POOLBEG PHARMA

POLB 001 Update

January 2024

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Jeremy Skillington

Chief Executive Officer

Poolbeg Well Positioned for Success

Industry Leading Team	• Experienced executive team successfully built 3 public life science companies • Three key former Amryt Pharma leaders joined Poolbeg with a track record of establishing and scaling sales infrastructures in the US & ROW
Revenue Focused Business Model	• Focused on near term revenue generation from commercial stage products • Deal focused - multiple partnering discussions ongoing
High Value Programmes for Partnering	• POLB 001 – Phase 2 ready - cancer immunotherapy-induced CRS (e.g. bispecific antibodies, CAR T cell therapy) and treatment for severe influenza • Oral encapsulation technology - targeting obesity with Oral GLP-1R agonist – entering clinic in 2024 • AI-led discovery programmes with CytoReason (Influenza) and OneThree Biotech (RSV)
Strong Financial Position	• Cash balance of £14.1m (30 June 2023) • Pivoting to revenue generation and cashflows

High Value Programmes

Actively engaging in partnering discussions

Product / Programme	Pre-Clinical	Phase I	Phase II	Phase III	Key Catalysts
POLB 001 Cancer immunotherapy-induced CRS					• Positive data from Phase 1b & *in vivo* study. Phase 2 enabling activities ongoing. Partnering ready
POLB 001 Severe influenza					• Positive data from Phase 1b challenge trial received - partnering ready
Oral Encapsulated GLP-1R Agonist Obesity & diabetes treatment					• Proof of technology clinical trial expected to commence H1 2024
Influenza AI Programme Utilising unique licensed human viral challenge data					• Outputs received Q2 2023 • Validation in 2024
RSV AI Programme Utilising unique licensed human viral challenge data					• Drug candidates identified and now prioritised following positive outputs from lab-based analysis.

Other Partnerships/Collaborations

- ✓ Ongoing strategic collaboration with Nasdaq listed company for the development of an optimised oral drug to treat a metabolic condition
- ✓ €2.3m in non-dilutive grant funding secured to develop a Phase I clinical trial ready oral vaccine candidate; Poolbeg led consortium including AnaBio Technologies, UCD and TCD

POLB 001: A Phase 2 Ready, Oral p38 MAPK inhibitor

Serving high unmet medical needs in patients receiving cancer immunotherapies

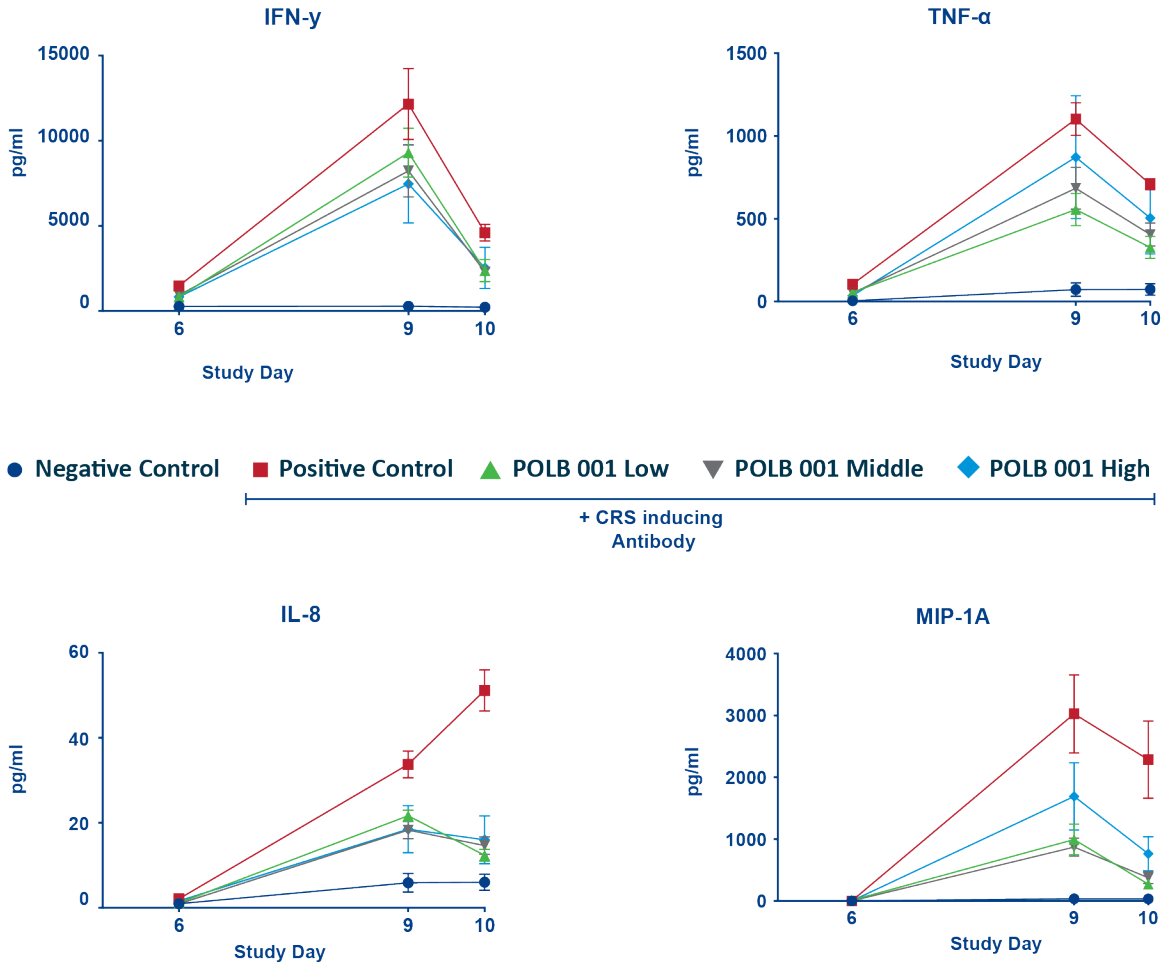
Compelling Data	• Phase 2 ready oral small molecule, excellent bioavailability • Strong pre-clinical data package • Safe & well tolerated in Phase I clinical trial	• Efficacy demonstrated in Phase 1b LPS human challenge trial – acute inflammatory model • Efficacy demonstrated in reducing cancer immunotherapy-induced CRS in an in vivo model
Strong Patent Portfolio	• Oncology patent applications filed in 2023, potential for **protection out to 2043** • **Recent data enhances** and facilitates the expansion of patent applications for POLB 001 in cancer immunotherapy-induced CRS • Granted patents for severe influenza out to 2038	
Significant Unmet Need	• **Cancer immunotherapies limited to specialised cancer centers**, largely due to CRS risk, which is rate-limiting and potentially life threatening • Require 7-10 day in-patient care during step-up dosing. CRS significantly extends hospital stay and healthcare resource utilisation, even when using currently available treatments. • An effective oral therapy to **prevent and treat** CRS has the potential to **enable broader use** of bispecific therapies in an **outpatient setting** • Current treatment options are **not sufficiently effective** in all patients • POLB 001 is well tolerated and suitable for oral **self-administration** • Tocilizumab is only available as an IV and is **off-label**	

[1]CAR T-Cell Therapy Market Analysis 2023-2030; Bispecific Antibodies Market Size, Share & Trends Analysis Report, Grand View Research

Positive In Vivo Results

Validates POLB 001's Potential to Address Cancer Immunotherapy-Induced CRS

- POLB 001 demonstrated efficacy in reducing CRS in an animal model of cancer immunotherapy-induced CRS
- Select humanized murine models offer the ability to investigate potent CRS with enhanced translatability to human disease
- Symptoms of CRS were significantly improved by POLB 001, accompanied by a reduction in key proinflammatory cytokines
- The data strengthens and facilitates the expansion of patent applications for POLB 001 in cancer immunotherapy-induced CRS



