

POLYGON Therapeutics unveils PLG-105, a first-in-class anti-TREM-1 program for cardiovascular disease, supported by landmark human data published in the European Journal of Preventive Cardiology

- **Large prospective study in more than 9,000 apparently healthy participants identifies soluble TREM-1 (sTREM-1) as a strong and independent predictor of future cardiovascular events**
- **Participants with the highest sTREM-1 levels showed a >10-fold increased risk of major cardiovascular events over 10 years**
- **These results have been validated in another independent prospective cohort**
- **Findings provide strong translational support for PLG-105, POLYGON's anti-TREM-1 therapeutic program in atherosclerotic cardiovascular disease (ASCVD)**

PARIS, France, June 17th, 2026 — POLYGON Therapeutics, a biotechnology company developing cardio-immunology therapies, today announced the publication of a major prospective cohort study validating soluble TREM-1 (sTREM-1) as an independent predictor of cardiovascular disease (CVD). The study, **published in the European Journal of Preventive Cardiology**, provides important human translational evidence supporting POLYGON's first-in-class anti-TREM-1 program, PLG-105, in atherosclerotic cardiovascular disease (ASCVD).

The study was **conducted in the Paris Prospective Study III (PPS3)**, a community-based cohort of **9,097 participants** free of cardiovascular disease at baseline and **followed for a median of 10 years**. Investigators measured plasma sTREM-1 levels and assessed their association with future cardiovascular events, including coronary heart disease, stroke, heart failure and peripheral artery disease.

Participants with the highest sTREM-1 levels (>290 pg/mL) experienced a greater than 10-fold increased risk of cardiovascular events compared with those with the lowest levels (<200 pg/mL), independently of established cardiovascular risk factors including LDL cholesterol, blood pressure, CRP, IL-6, glycaemia and renal function. The **findings were externally validated** in the independent Swiss CoLaus|PsyCoLaus cohort.

Adding sTREM-1 to established cardiovascular risk models significantly **improved risk prediction and patient reclassification performance**, highlighting its potential utility for patient stratification and biomarker-driven clinical development.

"These findings provide important human validation of the TREM-1 pathway in cardiovascular disease and strengthen the translational rationale for investigating TREM-1 inhibition in ASCVD" said **Prof. Hafid Ait-Oufella**, Co-Founder & Chief Scientific Officer, POLYGON Therapeutics.

"The magnitude and consistency of the association observed in this study are remarkable," added **Prof. Peter Libby**, Mallinckrodt Professor of Medicine, Harvard Medical School and Brigham and Women's Hospital. *"These findings support the relevance of the TREM-1 pathway in cardiovascular disease biology and warrant further investigation of therapeutic approaches targeting this pathway."*

TREM-1 is an immuno-metabolic receptor expressed on myeloid cells that amplifies inflammatory signaling within the atherosclerotic plaque environment. Preclinical studies suggest that TREM-1 contributes to multiple immuno-metabolic mechanisms involved in plaque progression and destabilization, including inflammatory cell recruitment, lipid uptake, oxidative stress and cytokine production.

PLG-105 is POLYGON's therapeutic candidate designed to inhibit the TREM-1 pathway in chronic cardiovascular disease. The company strongly believes that targeting this upstream immune amplifier may offer a differentiated approach to reducing residual inflammatory cardiovascular risk in ASCVD patients.

*"We believe these data provide strong human validation of the TREM-1 pathway as a promising immuno-metabolic therapeutic target in cardiovascular disease," said **Mohamed Abou Ali**, Co-Founder and Chief Executive Officer of POLYGON Therapeutics. "PLG-105 was designed to translate this biology into a targeted therapeutic approach for patients who remain at high cardiovascular risk despite current standard of care."*

The company is currently advancing PLG-105 through lead optimization and IND-enabling activities.

ABOUT PLG-105

PLG-105 is POLYGON Therapeutics' anti-TREM-1 therapeutic program for atherosclerotic cardiovascular disease. TREM-1 (Triggering Receptor Expressed on Myeloid Cells-1) is an innate immune receptor involved in amplification of inflammatory responses within atherosclerotic plaques. Soluble TREM-1 (sTREM-1), generated through receptor shedding after engagement, may serve as a biomarker for pathway activation and patient stratification.

ABOUT POLYGON THERAPEUTICS

POLYGON Therapeutics is a Paris-based biotechnology company developing precision cardio-immunology therapies targeting inflammatory drivers of cardiovascular disease. The company combines translational human biology, biomarker-driven development and immunology expertise to develop novel therapeutic approaches in atherosclerotic cardiovascular disease.

For more information:

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Forward-Looking Statements: This press release contains forward-looking statements regarding POLYGON Therapeutics' plans, programs and expectations for PLG-105, including statements about its potential therapeutic benefits and clinical development strategy. These statements involve risks and uncertainties. Actual results may differ materially. POLYGON Therapeutics undertakes no obligation to update these statements.