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 5, 2024

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

Delaware	**001-40384**	**83-2377352**
(State or other jurisdiction of incorporation or organization)	**(Commission File Number)**	**(I.R.S. Employer Identification No.)**

27 West 24th Street, Suite 702	
New York, NY	**10010**
(Address of principal executive offices)	**(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 September 5, 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	Corporate Presentation dated September 5, 2024
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)

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: September 5, 2024

By: /s/ Brad Middlekauff
Name: Brad Middlekauff
Title: Corporate Secretary

TOURMALINE

Corporate Overview

September 2024

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.

This presentation contains trademarks, services marks, trade names and copyrights of the Company and other companies, which are the property of their respective owners. The use or display of third parties' trademarks, service marks, trade name or products in this presentation is not intended to, and does not, imply a relationship with the Company, or an endorsement of sponsorship by the Company. Solely for convenience, the trademarks, service marks and trade names referred to in this presentation may appear without the ®, TM or SM symbols, but such references are not intended to indicate, in any way, that the Company will not assert, to the fullest extent under applicable law, their rights or the right of the applicable licensor to these trademarks, service marks and trade name.

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

Experienced leadership team

Management Team

Sandeep Kulkarni, MD
Co-founder and Chief Executive Officer

Yung Chyung, MD
Chief Medical 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

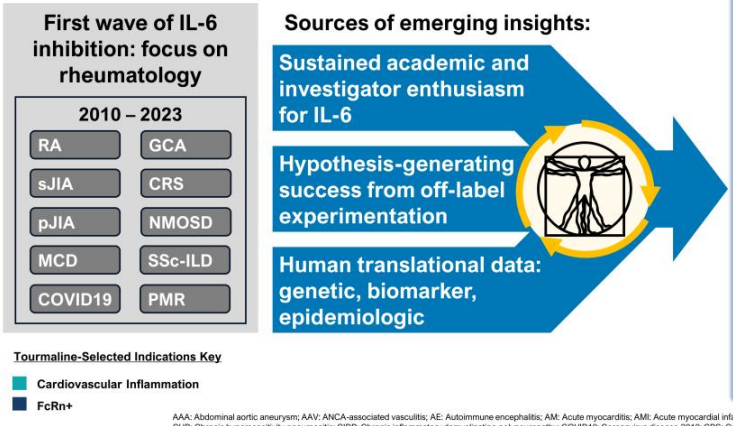
Parvinder Thiara

Sandeep Kulkarni, MD

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 strategic paths to significant value creation:** (1) FcRn+ and (2) cardiovascular inflammation
- **A late-stage clinical company:** pivotal Phase 2b spiriTED TED trial and Phase 2 TRANQUILITY CV trial ongoing, pivotal Phase 3 TED trial also expected to commence in 2H 2024
- **Accomplished leadership team:** extensive experience developing and commercializing antibodies for immune and inflammatory diseases
- **Well-financed:** cash expected to fund operations into 2027, enabling the delivery of key anticipated milestones for both strategic paths

We are in an IL-6 renaissance



Second wave of IL-6 Inhibition: driven by emerging insights

2024: Late-stage programs	2024+: Large body of potential indications		
AE	Cardio:	AAA	AM
AMI		Stroke	
ASCVD	Derm:	BP	PV
DMD	Endo:	Graves'	
HFpEF	GI:	CD	UC
MOGAD	Hem:	ITP	TTP
TED	Neph:	IgAN	MN
UME	Neuro:	CIDP	IBM
		MG	MS
	Ophth:	DME	NIU
	Resp:	CHP	IPF
		PAP	Sarcoid
	Rheum:	AAV	IgG4-RD
		SjS	

Tourmaline-Selected Indications Key

- Cardiovascular Inflammation
- FcRn+

AAA: Abdominal aortic aneurysm; AAV: ANCA-associated vasculitis; AE: Autoimmune encephalitis; AM: Acute myocarditis; AMI: Acute myocardial infarction; ASCVD: Atherosclerotic cardiovascular disease; BP: Bullous pemphigoid; CD: Crohn's disease; CHP: Chronic hypersensitivity pneumonitis; CIDP: Chronic inflammatory demyelinating polyneuropathy; COVID19: Coronavirus disease 2019; CRS: Cytokine release syndrome; DMD: Duchenne muscular dystrophy; DME: Diabetic macular edema; GCA: Giant cell arteritis; FcRn: neonatal Fc receptor; HFpEF: Heart failure with preserved ejection fraction; IBM: Inclusion body myositis; IgAN: IgA nephropathy; IgG4-RD: IgG4 related disease; IPF: Idiopathic pulmonary fibrosis; ITP: Idiopathic thrombocytopenic purpura; MCD: Multicentric castleman's disease; MG: Myasthenia gravis; MN: Membranous nephropathy; MOGAD: Myelin oligodendrocyte glycoprotein antibody-associated disease; MS: Multiple sclerosis; NIU: Non-infectious uveitis; NMOSD: Neuromyelitis optica spectrum disorder; PAP: Pulmonary alveolar proteinosis; pJIA: Polyarticular juvenile idiopathic arthritis; PMR: Polymyalgia rheumatica; PV: Pemphigus vulgaris; RA: Rheumatoid arthritis; Sarcoid: Sarcoidosis; sJIA: Systemic juvenile idiopathic arthritis; SjS: Sjögren's syndrome; SSc-ILD: Systemic sclerosis interstitial lung disease; TED: Thyroid eye disease; TTP: Thrombotic thrombocytopenic purpura; UC: Ulcerative colitis; UME: Uveitic macular edema

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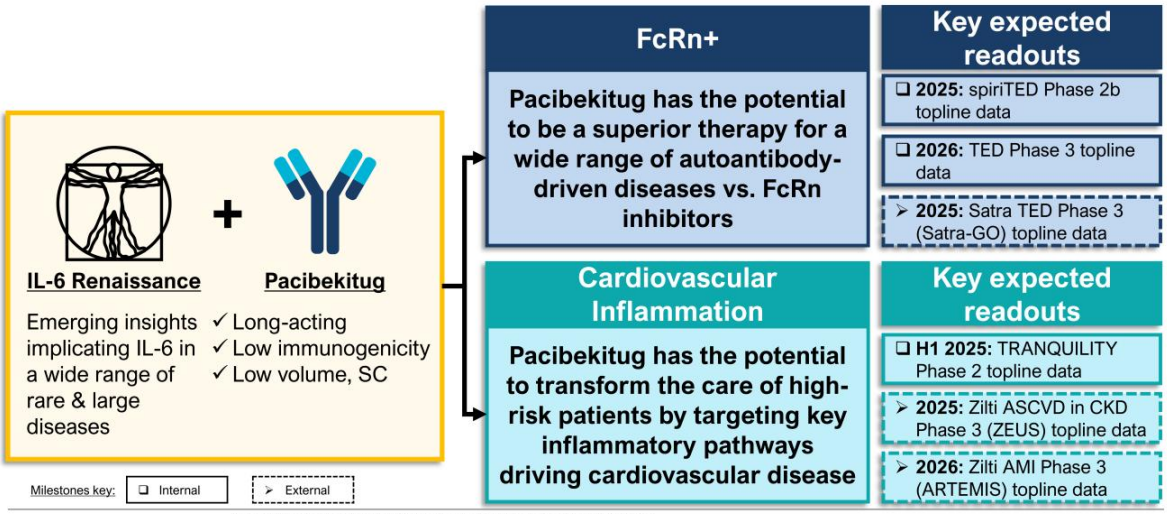
Pacibekitug: an anti-IL-6 antibody with the potential to deliver significant value to patients

Pacibekitug attributes observed to date	Potential value to patients
Long-acting with terminal half-life of ~7 weeks[1]	Dosing every 8 weeks[5] or quarterly[6]
>90% pathway inhibition after single 10mg dose[2]	Fast, deep, and durable impact across diseases
Fully human with ADAs in only 0.5% of pt[3]	Durable benefit without need to increase dose
High affinity to IL-6[4]	Volume of ≤1ml for SC injection[5]
Existing data from 448 study participants[1]	Generally well-tolerated safety profile observed to date

[1]Across six clinical trials in healthy volunteers and RA, SLE, and CD patients. [2]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. [3]Generated from Medarex transgenic mouse platform; across 448 subjects dosed with pacibekitug, only 2 subjects generated anti-drug antibodies (ADAs) following treatment. [4]Data on file. [5]To be assessed based on data from prior Phase 2 trials. [6]To be evaluated in CV Phase 2 trial.