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Dr Martin Kaiser, FRCP, FRCPath

Reader/Associate Professor in Molecular Haematology at The Institute of Cancer Research, Haematology Consultant at The Royal Marsden Hospital

Leading Expert in the Treatment of Haematological Malignancies at the Royal Marsden, London

ICR The Institute of Cancer Research

The ROYAL MARSDEN NHS Foundation Trust

RWTH AACHEN UNIVERSITY

- Team leader of the Myeloma Molecular Therapy group at the Institute of Cancer Research and Honorary Consultant Haematologist at The Royal Marsden NHS Foundation Trust
- 12 years as a consultant haematologist
- Specialist on the treatment myeloma patients
- Over 10 years experience as a PI on early and late-stage clinical trials
- Vice chair of the academic UK Myeloma Clinical Trials group (UKMRA)
- International policy roles

Growing Number of CRS Inducing Immunotherapies

CAR T Cell Therapies

YESCARTA® (axicabtagene ciloleucel) Suspension for IV infusion

KYMRIAH® (tisagenlecleucel) Suspension for IV infusion

CARVYKTI™ (ciltacabtagene autoleucel) Suspension for IV infusion

TECARTUS® (brexucabtagene autoleucel) Suspension for IV infusion

Breyanzi™ (lisocabtagene maraleucel) SUSPENSION FOR IV INFUSION

Abecma® (idecabtagene vicleucel) SUSPENSION FOR IV INFUSION

Bispecific Antibodies

BLINCYTO® (blinatumomab) for injection
35 mcg single-dose vial

ELREXFIO™ (elranatamab-bcmm)
INJECTION FOR SUBCUTANEOUS USE | 44 mg/1.1 mL 76 mg/1.9 mL

TALVEY™ (talquetamab-tgvs) Injection for subcutaneous use
2 mg/mL and 40 mg/mL

TECVAYLI® (teclistamab-cqyv) Injection for subcutaneous use
10 mg/mL and 90 mg/mL

COLUMVI™ glofitamab-gxbm
injection for intravenous use 2.5 mg | 10 mg

CRS Management

ACTEMRA® tocilizumab

NDC 70069-025-01 Rx only
Dexamethasone Sodium Phosphate Injection, USP
100 mg /10 mL
(10 mg/mL*)

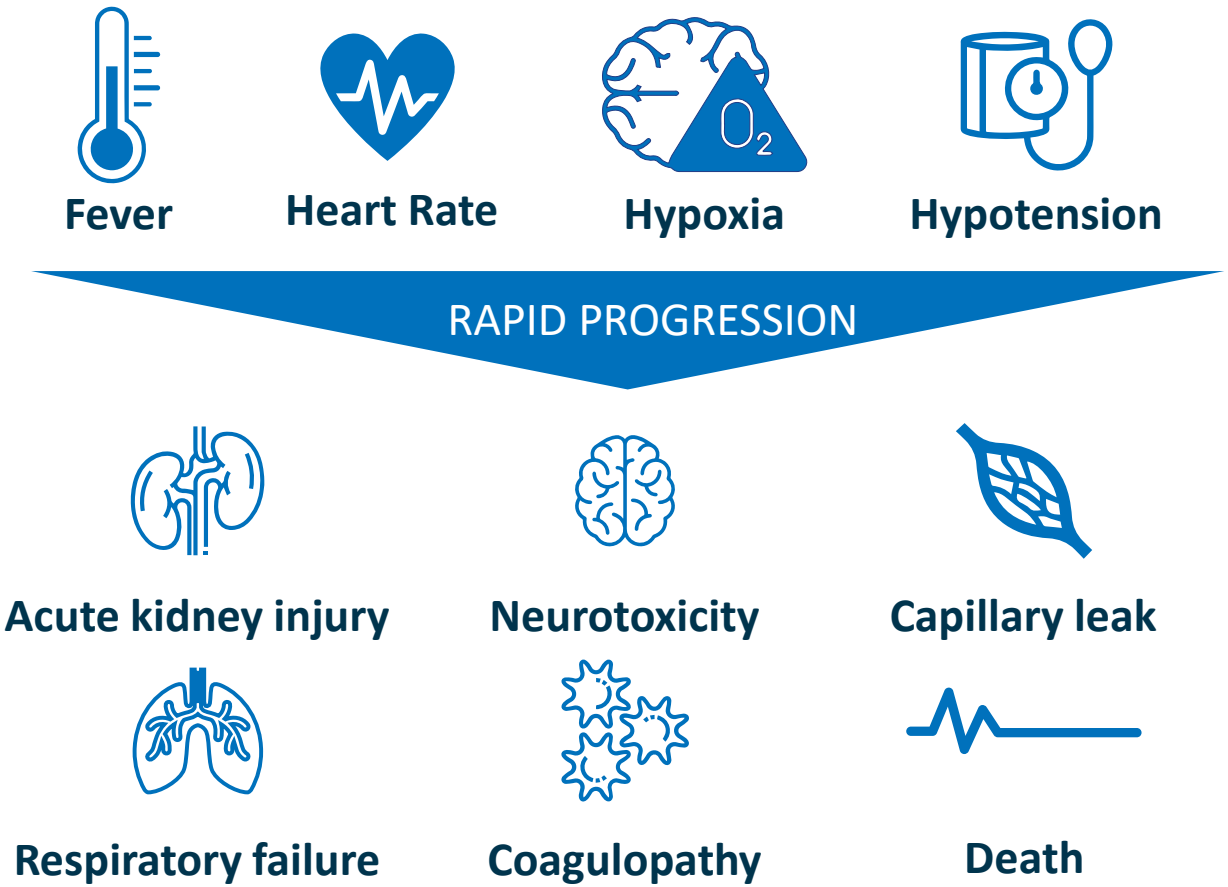
Kineret® (anakinra)

What is Cytokine Release Syndrome?

Severe life-threatening side effect of cancer immunotherapies

- A severe inflammatory response, which may be encountered as a side effect of some therapies and infections
- Broad range of symptoms can rapidly progress to a severe life-threatening reaction
- Even lower grades of CRS can lead to extended hospital stays while patients are closely monitored

