with significant market opportunity

- TED patients experience significant disease burden driven by inflammation, proptosis, double-vision, and pain
- ~30k new patients each year in the U.S. (average age at diagnosis is ~45)<sup>1,2</sup>
- ~80%<sup>3</sup> of moderate-to-severe TED patients not receiving an FDA-approved treatment, which we believe may be related to significant limitations such as risk of permanent hearing impairment / loss:
  - Vast majority of US treaters report unmet need across all aspects of treatment (efficacy, safety, administration)<sup>4</sup>

### 2 Extensive third-party clinical support that IL-6 inhibition may address key unmet needs

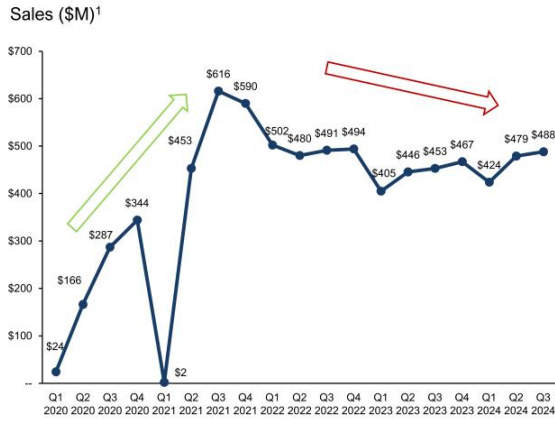
- 50+ publications with 350+ patients demonstrate the therapeutic potential of IL-6 pathway inhibition in TED
- IL-6 may play a more central and upstream role in TED pathogenesis than IGF-1R or FcRn
- Many TED treaters already routinely utilize IL-6 inhibition in their practice<sup>4</sup>

### 3 Pacibekitug has best-in-disease potential in TED

- Deep inhibition of IL-6 pathway observed to date offers potential for durable efficacy across many endpoints
- Existing clinical database supports the potential for a well-tolerated profile at selected doses
- Q8W dosing would allow for a patient-friendly, low burden treatment course

# IGF-1R class limitations present a significant opportunity for novel therapeutic approaches in TED

## TEPEZZA U.S. revenues have been stagnating since 2021...



## ...believed to be due to real-world experience

### 1. Safety issues: Risk of potentially permanent hearing loss<sup>2</sup>

#### WARNINGS AND PRECAUTIONS

- **Hearing Impairment Including Hearing Loss:** TEPEZZA may cause severe hearing impairment including hearing loss, which in some cases may be permanent. Assess patients' hearing before, during, and after treatment with TEPEZZA and consider the benefit-risk of treatment with patients

### 2. Limited durability: Growing real-world effectiveness data reveals larger than anticipated number of non-responders / high relapse rate<sup>3,4</sup>

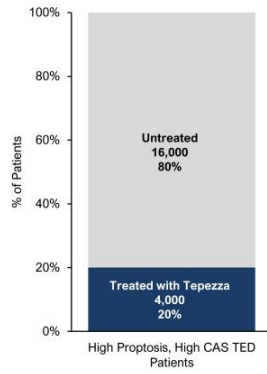
- ### 3. High level of inconvenience & complexity:
- IV Q3W (n=8)<sup>2</sup> but limited access to infusion centers<sup>5</sup>
  - Numerous visits and high time commitment (HCPs and patients)<sup>5</sup>
  - Need for serial audiograms, as per label<sup>2,6</sup>
  - Burdensome reimbursement approval process<sup>7</sup>

# Despite an FDA-approved medicine, the vast majority of moderate-to-severe TED patients remain untreated

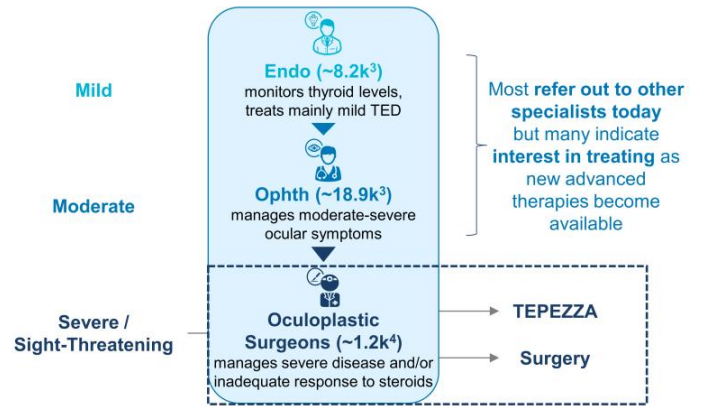
Most TED patients are not receiving TEPEZZA...