Two strategic paths to unlock major value creation



The timing of regulatory and clinical trial milestones are subject to change and additional discussion with the FDA
AMI: acute myocardial infarction; ASCVD: atherosclerotic cardiovascular disease; CKD: chronic kidney disease; Satra: satralizumab; Zilti: ziltivekimab

Clinical development plan for pacibekitug

Strategy	Indication	Preclinical	Phase 1	Phase 2	Phase 3	Expected key milestones
FcRn+	Thyroid Eye Disease (TED)	spiriTED				Phase 2b topline data expected in 2025
						Phase 3 expected to begin in H2 2024
Cardiovascular Inflammation	Atherosclerotic Cardiovascular Disease (ASCVD)	TRANQUILITY				Phase 2 topline data expected in H1 2025

Expect to announce at least one additional indication in 2024

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

FcRn+

FcRn inhibition has garnered substantial attention to date, however significant unmet need persists

What is FcRn?[1]

- Neonatal Fc receptor (FcRn) inhibition observed to lower IgG antibodies
- Mechanism relevant in disorders mediated by pathogenic IgG autoantibodies
- Two anti-FcRn therapies approved for myasthenia gravis with additional supportive data in CIDP, RA, and TED[2,3,4]

FcRn market adoption

- First approved FcRn inhibitor annualizing ~$1.5B sales in 2nd year of launch in MG[5]
- FcRn companies account for >$30B in market capitalization[6]

Key limitations of FcRn inhibition[7]

- **Efficacy limitations:** incomplete clinical response observed
- **Lack of durable efficacy:** clinical worsening occurs soon after cessation of therapy
- **High burden dosing profile:** burdensome weekly or biweekly IV or high-volume SC infusions/injections
- **Unknown long-term safety profile:** uncertain rate of infectious or other complications from sustained non-specific reduction of total IgG

[1]Pyzik et al., Nat Rev Immunol (2023). [2]Chronic inflammatory demyelinating polyneuropathy (CIDP): ARGX, "argenx Reports Posit Topline Data from ADHERE study..." July 17, 2023. [3]Rheumatoid arthritis (RA): Taylor et al., presentation at ACR Convergence (2023). [4]Thyroid eye disease (TED): Kahaly et al., J Clin Endocrinol Metab (2023). [5]ARGX company reports and filings. [6]FactSet as of 12/29/23; assumes Momenta acquisition for $6.5B, UCB market capitalization not included. [7]VYVGART, VYVGART HYTRULO, and RYSTIGGO FDA labels.

Pacibekitug has broad potential beyond autoantibody reduction

An FcRn+ opportunity

Modes of action for IL-6 inhibition[1,2]

IL-6 inhibition impacts:

- Pathogenic B-cell and plasma cell proliferation
- Pathogenic Th17 and Tfh cell proliferation and differentiation
- Acute phase proinflammatory signaling
- Circulation of pathogenic autoantibodies

Potential benefits of IL-6 inhibition versus FcRn inhibition

	IL-6 inhibition[1,2,3]	FcRn inhibition[4,5,6]
Autoantibody reductions	✓	✓
Inhibition of autoantibody production	✓	✗
Anti-inflammatory effects beyond autoantibody reduction	✓	✗
Durability of effect	✓	✗
Low administration burden	✓	✗
Favorable long-term safety profile observed to date	✓	?

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[1]Cabezas et al., Front Immunol (2022). [2]Dienz et al., J Exp Med (2009). [3]Tourmaline PK/PD modelling. [4]Howard et al., Lancet Neurol (2021). [5]Patel and Bussel, J Allergy Clin Immunol (2020). [6]VYVGART, VYVGART HYTRULO, and RYSTIGGO FDA labels.

TED: our beachhead indication designed to validate pacibekitug's FcRn+ 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)[1,2]
   - ~80%[3] 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)[4]

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[4]

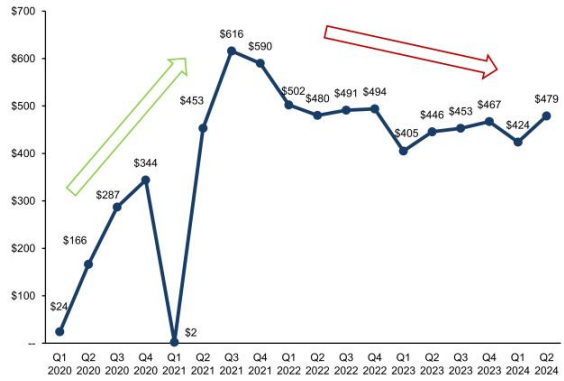
3. **Pacibekitug has best-in-disease potential in TED**
   - Deep inhibition of IL-6 pathway observed to date offers potential for durable efficacy across many endpoints
   - Existing clinical database supports the potential for a well-tolerated profile at selected doses
   - Q8W dosing would allow for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

[1]Lazarus, Best Pract. Res. Clin. Endocrinol. Metab. (2012). [2]Bartalena et al., Front. Endocrinol. (2020). [3]Horizon Q3 2022 earnings call. [4]Tourmaline market research.

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

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

Sales ($M)[1]



…believed to be due to real-world experience

1. **Safety issues:** Risk of potentially permanent hearing loss[2]

> **----------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[3,4]

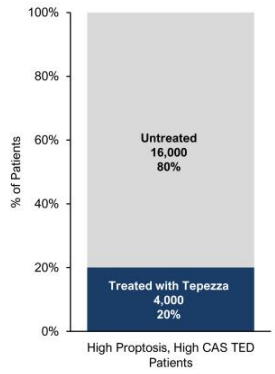
3. **High level of inconvenience & complexity:**
   - IV Q3W (n=8)[2] but limited access to infusion centers[5]
   - Numerous visits and high time commitment (HCPs and patients)[5]
   - Need for serial audiograms, as per label[2,6]
   - Burdensome reimbursement approval process[7]

[1]Horizon and Amgen company reports and filings. [2]TEPEZZA FDA label. [3]Kahaly et al., Thyroid (2021) (ATA 2021 presentation). [4]Rosenblatt et al., Ophthalmic Plast Reconstr Surg (2023). [5]Tourmaline market research. [6]Chow and Silkiss, BMJ Case Rep (2022). [7]Horizon Therapeutics Public Ltd. Co. Q2 2023 Form 10-Q.

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

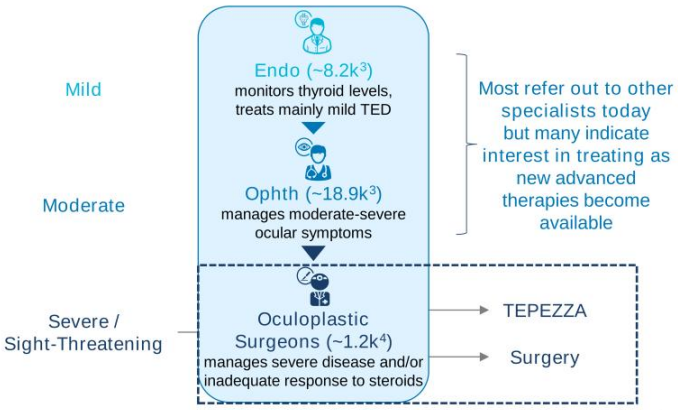
Most TED patients are not receiving TEPEZZA…

TEPEZZA US LTM penetration[1]



…or only get it relatively late in the treatment journey[2]

Simplified Treatment Journey[2]



[1]Horizon Q3 2022 earnings call; LTM = last twelve months. [2]Tourmaline market research; endo = endocrinologist; ophth = ophthalmologist. [3]AAMC 2022 Physician Specialty Data Report. [4]Hussey and Tao, Orbit (2022).