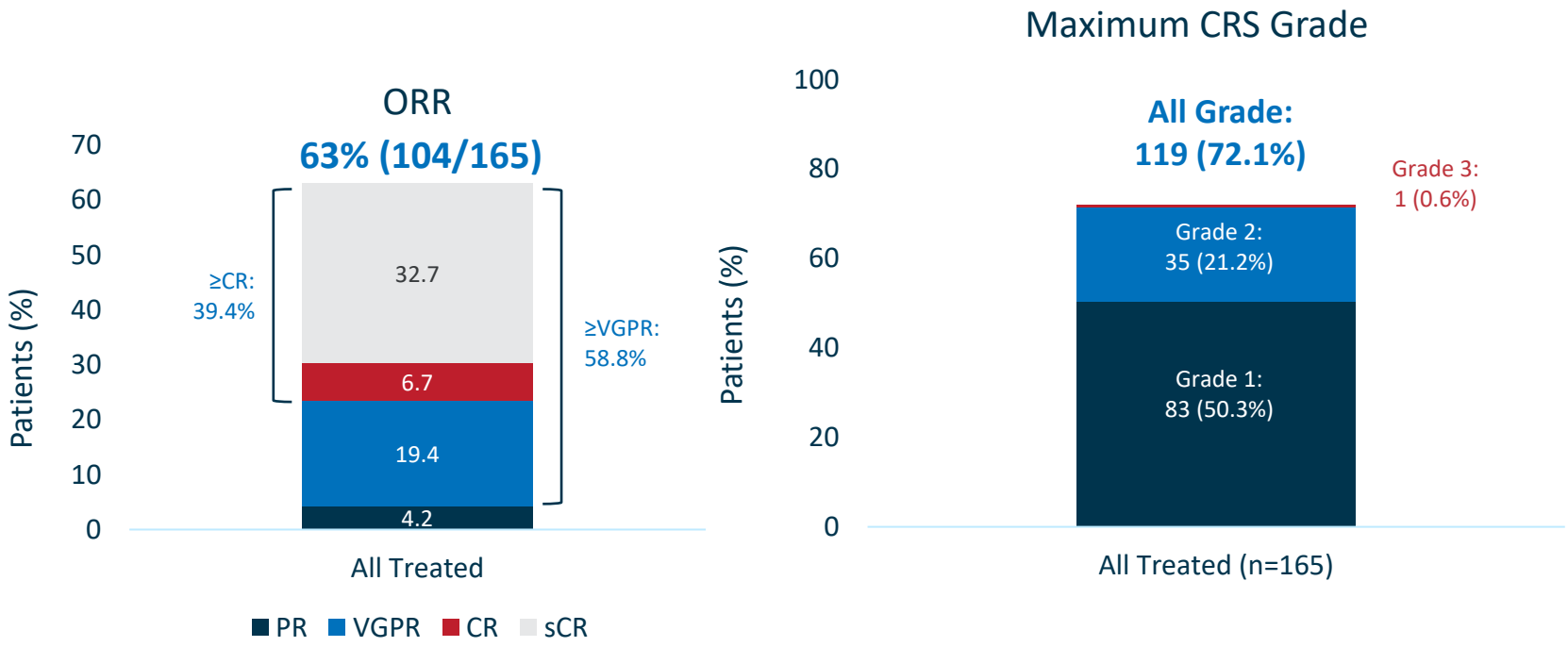
Clinical Manifestations of CRS



Bispecific Antibodies Have Immense Response Rates in Late-Stage Cancer Patients, but it Comes With Challenges

4th Line Refractory/Relapsed Myeloma Patients Treated with Teclistamab

- MajesTEC-1 clinical trial (N = 165)
- Week 1: Step-up doses of Teclistamab
- Week 2 onwards: Weekly S.C. Teclistamab
- Primary endpoint: ORR*
- Median duration of response: 18.4 months



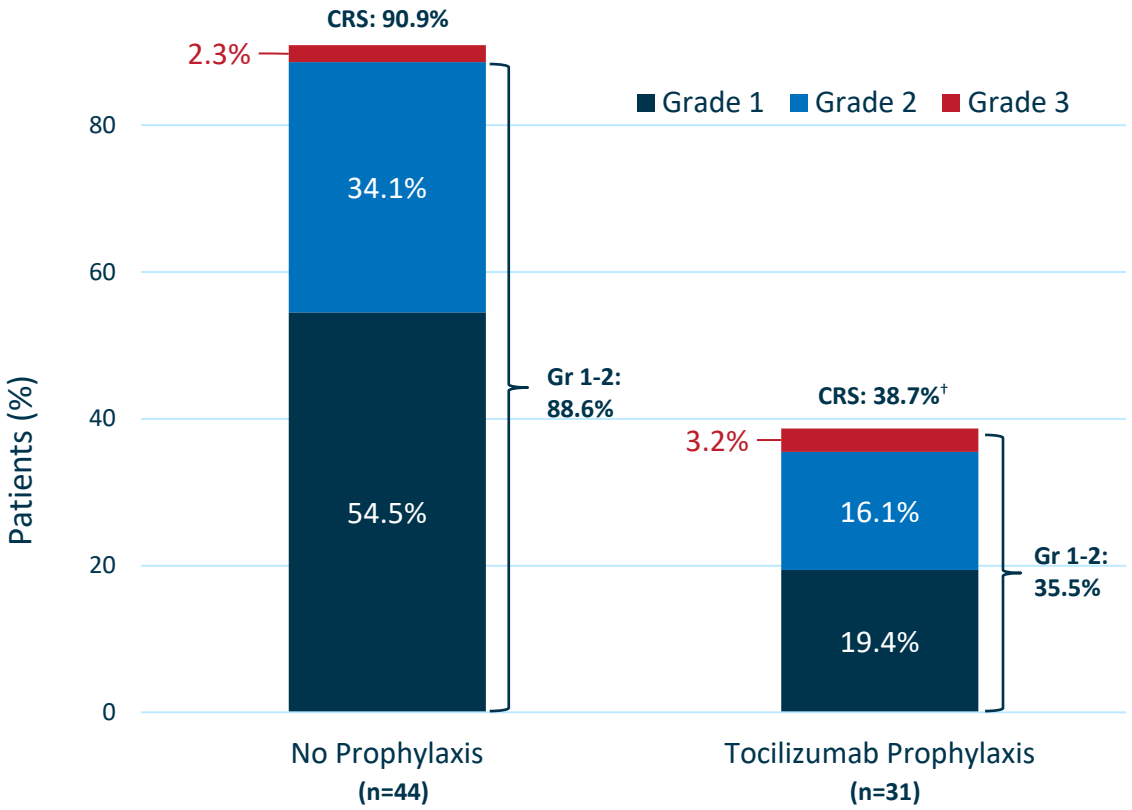
*ORR = Overall Response Rate

High Levels of CRS persist with Current Treatment Options

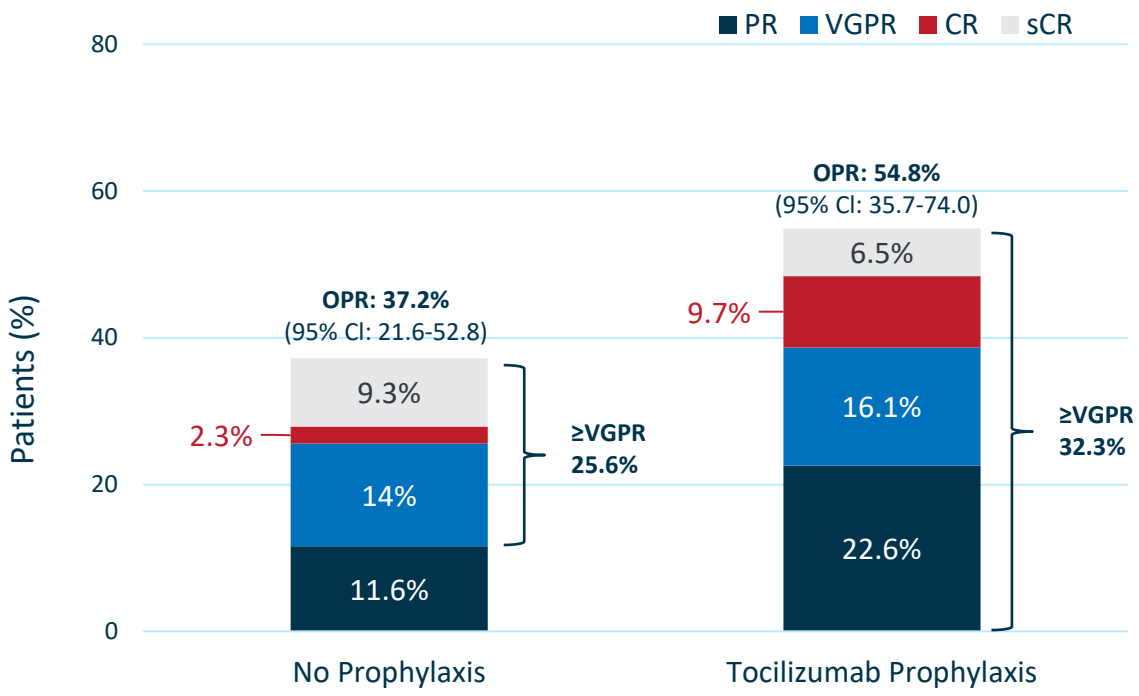
No approved prophylactic

Investigator initiated studies have examined the effect of prophylactic tocilizumab, including Multiple Myeloma patients treated with Cevostamab (shown), however CRS persists.