...or only get it relatively late in the treatment journey<sup>2</sup>

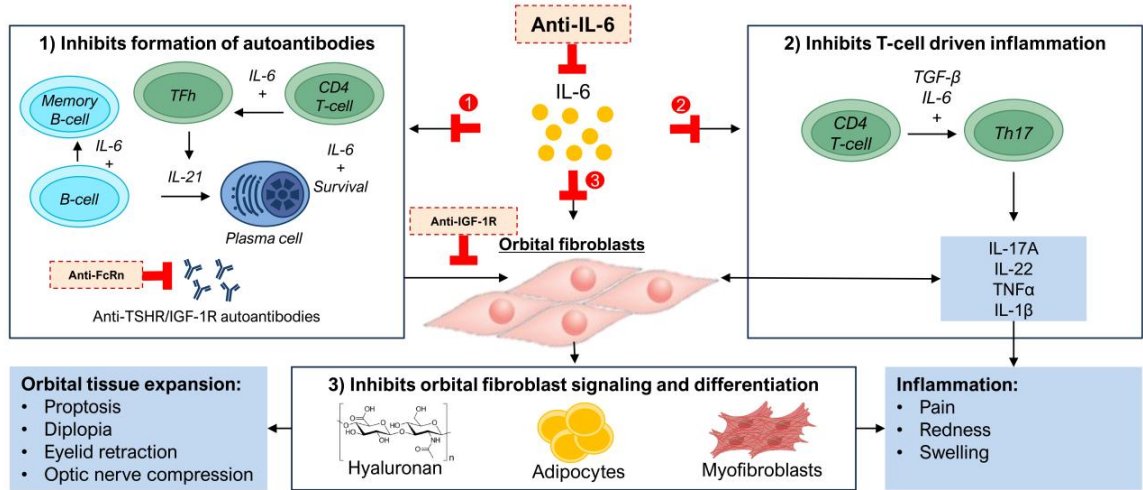
TEPEZZA US LTM penetration<sup>1</sup>



Simplified Treatment Journey<sup>2</sup>



# IL-6 inhibition has the potential to address a central and upstream driver of TED



# Over 50 publications support the therapeutic potential of IL-6 pathway inhibition in TED

Study Details				Key Endpoints			Study Details				Key Endpoints		
First author	Year	Study type	N treated	Proptosis response rate	CAS response rate	% autoantibody reduction	First author	Year	Study type	N treated	Proptosis response rate	CAS response rate	% autoantibody reduction
Pérez-Moreiras	2021	Retro	54	78	89	75	Copperman	2019	CS	2	100	0	NR
Sánchez-Bilbao	2020	Obs	48	NR	NR	NR	Coy	2019	CS	2	NR	50	NR
Alianza-Mateo	2016	Retro	29	NR	NR	NR	Sierra Osorio	2020	CS	2	100	100	NR
Lee	2024	Prosp	19	11	47	56	Park	2021	CS	2	100	100	NR
Pérez-Moreiras	2014	Prosp	18	72	100	76	Abellon-du Payrat	2022	CS	2	100	50	NR
Pérez-Moreiras	2018	RCT	15	93	60	NS	Butnaru	2013	CR	1	NR	100	NR
de la Fuente Bursón	2020	Retro	15	NR	NR	NR	Gómez Rodríguez	2014	CR	1	NR	100	NR
Pereira	2023	Retro	14	NR	NR	NR	Bielefeld	2017	CR	1	CI	NR	NR
Habroosh	2024	Prosp	13	100	31	68	Canas	2018	CR	1	100	NR	NR
Boutzios	2023	Obs	12	NR	NR	84	Pascual-Camps	2018	CR	1	NR	NR	NR
Pampin-Sánchez	2022	Retro	11	75	73	NR	Garreta Fontelles	2019	CR	1	NR	NR	93
Moi	2022	Retro	10	CI	80	75	Mehmet	2020	CR	1	0	NR	NR
Cortez	2022	Prosp	10	10	100	81	Kaplan	2020	CR	1	NR	0	85
Silkiss	2020	CS	9	CI	56	74	Cayon-Blanco	2020	CR	1	NR	100	NR
Smith	2021	Retro	9	78	100	54	Tran	2020	CS	1	NR	NR	NR
Bielefeld	2019	Obs	8	NR	NR	NR	Ruiz	2021	CR	1	NR	NR	NR
Ceballos-Marcias Jose	2020	CS	8	NR	75	41	Albrashdi	2022	CR	1	100	NR	NR
Benedjaj	2020	Retro	7	NR	NR	NR	Cezara	2022	CR	1	NR	0	NR
Moás	2022	Obs	7	NR	NR	92	Mohamed	2022	CS	1	0	0	NR
Toro-Tobon	2023	Retro	6	50	NR	NR	Moleiro	2022	CR	1	100	NR	86
de Pablo Gomez	2018	CS	5	NR	60	NR	Almazrouei	2023	CR	1	NR	NR	NR
Navarrete	2022	Retro	5	NR	NR	NR	Cuculescu	2023	CR	1	CI	0	NR
Ribi	2017	CS	3	33	67	NR	Nirmalan	2023	CS	1	NR	NR	NR
Maldiney	2020	CS	3	67	NR	NR	Pramono	2023	CR	1	NR	NR	NR
Stevens	2022	Retro	3	100	67	NR	Rymuza	2024	CR	1	100	0	8
Russell	2017	CS	2	NR	0	NR							
Sy	2017	CS	2	CI	50	69							
							<b>Weighted Mean</b>				<b>68%</b>	<b>72%</b>	<b>71%</b>
							<b>Smith 2017 (tepro Phase 2)</b>				<b>71%</b>	<b>69%</b>	<b>N/A</b>
							<b>Douglas 2020 (tepro Phase 3)</b>				<b>83%</b>	<b>59%</b>	<b>N/A</b>