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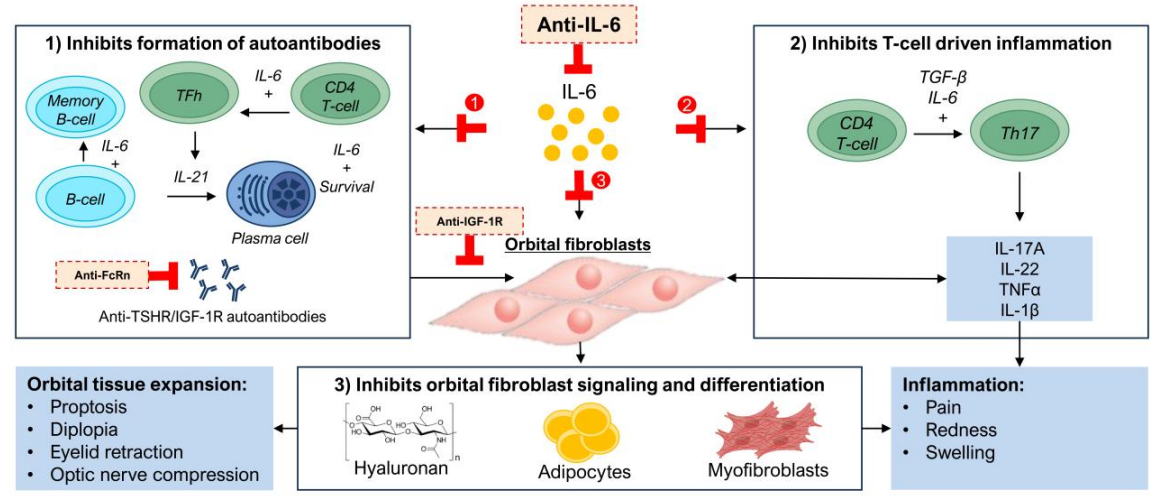
IL-6 inhibition has the potential to address a central and upstream driver of TED



Adapted from Huang et al., Eye (2018); Hodgson and Rajaii, Ophthalmol Ther (2020); Fang et al, Front Endocrinol (2021); Smith et al., Eye (2019); and Cabezas et al., Front. Immunol. (2022)

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

Study Details				Key Endpoints		
First author	Year	Study type	N treated	Proptosis response rate	CAS response rate	% autoantibody reduction
Pérez-Moreiras	2021	Retro	54	78	89	75
Sánchez-Bilbao	2020	Obs	48	NR	NR	NR
Atienza-Mateo	2018	Retro	29	NR	NR	NR
Lee	2024	Prosp	19	11	47	56
Pérez-Moreiras	2014	Prosp	18	72	100	76
Pérez-Moreiras	2018	RCT	15	93	60	NS
de la Fuente Bursón	2020	Retro	15	NR	NR	NR
Pereira	2023	Retro	14	NR	NR	NR
Habroosh	2024	Prosp	13	100	31	68
Boutzios	2023	Obs	12	NR	NR	84
Pampín-Sánchez	2022	Retro	11	75	73	NR
Moi	2022	Retro	10	CI	80	75
Cortez	2022	Prosp	10	10	100	81
Silkiss	2020	CS	9	CI	56	74
Smith	2021	Retro	9	78	100	54
Bielefeld	2019	Obs	8	NR	NR	NR
Ceballos-Marcias Jose	2020	CS	8	NR	75	41
Bennedjai	2020	Retro	7	NR	NR	73
Moás	2022	Obs	7	NR	NR	92
Toro-Tobon	2023	Retro	6	50	NR	NR
de Pablo Gomez	2018	CS	5	NR	60	NR
Navarrete	2022	Retro	5	NR	NR	NR
Ribi	2017	CS	3	33	67	NR
Maldiney	2020	CS	3	67	NR	NR
Stevens	2022	Retro	3	100	67	NR
Russell	2017	CS	2	NR	0	NR
Sy	2017	CS	2	CI	50	69

Study Details				Key Endpoints		
First author	Year	Study type	N treated	Proptosis response rate	CAS response rate	% autoantibody reduction
Copperman	2019	CS	2	100	0	NR
Coy	2019	CS	2	NR	50	NR
Sierra Osorio	2020	CS	2	100	100	NR
Park	2021	CS	2	100	100	NR
Abeillon-du Payrat	2022	CS	2	100	50	NR
Butnaru	2013	CR	1	NR	100	NR
Gómez Rodríguez	2014	CR	1	NR	100	NR
Bielefeld	2017	CR	1	CI	NR	NR
Canas	2018	CR	1	100	NR	NR
Pascual-Camps	2018	CR	1	NR	NR	NR
Garreta Fontelles	2019	CR	1	NR	NR	93
Mehmet	2020	CR	1	0	NR	NR
Kaplan	2020	CR	1	NR	0	85
Cayon-Blanco	2020	CR	1	NR	100	NR
Tran	2020	CS	1	NR	NR	NR
Ruiz	2021	CR	1	NR	NR	NR
Albrashdi	2022	CR	1	100	NR	NR
Cezara	2022	CR	1	NR	0	NR
Mohamed	2022	CS	1	0	0	NR
Moleiro	2022	CR	1	100	NR	86
Almazrouei	2023	CR	1	NR	NR	NR
Cuculescu	2023	CR	1	CI	0	NR
Nirmalan	2023	CS	1	NR	NR	NR
Pramono	2023	CR	1	NR	NR	NR
Rymuza	2024	CR	1	100	0	8
Weighted Mean				**68%**	**72%**	**71%**
Smith 2017 (tepro Phase 2)				**71%**	**69%**	**N/A**
Douglas 2020 (tepro Phase 3)				**83%**	**59%**	**N/A**

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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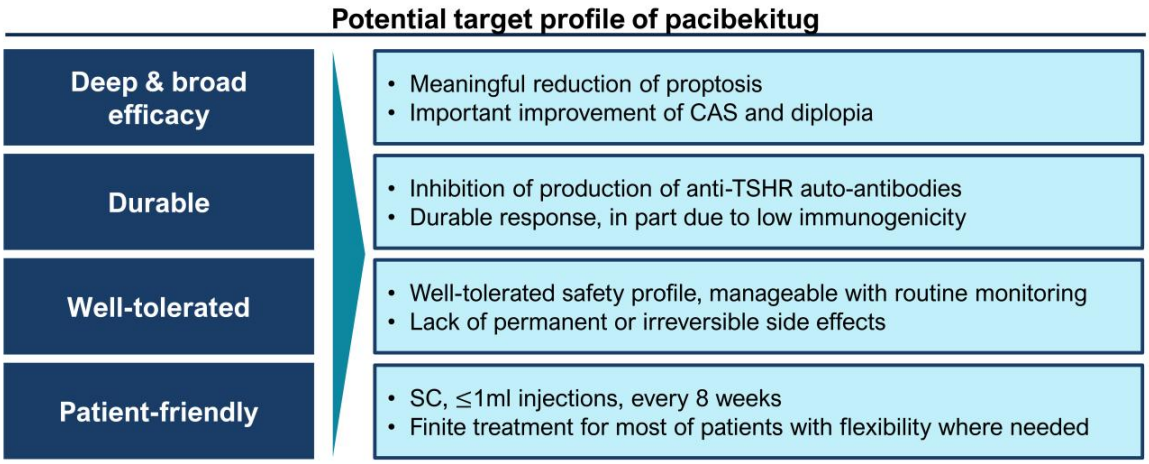
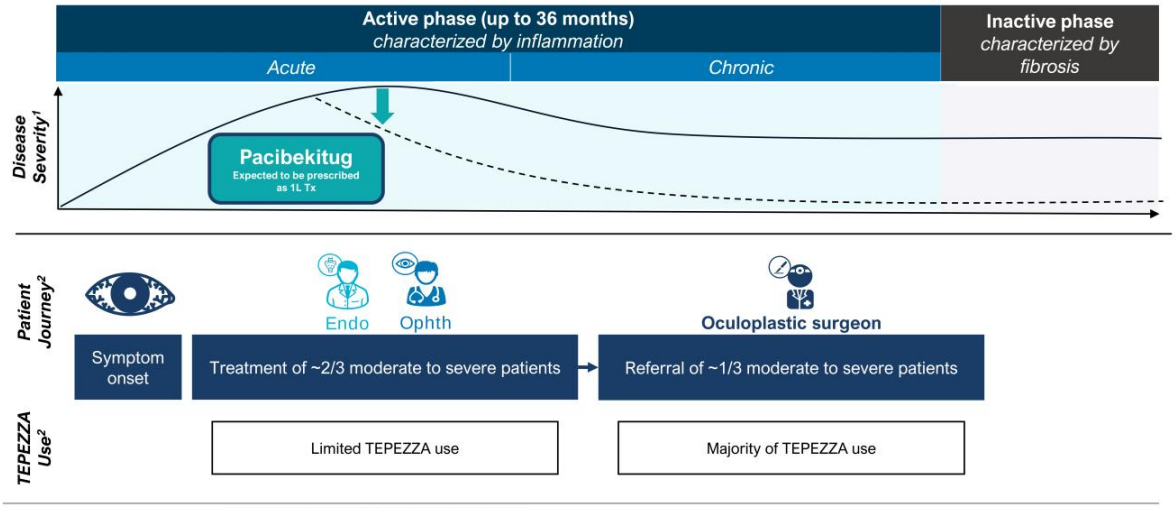
Proptosis response rate is generally defined in the data outlined here as a ≥2 mm proptosis improvement in the worse eye at baseline without any worsening in the other eye. CAS response rate is generally defined in the data outlined here as a CAS of 0 or 1. Studies referenced in this table represent 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