Incidence and Severity of CRS

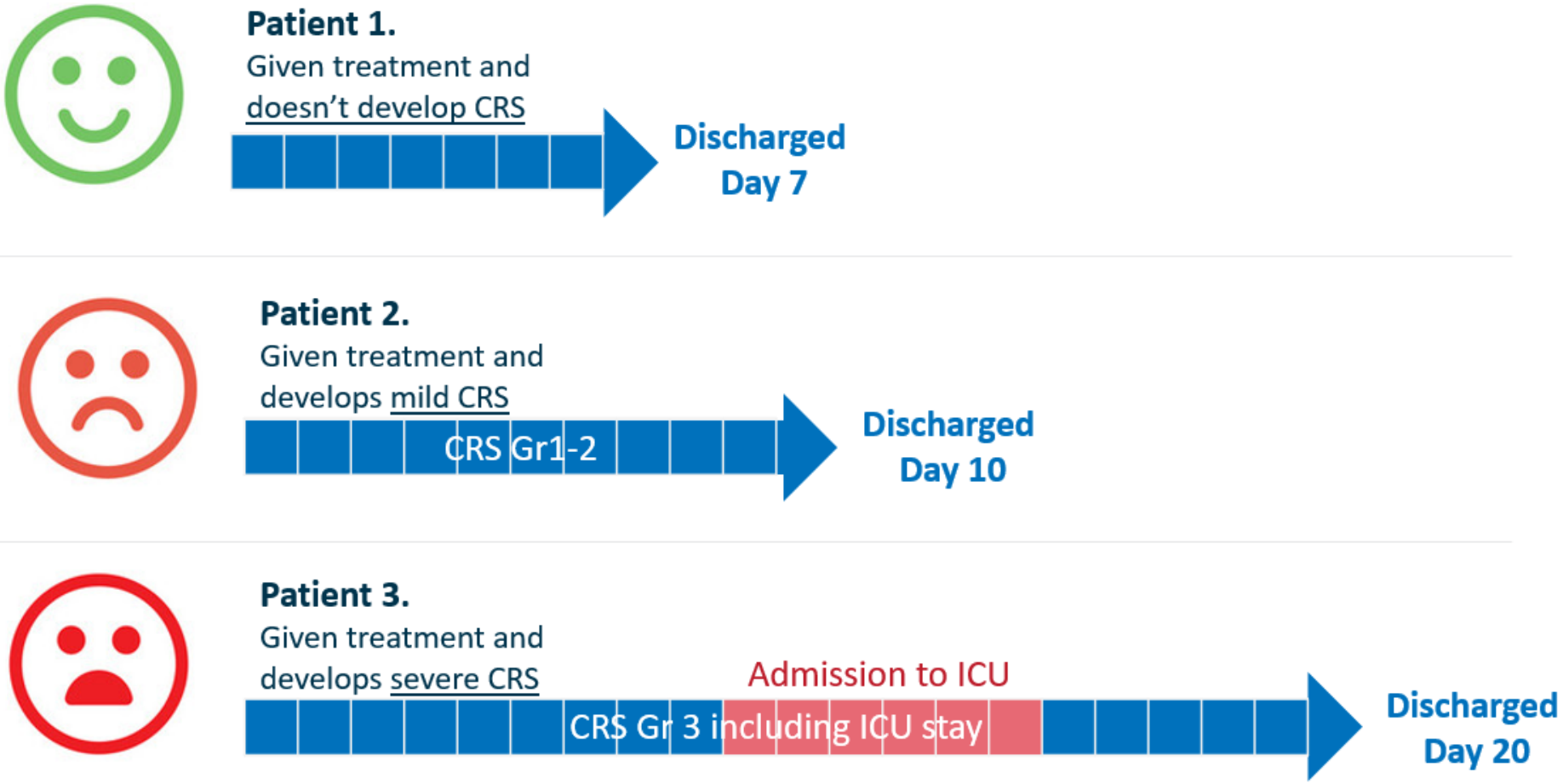


Response Rates to Cevostamab



Source: Genentech, EHA poster. **Data cut-off: August 22, 2022:** *CRS reported using ASTCT 2019 criteria; †p<0.001 for comparison vs overall CRS rate in the no prophylaxis arm using a proportions test; CRS, cytokine release syndrome; Gr, Grade . *CR, complete response; ORR, objective response rate; PR, partial response; sCR, stringent complete response; VGPR, very good partial response

Development of CRS Significantly Extends In-Patient Stay During Step-Up Dosing of Bispecific Antibodies or CAR-T therapy



Diagrammatic representation of 3 patients administered bispecific antibodies for the treatment of R/R multiple myeloma based on anecdotal feedback from a consultant haematologist. DATA PRESENTED IS HYPOTHETICAL AND FOR ILLUSTRATIVE PURPOSES ONLY

Summary

- CRS is a serious medical condition that causes morbidity, significant healthcare resource utilization and potential mortality risk
- Rapid growth in research, development and approval of cancer immunotherapies
- CRS risk limits delivery of cancer immunotherapies to specialist cancer centres
- Existing treatments are available to manage CRS in a hospital setting but there remains a significant unmet medical need
- An oral therapy that could prevent or treat CRS would be beneficial to patients and healthcare system

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David Allmond

Chief Business Officer

CRS is a Rate Limiting Side Effect Associated with Emerging Immunotherapies in Cancer

Even mild to moderate CRS impacts seamless delivery of potentially life-saving treatments

- Up to 70 - 95% of patients suffer CRS related side effects with immunotherapies in cancer
- Severe cases of CRS are life-threatening and may require intensive supportive care
- Mild to moderate CRS can result in extended hospitalisation and high consumption of healthcare resources
- Advancements of immunotherapies in cancer is driving the need for effective CRS management

Oral administration of POLB 001 to prevent or treat CRS has the potential to enable broader use of immunotherapies

Novel strategies are needed for the management of CRS to enable outpatient delivery of immunotherapies in cancer

POLB 001 Demonstrated Strong Efficacy/Safety Profile in Phase 1 Clinical Trials

POLB 001 was widely distributed, reduced the inflammatory response and inhibited p38 MAPK activation and signaling following LPS challenge

- Excellent safety profile across two clinical studies
- Potent target inhibition confirmed
- Major reduction of key inflammatory markers
- Clear dose response relationship observed

- Well tolerated drug that attenuates excessive immune responses without completely ablating the immune response
- Shows promise of no undue suppression of effective immune responses in already immunocompromised patients

ASH Abstract And Poster Presentation

Presentation at 65th American Society of Hematology (ASH) Annual Meeting to provide insight into POLB 001's potential to treat CRS associated with cancer immunotherapies

#2093. POLB 001, an oral broad-spectrum anti-inflammatory with the potential to prevent Cytokine Release Syndrome

