

# **Bitterroot Bio**

## **Category:**

Best Startup

## **Company Name:**

Bitterroot Bio

## **Turnover and/or Funding:**

\$142 M Series A raise, led by ARCH Ventures, Deerfield Partners, Google Ventures (GV).

## **Sub-Category:**

Biotechnology

## **Corporate history (creation, key milestones, main funding,...)Information on Condition / Disease and need for solution / product (prevalence, existing treatments / solutions):**

Founded in 2021, Bitterroot Bio is a pioneer in the field of cardio-immunology, which investigates the interplay between the immune system and cardiovascular health. Our research seeks to uncover critical roles that immune modulators play in the progression of cardiovascular disease, the leading cause of death worldwide (17.9 million deaths annual, per WHO 2021)<sup>1</sup>

BRB-002, our lead program targeting CD47 is designed to address the root causes of atherosclerosis, a cardiovascular disease characterized by the buildup of plaque in the walls of arteries that can lead to heart attacks and stroke. Through our novel approach, we hope to address the large and growing unmet need in patients who face the risk of heart attacks, despite being on standard of care therapy.

Residual risk persists in patients even when traditional risk factors are well controlled, such as LDL ("bad") cholesterol and blood pressure. Research over the last decade has shown that novel factors like inflammation and immune response continue to contribute to cardiovascular events. Tackling this residual risk through immune modulation is a major focus for Bitterroot, and through this work we hope to improve long-term outcomes in patients with atherosclerotic cardiovascular disease (ASCVD).

## **Milestones:**

Founding - Company incorporation September 2021

Series A \$142 M Raise - Company launches out of stealth June 2023

First patient dosed in First-in-Human BRB-002 Phase 1 Study - April 2024

First-in-Human BRB-002 Phase 1 Results - January 2025 (topline), March 2025 (full results)

First-in-Patient BRB-002 Phase 2a Initiation - Mid-2025

## **History of the development of the solution/product (Intellectual Property, preclinical and clinical datas, development collaborations):**

BRB-002 is an investigational, novel fusion protein designed to inhibit CD47 cell surface receptor, commonly referred to as a "don't eat me" cellular signal. Through the blockade of CD47, we believe we can induce the activation of macrophages and restore efferocytosis to clear out the necrotic cells and associated cellular debris found within atherosclerotic plaque, the primary driver of ASCVD. As a short-term goal of therapy, we expect to see a reduction in vascular inflammation, a key characteristic of ASCVD driven by pro-inflammatory necrotic plaque cells. Over the long-term, on the order of months to years, our goal of therapy with BRB-002 is a structural reduction in plaque burden, which would be a fundamental scientific and clinical breakthrough in the treatment of ASCVD. With these short- and long-term goals we aspire to improve outcomes for ASCVD patients, reducing the rate of future heart attacks.

BRB-002 entered preclinical development in 2021 and advanced into a Phase 1 healthy volunteer study April 2024. Topline results from this study were reported January 2025, followed by a poster presentation at the American College of Cardiology Scientific Sessions in March 2025. A Phase 2a study is expected to initiate in the first half of 2025.

We have generated robust preclinical datasets in mouse models of atherosclerosis (ApoE deficient mouse model) demonstrating that the inhibition of CD47 can indeed lead to a reduction in vascular inflammation and plaque burden. These results were presented in 2023 at the American Heart Association Scientific Sessions.

One of our co-founders, Dr. Nicholas Leeper of Stanford University, has also published a retrospective analysis evaluating a small cohort of patients in a clinical trial evaluating an anti-CD47 monoclonal antibody in an oncology setting. Coincidentally, through PET/CT imaging, Dr. Leeper observed a reduction in carotid vascular inflammation over the course of 8 weeks. This seminal analysis was published as correspondence in the New England Journal of Medicine in 2021 and is viewed as the foundational data supporting the founding of Bitterroot Bio.

Our Phase 1 data on BRB-002 was recently presented at the American College of Cardiology Scientific Sessions, and showed an excellent safety and tolerability profile

for the molecule paired with robust evidence of target engagement.

Our Phase 2a trial called MATADOR, is evaluating BRB-002 in patients with established atherosclerosis disease. This study has initiated and is examining the safety and tolerability of multiple doses of BRB-002, as well as its impact on carotid vascular inflammation. Positive results recapitulating the findings Dr. Leeper observed in his retrospective New England Journal of Medicine analysis would demonstrate the very first clinical proof-of-concept for BRB-002 in the field of cardiovascular medicine.

Regarding intellectual property, we have granted and pending patents covering the broad application of CD47 in the cardiovascular space. We also have entered into an exclusive license with Stanford for intellectual property that covers the use of anti-CD47 agents for vascular inflammation.

### **Why this drug or device is innovative, the broad implications for future research, and/or how it will improve the human condition:**

BRB-002 is among the first investigational therapies leveraging the interplay between the immune and cardiovascular systems for the benefit ASCVD patients. Current standard-of-care therapies are grounded in lipid-lowering approaches, thus by leveraging the immune system, BRB-002 may ultimately provide a ground-breaking and novel approach to treating ASCVD.

Indeed, by pursuing an immuno-modulating approach with BRB-002, we believe we have a path to uniquely and directly address the residual risk remaining in patients previously referenced.

More broadly, positive clinical results supporting our therapeutic hypothesis for BRB-002 would be paradigm shifting as they could potentially serve to validate the broader field of cardio-immunology, shepherding in new, next-generation treatments for ASCVD, beyond lipid lowering approaches.

### **Please provide appropriate references (PubMed, Abstract, Website):**

1: [https://www.who.int/news-room/fact-sheets/detail/cardiovascular-diseases-\(cvds\)](https://www.who.int/news-room/fact-sheets/detail/cardiovascular-diseases-(cvds))

Effect of CD47 Blockade on Vascular Inflammation - The New England Journal of

Medicine - Leeper et al.

- <https://www.nejm.org/doi/pdf/10.1056/NEJMc2029834>

BRB-002 Preclinical Data

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[https://brbio.com/wp-content/uploads/2023/11/2023-AHA-ePoster-Slide\\_BRB-002-vFINAL\\_b.pdf](https://brbio.com/wp-content/uploads/2023/11/2023-AHA-ePoster-Slide_BRB-002-vFINAL_b.pdf)

BRB-002 Phase 1 Results

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[https://brbio.com/wp-content/uploads/2025/03/ACC\\_Poster\\_No\\_QR\\_29MAR25\\_FINALVers.pdf](https://brbio.com/wp-content/uploads/2025/03/ACC_Poster_No_QR_29MAR25_FINALVers.pdf)

## **References File Document upload:**

N/A