Market research indicates pacibekitug's potential to become an optimal first-line therapy and market leader in TED



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.

Pacibekitug offers the potential to stop disease progression in the inflammatory active phase



[1]Adapted from Bartley, Arch Ophthalmol. (2011). [2]Tourmaline market research.

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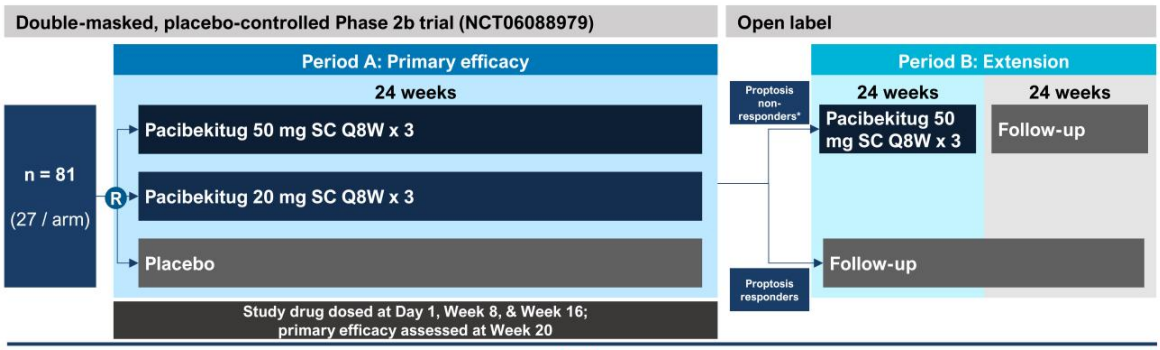
spiriTED pivotal trial in first-line TED



Study population:
- Moderate-to-severe TED, with proptosis ≥ 3mm above normal (based on race and gender)
- Active phase, with symptom onset ≤ 15 months, CAS ≥ 4 and positive TSI
- First-line setting, with cap on prior corticosteroid use (< 1g methylprednisolone or equivalent)

Primary efficacy endpoint:
- Proptosis response rate at week 20

Additional endpoints:
- CAS
- Diplopia
- QoL, safety, PK/PD/ADA

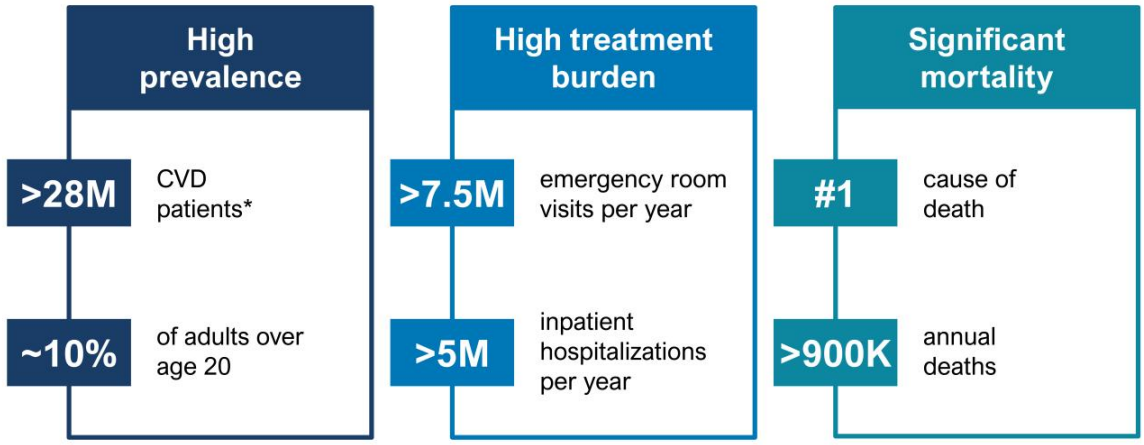
*Any patient who receives rescue therapy/intervention in Period A will not receive pacibekitug in Period B and will instead undergo follow-up only

Cardiovascular Inflammation

Pacibekitug could address a critical but poorly-addressed risk factor in cardiovascular diseases

- IL-6 driven inflammation has increasingly been validated as a critical modifiable risk factor driving residual cardiovascular risk
- The potential of IL-6 inhibition spans a broad range of cardiovascular indications, affecting tens of millions of patients globally
- Converging lines of human evidence across multiple settings support the transformative potential of IL-6 inhibition
- IL-6 inhibition is being evaluated in multiple cardiovascular outcomes trials, and Tourmaline is well-positioned to capitalize on emerging clinical enthusiasm
- Pacibekitug's potentially best-in-class profile, including quarterly subcutaneous administration, is being evaluated in the Phase 2 TRANQUILITY study and is anticipated to be Phase 3-ready in 2025

Cardiovascular disease continues to be the largest area of unmet medical need in the US[1]



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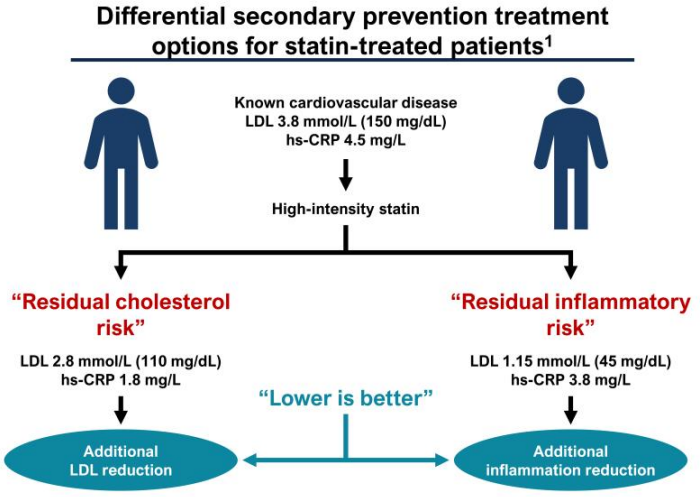
[1]Tsao et al., Circulation (2023). *Includes coronary heart disease, heart failure and stoke; excludes hypertension
CVD: Cardiovascular disease.