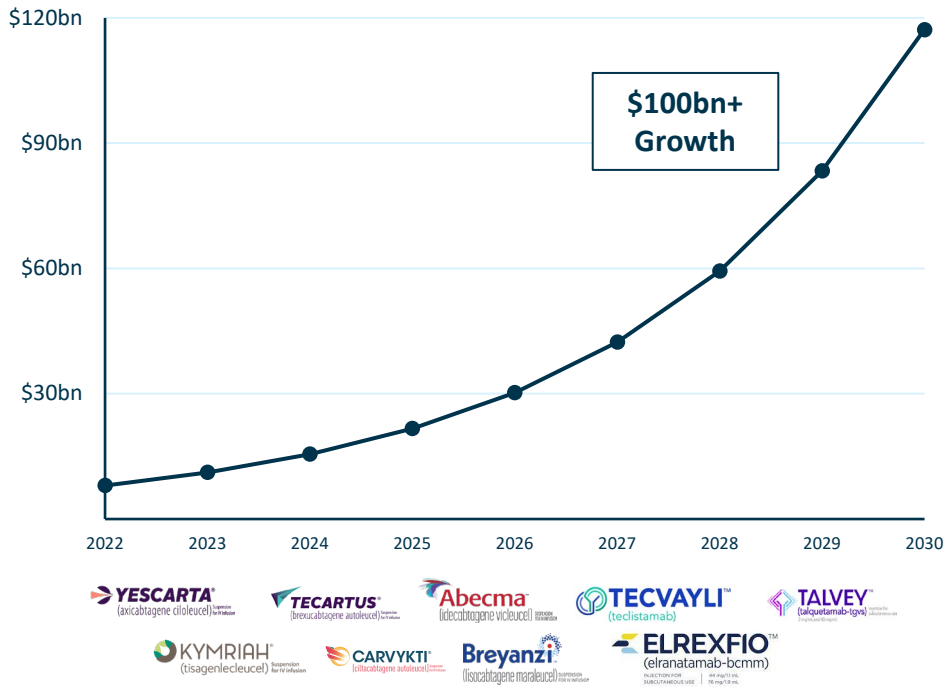
Emma Searle, MD, Liam Tremble, PhD, Rakesh Popat, MBBS, PhD, Digna de Bruin, MD. PhD., Matthijs Moerland, PhD., and Brendan Buckley, Prof, MD.

- POLB 001 has the potential to revolutionise the impact of cancer immunotherapies by enabling safer and broader use in an outpatient setting

Significant Market Opportunity in a Rapidly Growing Field

CRS is rate limiting in delivering cancer immunotherapies

Bispecific Antibody & CAR T Therapy[1]



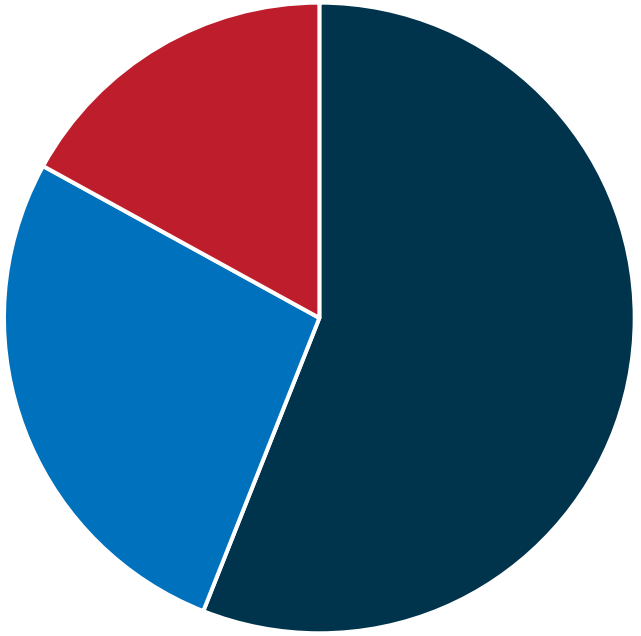
- In the U.S. alone, almost 2 million new cancers occurred in 2023 which is estimated to increase to **24.58 million cases by 2030** [1,2]
- Bispecific Antibody and CAR T Therapy market expected to show **exponential growth,** similar to antibodies in the early 2000s[3,4]
- The field of cancer immunotherapies, including CAR T and bispecific antibodies, is burgeoning and expected to grow to **>$100bn USD[4] by 2030**
- CAR-T and Bispecific Antibodies are rapidly moving into **earlier lines of treatment** in many tumour types
- **CRS is rate limiting** for these potentially life saving therapies, which can only be delivered in specialist cancer centres, requiring hospitalisation and significant use of healthcare resources
- There are currently very **few approved therapies** for the management of CRS
- Opportunity for new innovations to enable broader, safer delivery of these therapies to the cancer patients who need them

[1]The American Cancer Society (ACS)
[2]The International Agency for Research on Cancer (IARC)
[3] Evaluate Pharma, concensus forecast sales, accessed December 2022
[4] CAR T-Cell Therapy Market Analysis 2023-2030; Bispecific Antibodies Market Size, Share & Trends Analysis Report, Grand View Research

POLB 001 > US $1Bn Market Opportunity

In Multiple Myeloma, High Grade Lymphoma and Acute Lymphoblastic Leukaemia alone

US Haematological Cancer Patients Receiving Immunotherapies



n = 28,000 patients

- Target Profile - **Oral prophylaxis of CRS** induced by cancer immunotherapies
- **US 3rd line+ Multiple Myeloma, High Grade Lymphoma and Acute Lymphoblastic Leukaemia patients only** receiving CAR-T and Bispecific therapy
- Increase cancer immunotherapy penetration to 2040 due to wider adoption and **outpatient administration**
- **Significant upside** potential across additional haematological malignancies, solid tumours and immune inflammatory diseases

Sources; Data Monitor, Evaluate, Cogvio and Management Estimates

Independent Advisory Board Supportive of POLB 001's Potential

International KOLs, Payers and Clinical Trial Experts in Haematology

Key insights

- Confirmed unmet need in multiple myeloma and Lymphoma – ability to ensure safe, efficient delivery of bispecific therapies
- Confirmed attractiveness of POLB 001 Target Product Profile to meet unmet need in clinical practice to enable safer broader delivery of immunotherapies in cancer
- Currently administration of immunotherapies limited to specialist cancer centres with long hospital stays and high consumption of healthcare resources
- POLB 001 profile attractive as a potential oral therapy to prevent and treat CRS

"Patients undergoing cancer immunotherapy treatment that suffer with CRS can be critically ill which, alongside a weakened immune system, can further increase their risk of infection. **Preventing CRS in the first instance would have a significant impact on patient health and wellbeing as well as reducing the burden on the healthcare system.** Current CRS treatments require intravenous infusion, which is difficult to deliver out of hospital, and some can only be used off label in combination with bispecific antibodies. If there was a therapy that was orally delivered, a whole lot of infrastructure requirement falls away." **Dr Martin Kaiser, ICR, UK**

"Bispecific antibodies will only be delivered in specialist cancer centres until there is a way to make them safer. **POLB 001 could make treatment safe enough to extend bispecifics to a much wider patient population**."
Prof. Gareth Morgan, NYU Langone, US

Summary

POLB 001 has a comprehensive pre-clinical and clinical data package

CRS is a rate limiting side effect associated with emerging immunotherapies in cancer

International key opinion leader insights support the potential of POLB 001 to manage CRS

> US $1Bn market opportunity for POLB 001 in a rapidly growing field of cancer immunotherapies

Pharma are seeking an effective solution for CRS to expand the market for cancer immunotherapies
An oral therapy to prevent and treat CRS could enable safer and broader use of these innovative therapies

Industry Leading Team

Revenue Focused Business Model

High Value Programmes for Partnering

Strong Financial Position

Appendix

Proven Leadership Team

Experience in commercialising and developing innovative medicines

Cathal Friel
Chairman

- ✓ Founder of Raglan Capital, completing 4 IPOs (Amryt Pharma, hVIVO & Poolbeg Pharma)