We believe many of these reports may underestimate the true efficacy of IL-6 inhibition

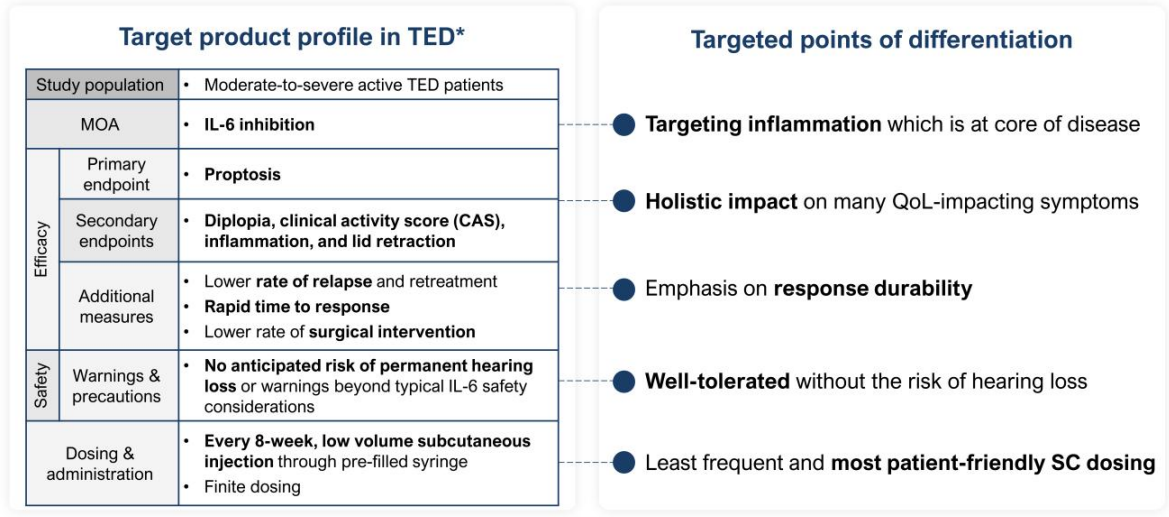
- 350+ mostly steroid-refractory patients
- Late IL-6 inhibition (>9 months post symptom onset) when disease may have exited active phase
- Exposure to IL-6 inhibition may have been suboptimal (<6 months)
- Tourmaline market research with over 100 TED treaters suggests many HCPs already routinely utilize IL-6 inhibition in their practice

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Proptosis response rate is generally defined in the data outlined here as a ≥2 mm proptosis improvement in the worse eye at baseline without any worsening in the other eye. CAS response rate is generally defined in the data outlined here as a CAS of 0 or 1. Studies referenced in this table represent investigator-led studies and were not designed with the intent of generating evidence for an approval of tocilizumab or sarilumab in TED. The majority of these studies were not designed with power to detect statistical significance. Retro: retrospective, Obs: observational, Prosp: prospective, RCT: randomized controlled trial, CS: case series, CR: case report, NR: not reported, NS: not significant, CI: clear improvement, Tepro: teprotumumab. Publications available upon request.