Many patients suffering from cardiovascular diseases continue to experience residual inflammatory risk

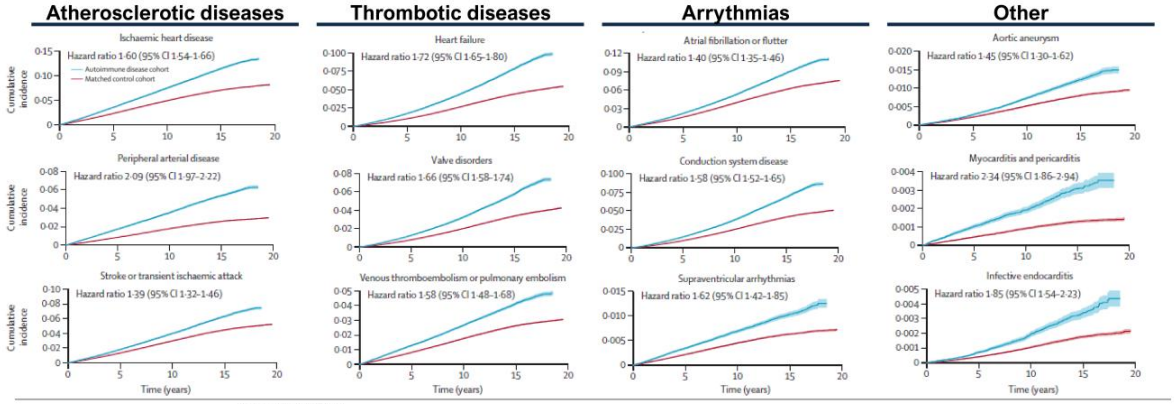


- A growing body of evidence supports addressing **residual inflammatory risk** in cardiovascular disease patients whose inflammation is not well-controlled on existing therapies, such as statins.
- As of August 2024, the European Society of Cardiology guidelines **recommend hs-CRP screening** for patients with suspected chronic coronary syndrome[2]

[1]Adapted from Ridker, Eur Heart J (2016). [2]Vrints et al., Eur Heart J (2024).

Inflammation is a strong predictor of risk across several cardiovascular indications

- Landmark study of >440,000 patients with chronic inflammatory disorders
- Each of the 19 most common autoimmune diseases showed increased CV risk
- Excess risk reflected in a wide range of cardiovascular diseases beyond ASCVD
- Risk elevation was not explained by traditional risk factors such as cholesterol, body-mass index, and diabetes



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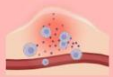
Conrad et al., Lancet (2022).
ASCVD: atherosclerotic cardiovascular disease

Significant unmet need for targeted anti-inflammatory therapies for cardiovascular diseases

Atherothrombotic Pathways	Thrombosis	Hypertension	Atherogenic lipoproteins	Diabetes, Insulin resistance, Obesity	Inflammation
					
Biomarkers	**None readily available**	**Blood pressure**	**ApoB, Non-HDL-C, LDL-C, Triglycerides, Lipoprotein(a)**	**HbA1c, Fasting glucose, Weight**	**C-reactive protein**
Approved Therapies	Aspirin P2Y12R inhibitors Factor Xa inhibitor PAR-1 antagonist	ACEI/ARB Calcium channel blocker Thiazide diuretic Renin inhibitor Beta-blocker Mineralocorticoid antagonist	Statins PCSK9 inhibitors Icosapent ethyl NPC1L1 inhibitor ACL inhibitor Bile acid sequestrants MTP inhibitor ANGPTL3 inhibitor Apheresis	SGLT2 inhibitors GLP-1 agonists GIP/GLP-1 agonist	Colchicine
Therapies in Development	Factor XI/XIa inhibitors	Angiotensinogen inhibitor Aldosterone synthase inhibitors Endothelin antagonist Renal denervation Baroreceptor activation	CEPT inhibitor Lipoprotein(a) inhibitors ApoC3 inhibitor Fibrates CRISPR PCSK9 base editing	GIP/GLP-1/glucagon agonists Amylin agonists GIP-1/amylin agonists	IL-6 inhibitors NLRP3 inhibitors

ACEI: angiotensin-converting enzyme inhibitor, ANGPTL3: angiopoietin-like protein 3, ApoB: apolipoprotein B, ARB: angiotensin receptor blocker, GLP-1: glucagon-like peptide-1, MTP: microsomal triglyceride transfer protein, NPC1L1: Niemann-Pick C1-Like 1, PAR: protease-activated receptors, PCSK9: proprotein convertase subtilisin/ kexin type 9, SGLT2: sodium-glucose cotransporter 2

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

RESEARCH LETTER

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

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

Research Letter

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

RESEARCH ARTICLE

Circulating Interleukin-6 Levels and Incident Ischemic Stroke

A Systematic Review and Meta-analysis of Prospective Studies

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

ORIGINAL RESEARCH

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

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

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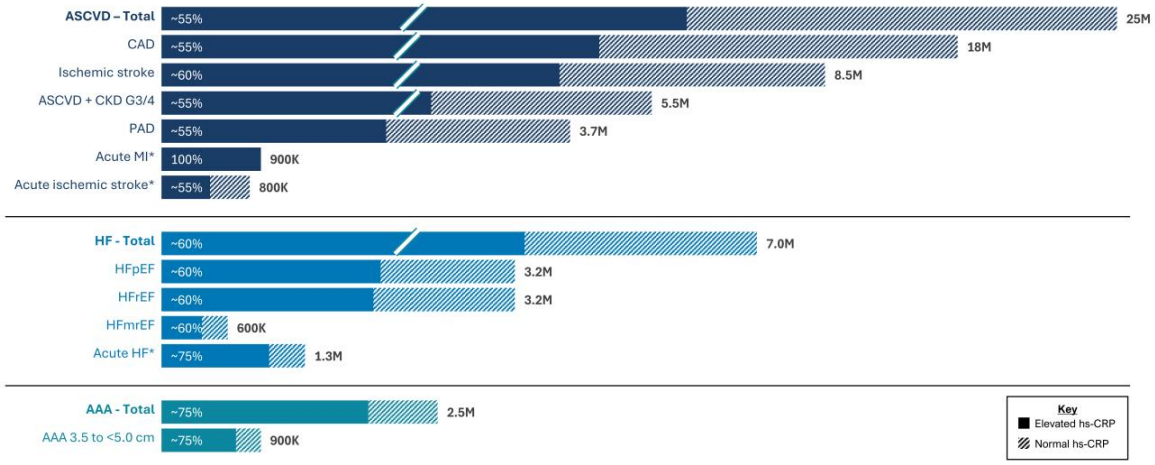
IL-6 inhibition has the potential to address millions of patients across a wide range of inflammation mediated CV conditions

Estimated US prevalence (2024)[1]

Populations are not mutually exclusive



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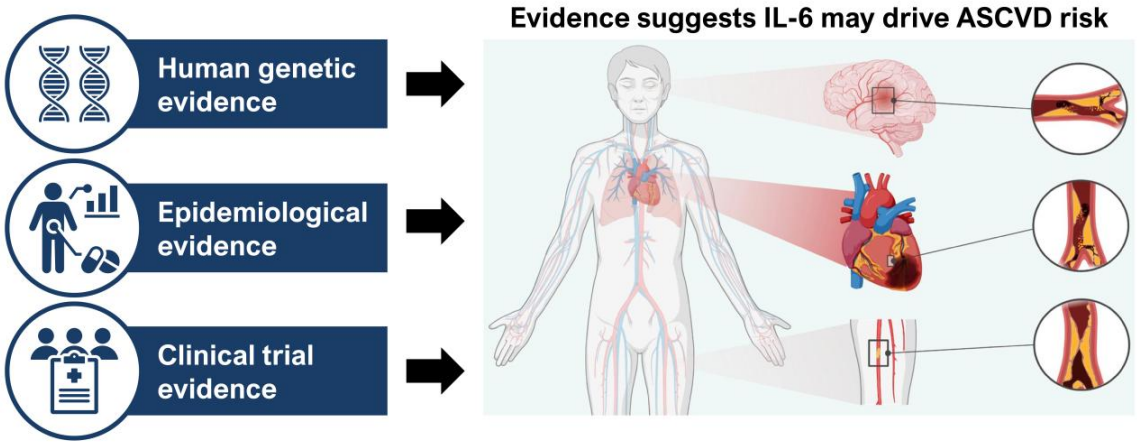
[1]Publications available upon request. *Annual incidence
AAA: abdominal aortic aneurysm. ASCVD: atherosclerotic cardiovascular disease. CAD: coronary artery disease. CKD: chronic kidney disease. HF: heart failure. HFmrEF: Heart Failure with Mid-Range Ejection Fraction. HFpEF: heart failure with preserved ejection fraction. HFrEF: heart failure with reduced ejection fraction. MI: myocardial infarction. PAD: peripheral artery disease.