Jeremy Skillington PhD
Chief Executive Officer

- ✓ Employee #1 at Inflazome - €380m exit to Roche
- ✓ Extensive BD experience with Genentech & HS Lifesciences

Ian O'Connell
Chief Financial Officer

- ✓ Co-founder of Open Orphan plc (renamed hVIVO plc) and one of Amryt Pharma's first team members
- ✓ Chartered Accountant with deep corporate finance experience

Additional Former Amryt Pharma Executive Team Members Joined Poolbeg:

David Allmond
Chief Business Officer

- ✓ Former CBO at Amryt Pharma – pivotal in establishing sales & marketing in EU, US and ex-US
- ✓ Previously CVP Global Marketing at Celgene and EMEA lead at Aegerion Pharmaceuticals

John McEvoy
Chief Legal Officer

- ✓ Former GC at Amryt Pharma since 2017 – pivotal in rapid growth through acquisition & Nasdaq listing
- ✓ Qualified lawyer in the US (New York), England & Wales, and Ireland

Laura Maher
VP Clinical Operations

- ✓ Former AD of Clinical Operations at Amryt Pharma
- ✓ Led the clinical research in Amryt Pharma's pipeline including Filsuvez®, the world's first approved epidermolysis bullosa treatment

Non-Executive Directors

A long history of success in the life sciences industry

Prof Luke O'Neill
Non-Executive Director

- ✓ Co-Founder Inflazome which was acquired by Roche in 2020 for €380m + milestones
- ✓ Previously scientific advisory board member of GSK & Pfizer

Eddie Gibson
Non-Executive Director

- ✓ Market access expert
- ✓ Supported numerous drug companies secure pricing and reimbursement

Prof Brendan Buckley
Non-Executive Director

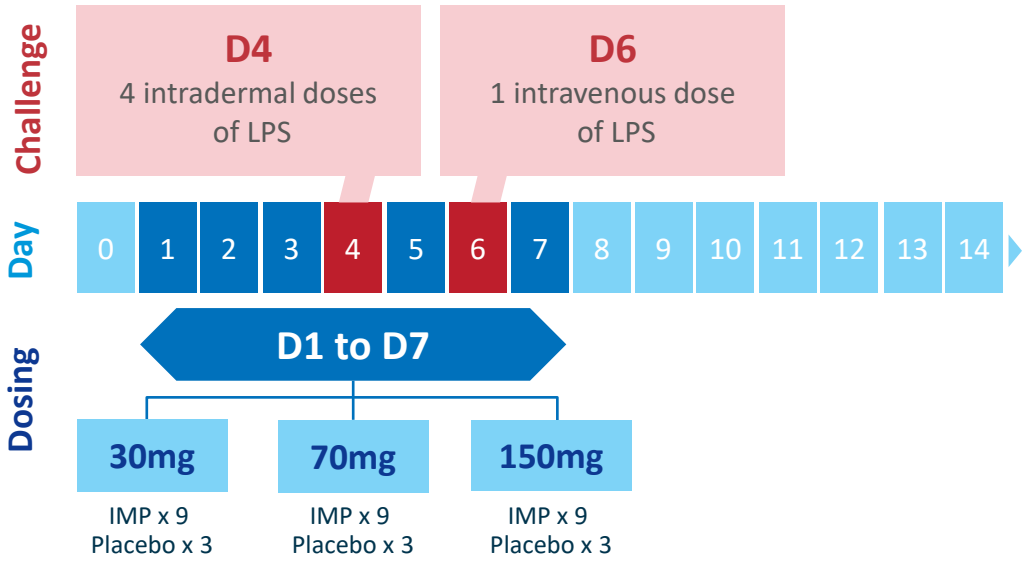
- ✓ Former Chief Medical Officer at ICON plc
- ✓ Former member of Committee for Orphan Medicinal Products & Scientific Advisory Group for Diabetes and Endocrinology at the EMA

POLB 001 – A Human LPS Challenge Trial

The challenge trial used LPS to evaluate the efficacy of POLB 001

Randomised, double-blind, placebo-controlled, multiple dose challenge trial in healthy volunteers

Trial design



Endpoints

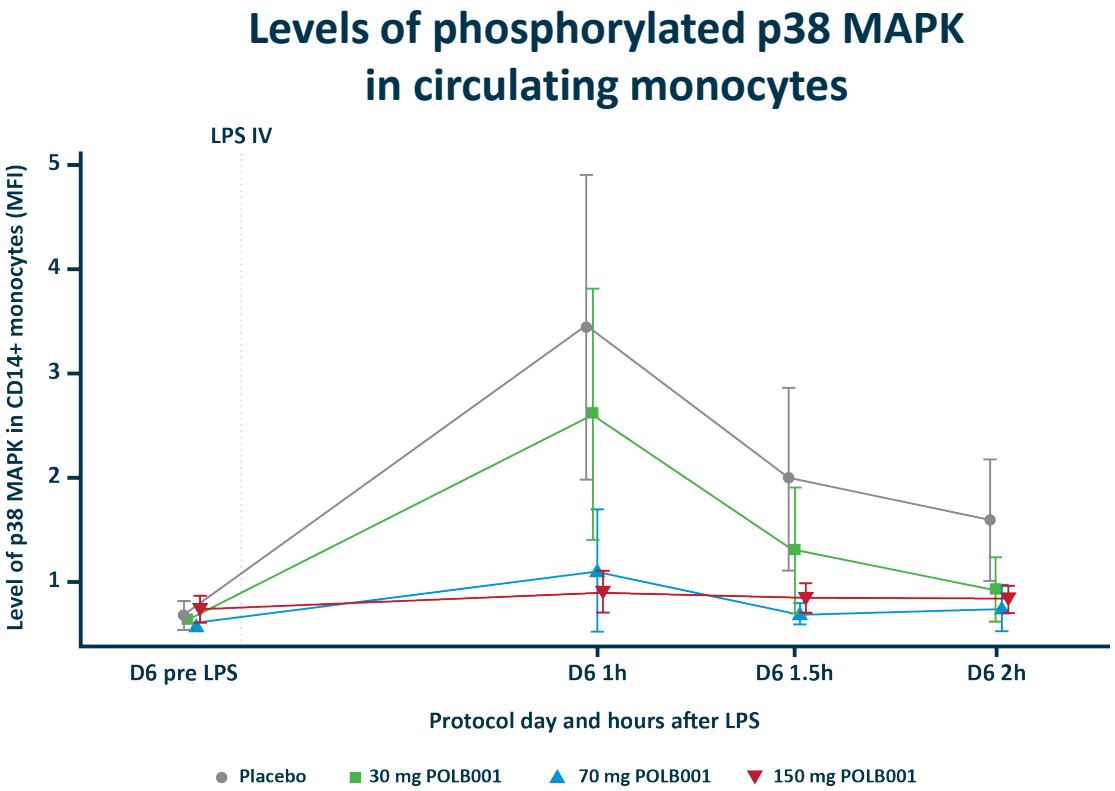
Intravenous LPS challenge

- Bloods (cytokines, vascular markers, CRP)
- *Ex-vivo* LPS response
- Safety & tolerability (inc. vital signs, AE's, ECG, Haematology)