# Pacibekitug's target product profile is expected to be well-differentiated in TED...

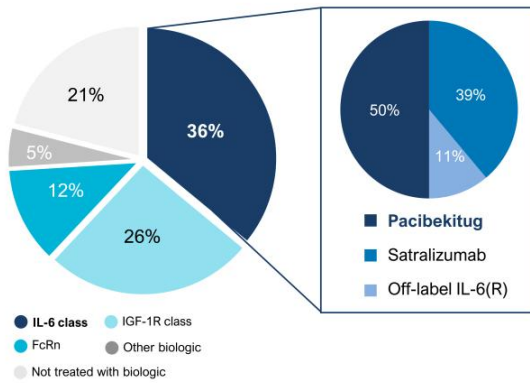


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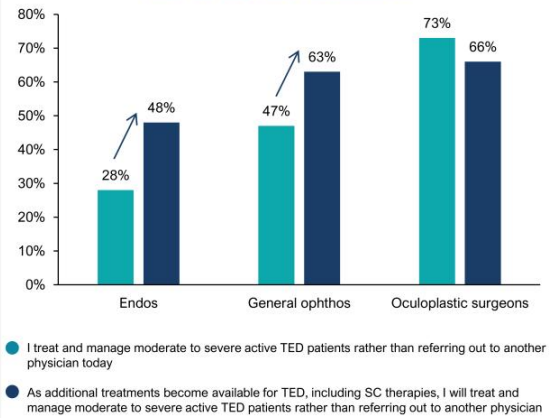
\*This target product profile outlines the desired characteristics of pacibekitug in TED. It will be informed by clinical data from Phase 2b and Phase 3 and additional evidence generated from other programs including from the real world. The characteristics presented reflect outcomes that may not be representative of pacibekitug. The results of past clinical trials may not be indicative of future results, and the results of future or ongoing clinical trials may not demonstrate some or any of the characteristics presented.  
MOA: mechanism of action, QoL: quality of life, TED: thyroid eye disease, SC: subcutaneous

## ...resulting in leading market share, capitalizing on increasing Rx from endocrinologists and ophthalmologists

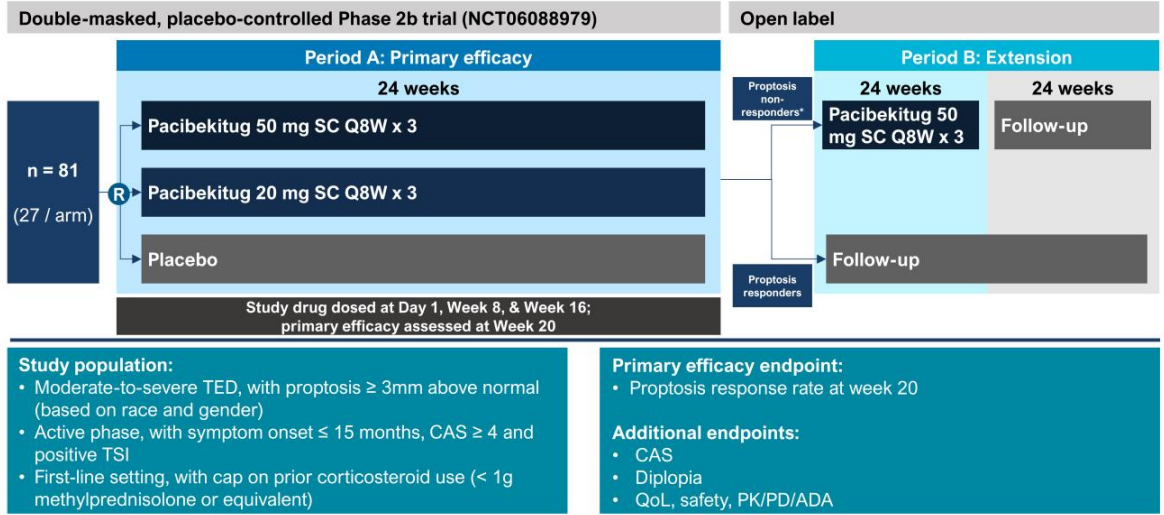
Pacibekitug ranked highest in future market share among 140 TED treaters in US<sup>1</sup>



Impact on Rx if SC therapies are available<sup>1</sup>





**spiriTED pivotal trial in first-line TED**



\*Any patient who receives rescue therapy/intervention in Period A will not receive pacibekitug in Period B and will instead undergo follow-up only

## Key upcoming milestones

Disease focus	Indication	Milestone	Expected timing
Cardiovascular inflammation	ASCVD	 Phase 2 topline data	Q2 2025
	AAA	Phase 2 trial start	Post-TRANQUILITY topline data
Autoimmune disease	TED	 Phase 2b topline data	H2 2025

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