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



ASCVD: atherosclerotic cardiovascular disease

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

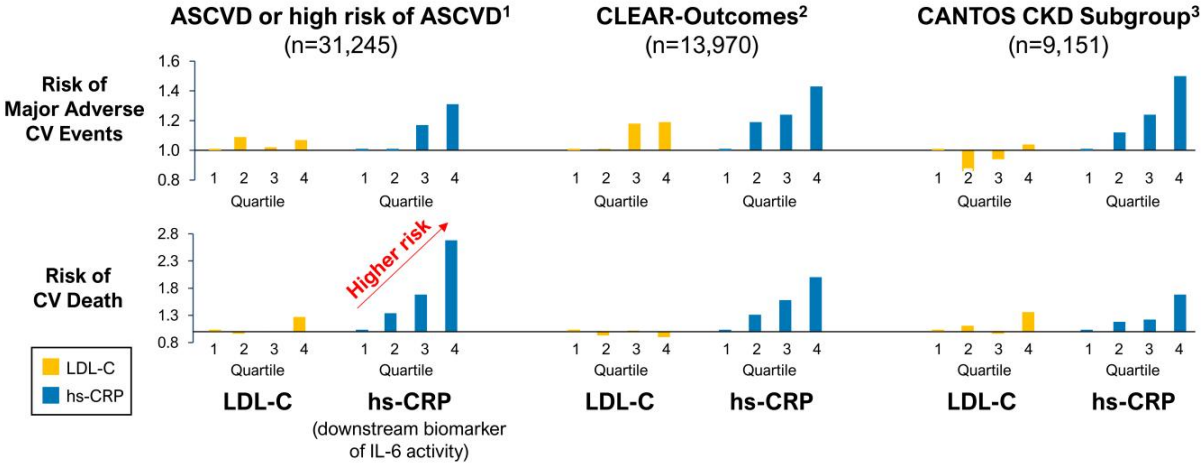
Concordance between results of human genetic studies and randomized clinical trials

Therapeutic target	Genetic Result	RCT Result
Lowering LDL-C to lower ASCVD risk[1,2]	Positive	Positive
Inhibiting IL-6 to treat polymyalgia rheumatica[3,4]	Positive	Positive
Lowering blood pressure to lower ASCVD risk[5,6]	Positive	Positive
Raising HDL-C to lower ASCVD risk[7,8]	Negative	Negative
Inhibiting LpPLA2 to lower ASCVD risk[9,10]	Negative	Negative
Inhibiting TNFα to treat multiple sclerosis[11,12]	Negative (harm)	Negative (harm)
Inhibiting IL-6 to lower ASCVD risk[13]	Positive	Trials Ongoing

"Probability of success for drug mechanisms with genetic support is 2.6 times greater than those without."[14]

[1]Ference et al., J. Am. Coll. Cardiol. (2012). [2]Casula et al., Pharm. Res. (2019). [3]Zhao et al., Ann Rheum Dis (2022). [4]Spiera eta al. N Engl Med (2023). [5]Wan et al., Hypertension (2021). [6]The Blood Pressure Lowering Treatment Trialists' Collaboration, Lancet (2021). [7]Voight et al., Lancet (2012). [8]Keene et al., BMJ (2014). [9]Gregson et al., Eur J Prev Cardiol. (2017). [10]Fras et al., Arch Med Sci. (2021). [11]Kang et al., Neurology (2021). [12]Lenercept Multiple Sclerosis Study Group, Neurology (1999). [13]Levin et al, Circulation Research (2021). [14]Minikel et al., Nature (2024).

Multiple observational studies show inflammation predicts future MACE even better than cholesterol in high-risk populations

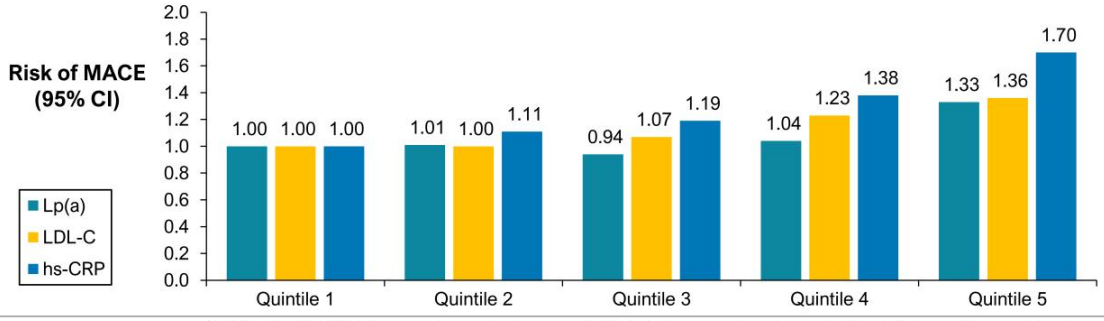


Hazard ratios shown. Major adverse cardiovascular events (MACE) include myocardial infarction, stroke, coronary revascularization, cardiovascular (CV) death.
CKD: chronic kidney disease. hs-CRP: high-sensitivity C-reactive protein. LDL: low-density lipoprotein cholesterol. Certain data in this presentation 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.
[1]Ridker et al., Lancet (2023). [2]Ridker et al., Circulation (2023). [3]Ridker et al., Eur Heart J (2022).

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[1]
(n=27,929)



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[1]Women's Health Study. MACE: CV death, MI, stroke, coronary revascularization. Increased risk defined as 1-relative risk, compared to lowest quintile of Lp(a) and hs-CRP population, adjusted for age, initial randomization treatment group, smoking (current, past, never), presence of diabetes, and Framingham blood pressure categories. Table 2. Ridker et al, NEJM (2024).

Analysis of CANTOS implicates IL-6 as a key ASCVD risk factor

Greater IL-6 pathway inhibition associated with greater CV benefit

Canakinumab Anti-inflammatory Thrombosis Outcomes Study (CANTOS) Trial Design[1]

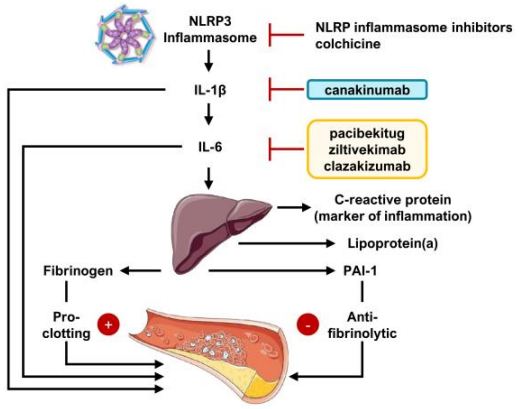
10,061 patients
- Stable CAD (post MI)
- On Statin, ACE/ARB, BB, ASA
- hs-CRP ≥2 mg/L

- Canakinumab 50 mg Q3M n = 2,170
- Canakinumab 150 mg Q3M n = 2,284
- Canakinumab 300 mg Q3M n = 2,263
- Placebo Q3M n = 3,344

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

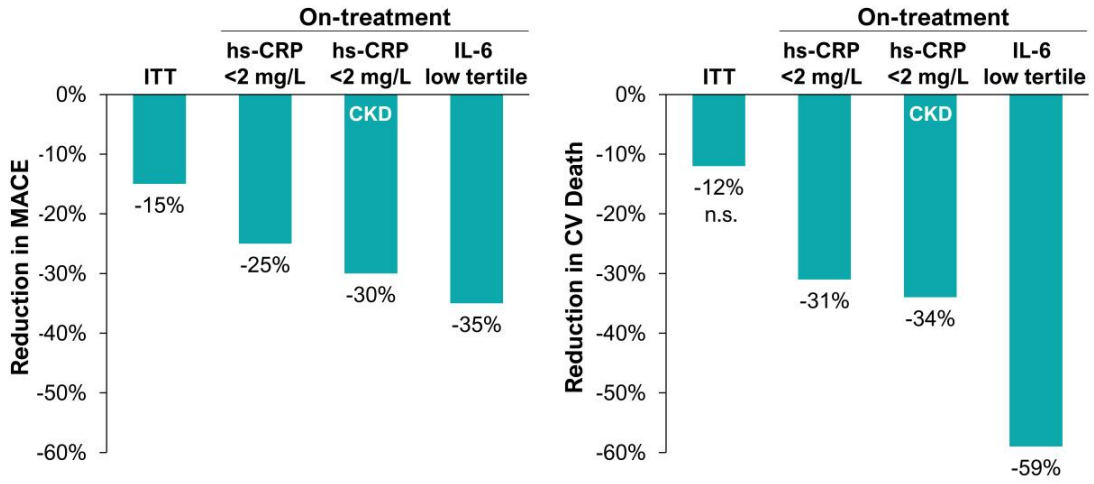
On-treatment analysis:
- Reduction in MACE & CV death stratified by on treatment hs-CRP reduction (pre-specified)
- Reduction in MACE & CV death stratified by on treatment IL-6 reduction