- **Local inflammatory responses** were also measured

Potent and Selective Inhibition of p38 MAPK Signaling

Effective target engagement demonstrated



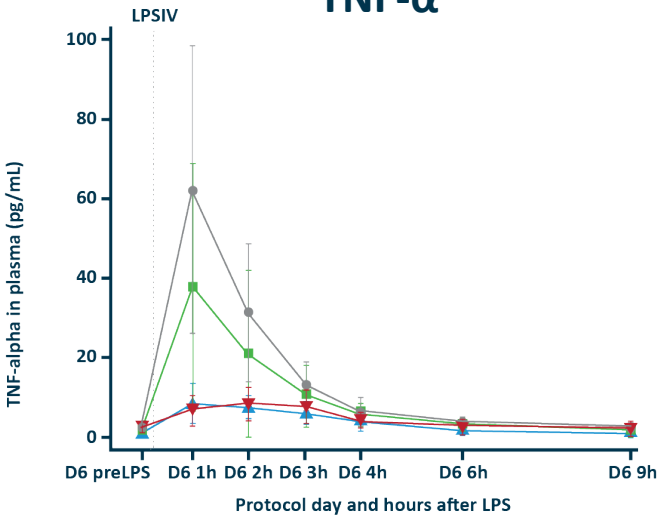
Blood samples were taken before and after administration of intravenous LPS. Peripheral blood samples were analyzed by flow cytometry. Monocytes were gated by FSC, SSC and CD14+. Data is presented as mean MFI values of phospho-p38 +/- SEM

- POLB 001 was **widely distributed**
- POLB 001 **inhibited p38 MAPK activation**
- POLB 001 i**nhibited *in vivo* and *ex vivo* responses** to LPS-induced TNF-α, an indirect measurement of p38 activity

Reduced Key Inflammatory Cytokines Following LPS Challenge

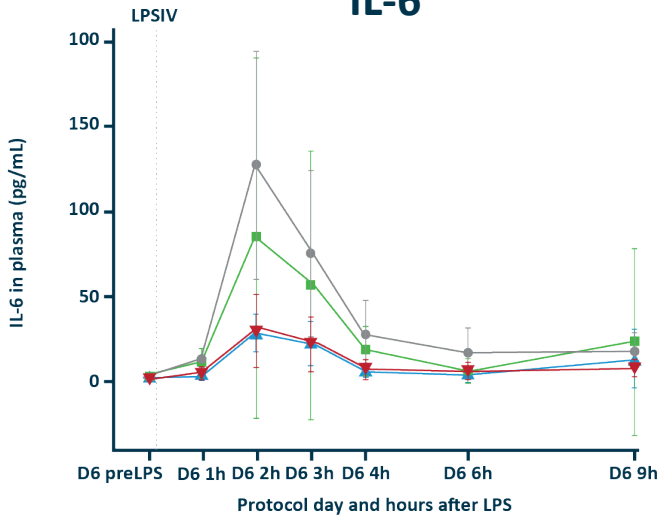
Dose dependent reductions, without ablation of immune function

TNF-α



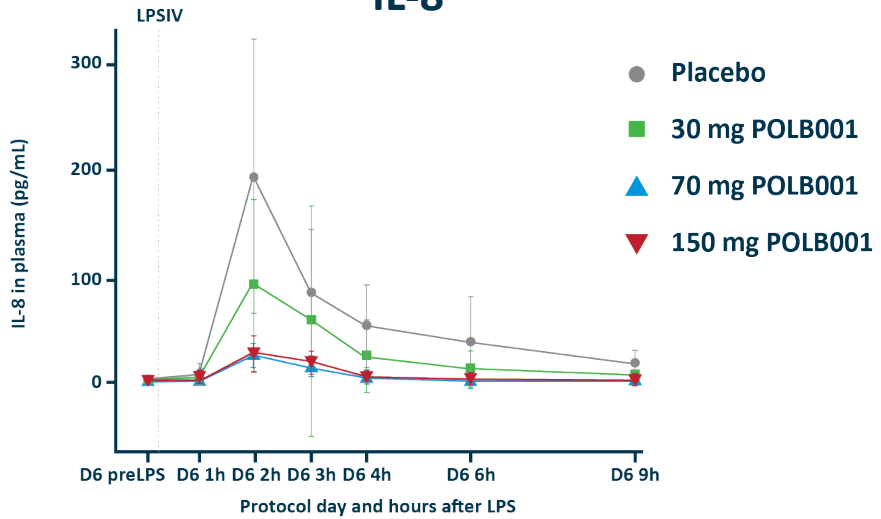
TNF-α reduction of **73.5% and 56.2%** seen for **70 mg and 150 mg doses respectively** (p = 0.0003†)

IL-6



IL-6 reduction of **57.4% and 63.5%** seen for **70 mg and 150 mg doses respectively** (p = 0.0002†)

IL-8



IL-8 reduction of **80.7% and 76.7%** seen for **70 mg and 150 mg doses respectively** (p < 0.0001†)

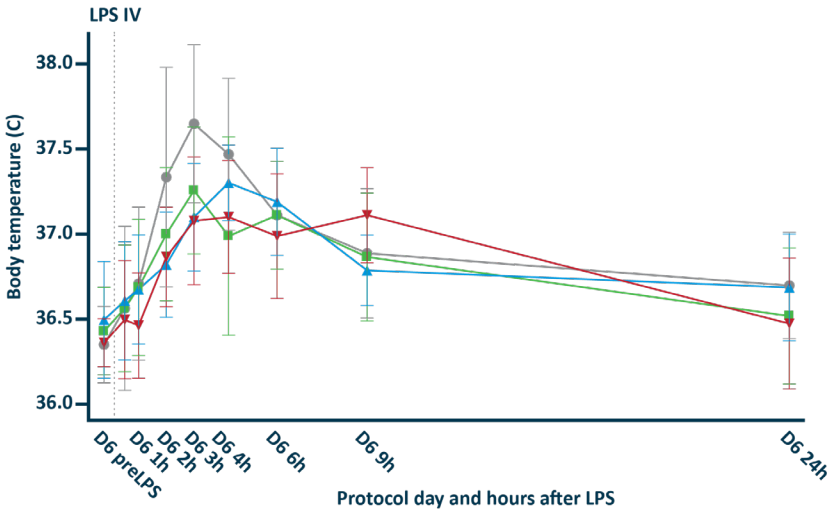
TNF-α, IL-6 and IL-8 levels decreased between 56-81% in subjects treated with 70 mg or 150 mg POLB 001 twice daily

†The exploratory analysis suggested statistically significant improvement in treatment (p<0.05) for the endpoints examined.

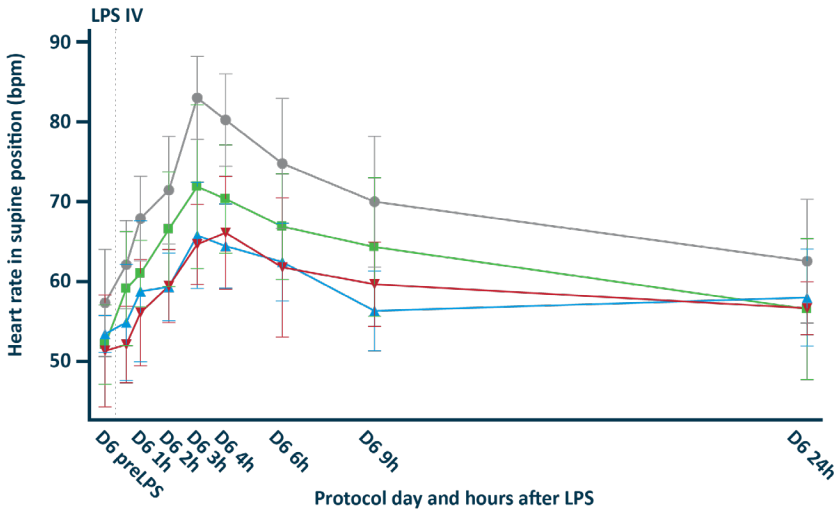
Reduced Key Indicators of LPS-Induced Systemic Inflammation

The reduction of systemic cytokines aligns with improvement in clinically meaningful endpoints