IL-1β is upstream of IL-6[2]



[1]Ridker et al., N. Engl. J. Med. (2017). [2]Adapted from Ridker et al., Circ. Res. (2016), Arnold et al., Eur. J. Cardiol. (2021) and Muller et al., J Lipid Res (2015)

Lessons from canakinumab (anti-IL-1β mAb):
"Lower is better" for downstream biomarkers of IL-6 activity



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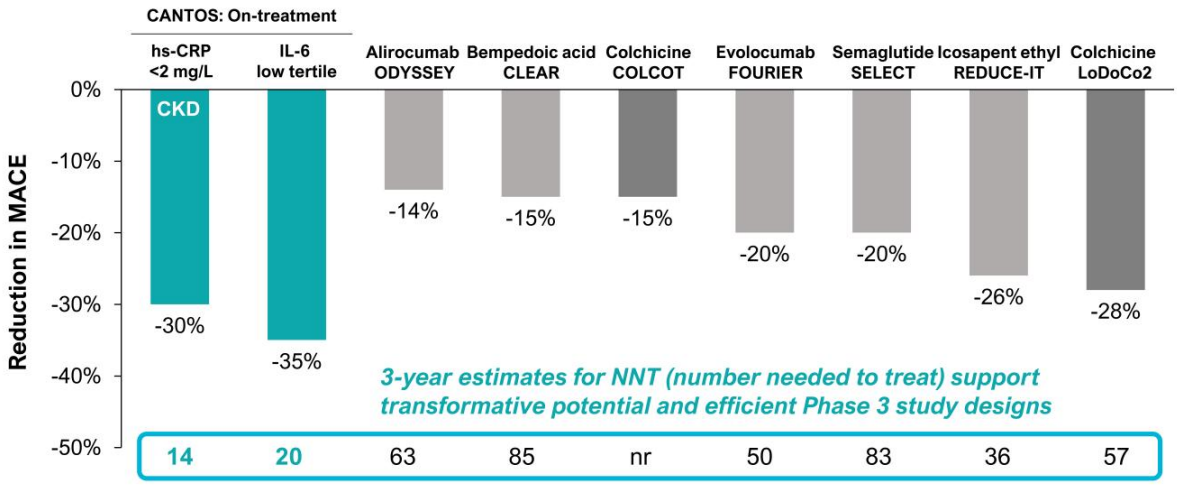
Reduction in MACE shown as 1-Hazard Ratio. ITT: intent to treat. MACE: major adverse cardiovascular events including CV death, myocardial infarction (MI), stroke. n.s.: not statistically significant. ITT CANTOS analysis presents data for 150mg dose group; values for CANTOS subanalyses combine all doses (50, 150, 300 mg). Ridker et al., NEJM (2017). Ridker et al., Lancet (2018). Adjusted for age, gender, smoking, hypertension, diabetes, BMI, baseline hs-CRP, baseline LDL-C. Ridker et al., Eur Heart J (2018). Adjusted for age, gender, smoking, hypertension, diabetes, BMI, baseline IL-6, baseline LDL-C. Ridker et al., JACC (2018).

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



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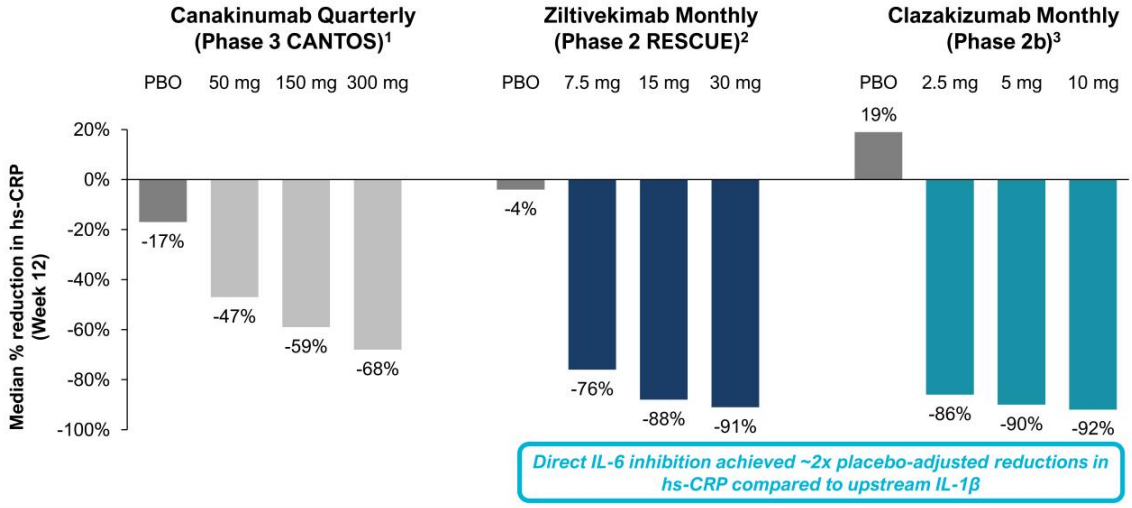
Reduction in MACE shown as 1-Hazard Ratio. MACE: major adverse cardiovascular events including CV death, myocardial infarction (MI), stroke except for: ODYSSEY OUTCOMES (all death, MI, ischemic stroke); COLCOT (CV death, MI, stroke, resuscitated cardiac arrest); LoDoCo2 (CV death, MI, ischemic stroke); main CANTOS analysis presents data for 150mg dose group; values for CANTOS subanalyses combine all doses (50, 150, 300mg); control arms were placebo + background SoC. 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-1β blockade



Direct IL-6 inhibition achieved ~2x placebo-adjusted reductions in hs-CRP compared to upstream IL-1β

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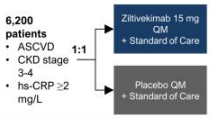
[1]Ridker et al., NEJM (2017). [2]Ridker et al., Lancet (2021). [3]Chertow, Nature (2024).
Certain data in this presentation are based on a cross-trial comparison and are not based on head-to-head clinical trials. Cross trial comparisons are inherently limited and may suggest misleading similarities or differences in outcomes. Results of head-to-head comparisons may differ significantly from those set forth herein.

Five Phase 3 CVOTs enrolling >24,000 patients

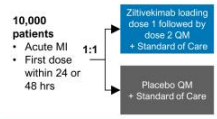
ZEUS: ASCVD w/CKD[1]



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

Secondary endpoints:
- Time to first occurrence of expanded MACE (above plus urgent coronary revascularization)
- Number of hospitalizations for HF or urgent HF visits
- Time to occurrence of CV death
- Time to first occurrence of composite CKD endpoint

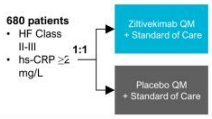
ARTEMIS: acute MI[2]



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

Secondary endpoints:
- Number of CV death, non-fatal MI, non-fatal stroke
- Time to first occurrence of composite MACE consisting of: all-cause mortality, non-fatal MI, and non-fatal stroke
- Time to first occurrence of MI (fatal and non-fatal)
- Time to occurrence of CV death

ATHENA: HFpEF[3]



Primary endpoint:
Change in KCCQ-CSS at 1 year

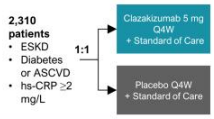
Secondary endpoints:
- Participant achieving threshold for clinically meaningful within-participant change in KCCQ CSS
- Participant achieving threshold for clinically meaningful within-participant change in 6-minute walk distance (6MWD)
- Participants improving 5 points or more in KCCQ-CSS

HERMES: HFpEF[4]

Primary endpoint:
Time to first occurrence of a composite HF endpoint (CV death, HF hospitalization, or urgent HF visit)

Secondary endpoints:
- Time to first occurrence of 4-point composite HF endpoint (CV death, HF hospitalization or urgent HF visit, non-fatal MI, non-fatal stroke)
- Number of CV deaths, HF hospitalizations or urgent HF visits
- Time to occurrence of CV death

POSIBIL6: ESKD[5]



Primary endpoint:
Time to first occurrence of CV death or MI

Secondary endpoints:
- Time to first occurrence of all-cause death or MI
- Time to first occurrence of CV death, MI, or ischemic stroke
- Time to first occurrence of CV death

Topline data readouts expected

2025	2026	2026	2027	2028

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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.
[1]Clinicaltrials.gov: NCT05021835. [2]Clinicaltrials.gov: NCT06118281. [3]Clinicaltrials.gov: NCT06200207 [4]Clinicaltrials.gov: NCT05636176 [5]Clinicaltrials.gov: NCT05485961 (Phase 3 portion only)

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

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

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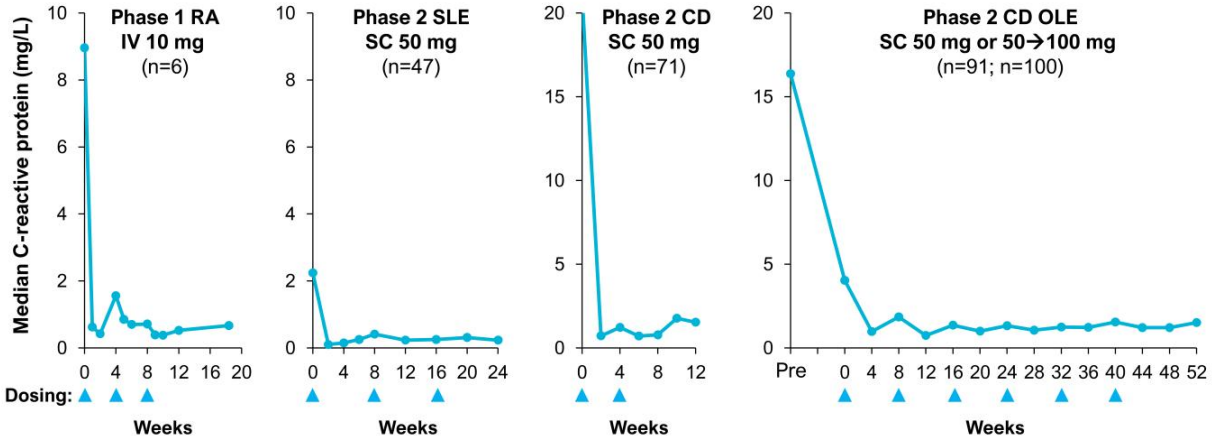
CD: Crohn's disease, CKD: chronic kidney disease, HD: hemodialysis, NDD: non-dialysis dependent, SLE: systemic lupus erythematosus. [1]Incidence of ADAs in repeat-dose studies calculated as reported per dosing arm. [2]Route of administration in planned or ongoing studies in patients with or at high-risk of ASCVD. [3]Clinicaltrials.gov NCT03926117. [4]Pergola et al., JASN (2021). [5]Ridker et al., Lancet (2021). [6]Wada et al., J Cardiol (2023). [7]Clinicaltrials.gov NCT01490450. [8]Clinicaltrials.gov NCT01545050. [9]Weinblatt et al., Arthritis Rheum (2015). [10]Clinicaltrials.gov NCT05485961.
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.

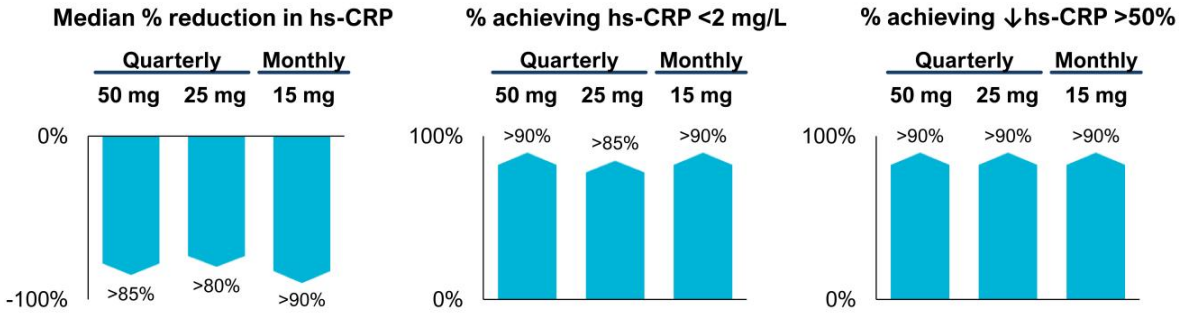
Pacibekitug achieved robust and durable suppression of CRP in patients with high-grade inflammatory autoimmune disorders



CRP: C-reactive protein, 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-TNFα. 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 14.3.4.1.5. 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



Ziltivekimab 15 mg monthly[1]
median % reduction: 88% | % achieving hs-CRP<2 mg/L: 82% | % achieving ↓hs-CRP>50%: 89%

Clazakizumab 5 mg monthly[2]
median % reduction: 90% | % achieving hs-CRP<2 mg/L: 82% | % achieving ↓hs-CRP>50%: 92%

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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 90 are shown. [1]Ridker et al., Lancet (2021). [2]Chertow, Nature (2024). 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)

Study population:

- CKD stage G3-4 (eGFR 15-59 ml/min/1.73m^2)
- hs-CRP ≥2 mg/L and <15 mg/L
- Exclude patients at higher risk for safety complications (e.g., immunocompromised patients)

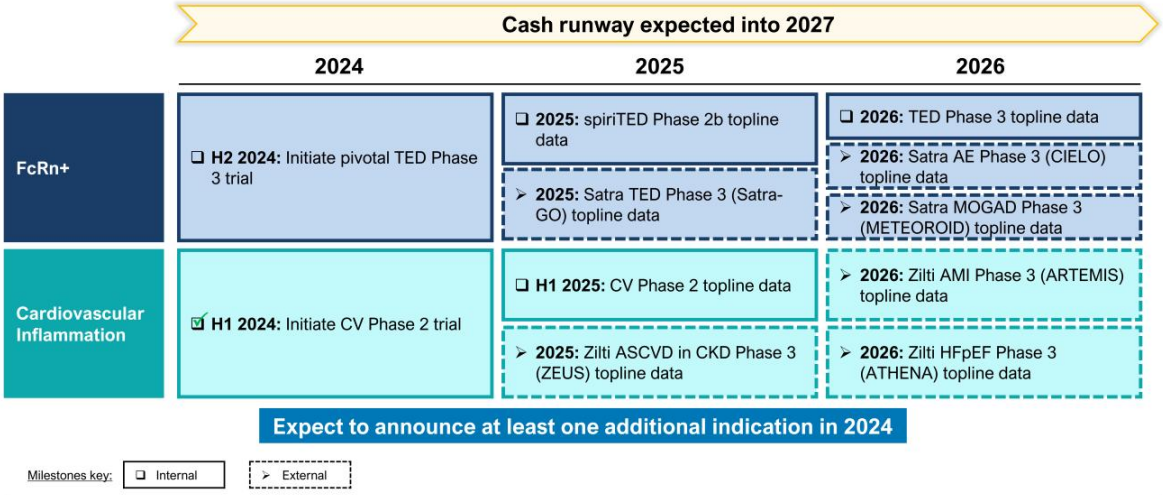
Primary efficacy endpoint:

- Change from baseline in hs-CRP

Additional endpoints:

- Other pharmacodynamic markers: serum amyloid A, fibrinogen, lipoprotein(a), and other biomarkers
- Safety and tolerability

Key milestones expected through 2026



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The timing of regulatory and clinical trial milestones are subject to change and additional discussion with the FDA
AE: autoimmune encephalitis; AMI: acute myocardial infarction; ASCVD: atherosclerotic cardiovascular disease; HFpEF: heart failure with preserved ejection fraction. MOGAD: myelin oligodendrocyte glycoprotein antibody-associated disease; Satra: satralizumab; TED: thyroid eye disease; Zilti: ziltivekimab


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