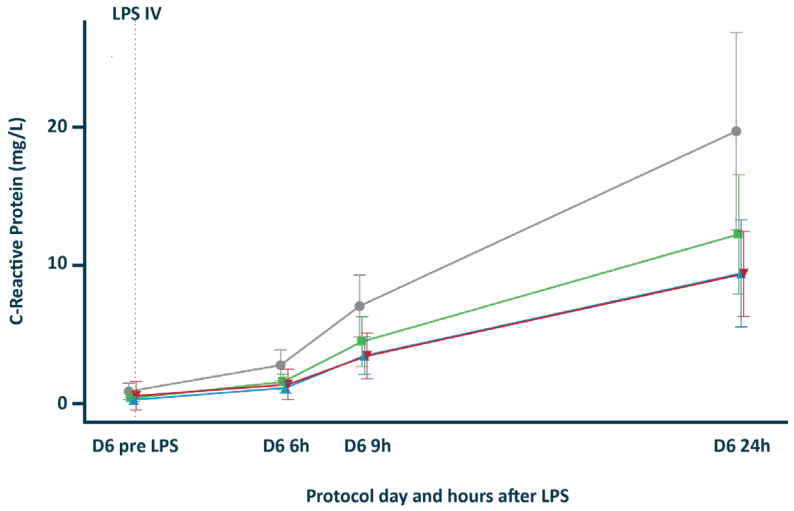
Mean Body Temperature



Heart Rate Rise (bpm)



C-Reactive Protein (CRP)



Placebo | 30 mg POLB001 | 70 mg POLB001 | 150 mg POLB001

No significant effect on body temperature with a trend towards reduction compared to placebo.

Suppressed increase in heart rate following IV LPS administration

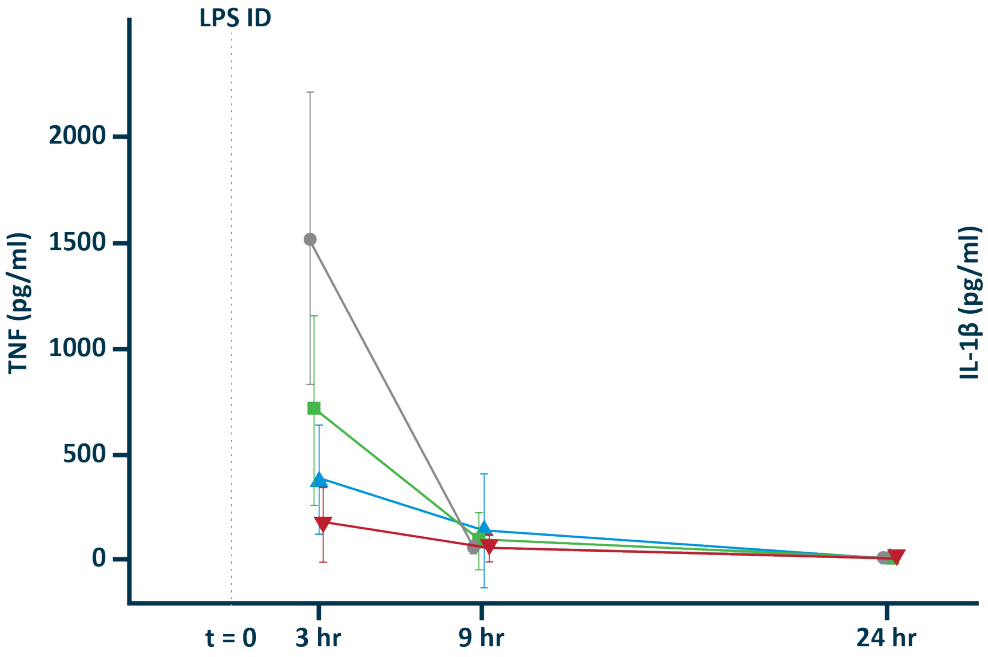
CRP level reduction of **33.1% and 33.3%** seen for **70mg and 150mg** doses respectively

Improvement in clinically meaningful endpoints

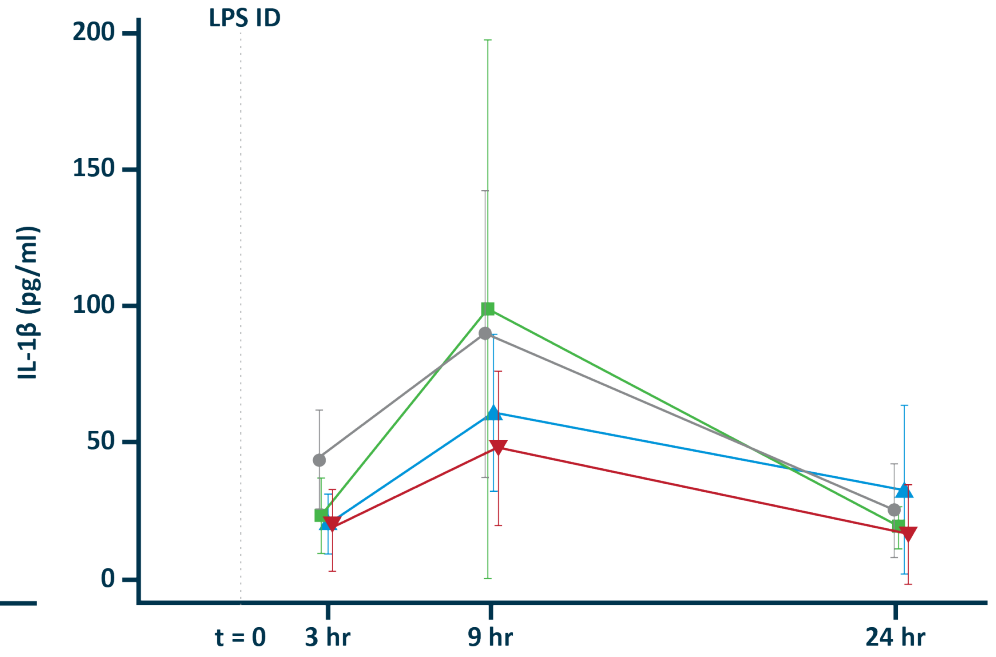
POLB 001 Effectively Reduced Inflammation in Tissue

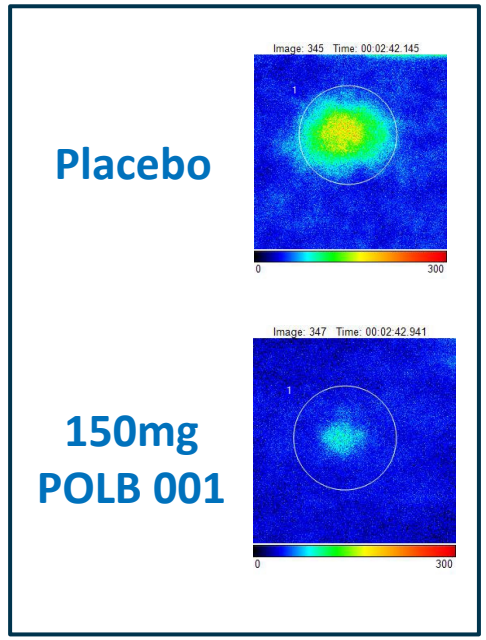
POLB 001 150 mg significantly reduced IL-1β† and TNF-α† responses in blister exudate compared to placebo

TNF-α in blister exudate



IL-1β in blister exudate





● Placebo ■ 30 mg POLB001 ▲ 70 mg POLB001 ▼ 150 mg POLB001

Results of LPS challenge study support initiation of Phase 2 study

†The exploratory analysis suggested statistically significant improvement in treatment ($p<0.05$) for the endpoints examined.

POOLBEG PHARMA

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