Disclaimer

Forward-Looking Statements

This document may contain forward-looking statements. Forward-looking statements are statements that are not historical facts and may be identified by words such as "plans", "targets", "aims", "believes", "expects", "anticipates", "intends", "estimates", "will", "may", "should" and similar expressions. Forward-looking statements include statements regarding objectives, goals, strategies, outlook and growth prospects; future plans, events or performance and potential for future growth; economic outlook and industry trends; developments in BenevolentAI's markets; the impact of regulatory initiatives; and/or the strength of BenevolentAI's competitors. These forward-looking statements reflect, at the time made, BenevolentAI's beliefs, intentions and current targets/aims. Forward-looking statements involve risks and uncertainties because they relate to events and depend on circumstances that may or may not occur in the future. The forward-looking statements in this release are based upon various assumptions based on, without limitation, management's examination of historical operating trends, data contained in BenevolentAI's records, and third-party data. Although BenevolentAI believes that these assumptions were reasonable when made, these assumptions are inherently subject to significant known and unknown risks, uncertainties, contingencies and other important factors which are difficult or impossible to predict and are beyond BenevolentAI's control.

Forward-looking statements are not guarantees of future performance and such risks, uncertainties, contingencies and other important factors could cause the actual outcomes and the results of operations, financial condition and liquidity of BenevolentAI or the industry to differ materially from those results expressed or implied by such forward-looking statements. The forward-looking statements speak only as of the date of this release. No representation or warranty is made that any of these forward-looking statements or forecasts will come to pass or that any forecast result will be achieved.
AGENDA

The Benevolent Platform™ & Business Model
Joanna Shields, CEO

Preliminary Results for the year ended 31 December 2022
Nick Keher, CFO

Pipeline review
Anne Phelan, CSO

Outlook
Joanna Shields, CEO
2022: A year of solid progress and growth for BenevolentAI

Enhanced the Benevolent Platform™, progressed our pipeline and delivered in commercial collaboration with AstraZeneca

**BEN-2293**: Completed Phase IIa study and expect top-line data in Q1 2023

**BEN-8744**: Submitted CTA in Dec 2022, expect to initiate a Phase I clinical trial in H1 2023

**BEN-28010**: Declared as a clinical candidate in July 2022, with preparation for IND-enabling studies ongoing

3 year collaboration expansion with AstraZeneca’s into 2 new disease areas

3 additional novel targets selected for AstraZeneca’s portfolio

3 in-house assets transitioned into lead optimisation

4 new in-house drug programmes generated using the Benevolent Platform™

**FDA approval** of COVID-19 treatment (baricitinib) first identified by BenevolentAI
BenevolentAI is a leading AI-enabled drug discovery & development company with a platform-generated pipeline.

**DISCOVERY**

Industry-leading AI platform uncovers novel biology across diseases and drug modalities

- Expansive knowledge graph with multimodal data foundations
- Disease and drug modality agnostic
- Generate predictions with the aim to increase the probability of success

**DEVELOPMENT**

Portfolio of first-in-class and best-in-class programs, discovered using our proprietary AI platform

<table>
<thead>
<tr>
<th></th>
<th>Discovery</th>
<th>Preclinical</th>
<th>Clinical</th>
</tr>
</thead>
<tbody>
<tr>
<td>BEN-2293</td>
<td>- Atopic Dermatitis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BEN-8744</td>
<td>- Ulcerative Colitis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BEN-9160</td>
<td>- ALS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BEN-28010</td>
<td>- Glioblastoma</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

1 asset in Phase II
3 assets in pre-IND/CTA
15 Platform-generated drug programmes
Powerful data foundations generate a 360° view of disease biology

Multimodal approach combines over 85 data sources to provide a holistic view of disease biology

Maximise our probability of clinical success by integrating disease traits, genetics and genomics data to generate endotype-specific target predictions

Breaks down silos across therapeutic areas to connect shared mechanisms across disease

Provides a proprietary integrated view of biomedical data that supports discovery and decision-making
The Benevolent Platform™ empowers scientists with industry-leading drug discovery AI

- Comprehensive data foundations
- Biology first
- Hypothesis driven

**TARGET IDENTIFICATION**

- Proprietary AI models reason across multi-modal data to discover novel targets
- Enables scientists to assess & select only the most promising targets to take into wet lab experiments
- Efficiently surfaces scientific evidence to support higher confidence decisions
- Data fed back into the Knowledge Graph to enhance future predictions
Our flexible business model unlocks multiple routes to value creation

**AI-Discovery Tools**
- Knowledge Graph
- Target Identification
- Precision Medicine
- Molecular Design

**OWNED PIPELINE**
- Platform-generated assets
- In-house development

**LICENSING**
- Platform-generated assets
- Out-licensed at IND, end Phase I or end II

**PLATFORM COLLABORATIONS**
- Economic Benefits
- Platform Validation
- Data generated enriches the Benevolent Platform™

**NON-COMMERCIAL COLLABORATIONS**
- ESG
- Platform Validation
- Data generated enriches the Benevolent Platform™
Preliminary Results for the year ended 31 December 2022

Nick Keher, CFO
### 2022 Financial highlights

<table>
<thead>
<tr>
<th></th>
<th>31 December 2022</th>
<th>31 December 2021</th>
</tr>
</thead>
<tbody>
<tr>
<td>Revenue</td>
<td>£10,560</td>
<td>£4,625</td>
</tr>
<tr>
<td>R&amp;D - Drug discovery</td>
<td>(£43,179)</td>
<td>(£27,129)</td>
</tr>
<tr>
<td>R&amp;D - Product &amp; technology</td>
<td>(£21,914)</td>
<td>(£19,963)</td>
</tr>
<tr>
<td>G&amp;A - Business operations</td>
<td>(£16,500)</td>
<td>(£13,944)</td>
</tr>
<tr>
<td>Underlying expenses related to share-based payments</td>
<td>(£23,731)</td>
<td>(£51,390)</td>
</tr>
<tr>
<td>Other income</td>
<td>166</td>
<td>90</td>
</tr>
<tr>
<td><strong>Normalised operating loss</strong></td>
<td>(£94,598)</td>
<td>(£107,711)</td>
</tr>
<tr>
<td>Normalised EPS (in pence)</td>
<td>(72.6)</td>
<td>(104.6)</td>
</tr>
<tr>
<td>Weighted average ordinary shares outstanding (in millions)</td>
<td>109.1</td>
<td>89.9</td>
</tr>
</tbody>
</table>

Revenue increase across AstraZeneca collaboration, with 3 additional novel targets in chronic kidney disease (x1) and idiopathic pulmonary fibrosis (x2).

DD spend increase driven by advancing pipeline into later stages of development, particularly BEN-2293 adaptive Phase I/II and BEN-8744 CTA filing enablement in Dec-22. Net 4 named programmes added into pipeline during the year.

P&T spend increase reflecting increased headcount, expected to plateau.

Bus Ops spend +18%, driven predominantly by listing status and expected to maintain at this level.

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1) Excludes exceptional costs related to the Business Combination
2) Normalised EPS also excludes taxation impact from exceptional items and finance income related to the Business Combination
Reported operating loss significantly driven by non-recurring costs of Business Combination.

Non-cash exceptional costs related to acceleration of share-based payments also incurred from Business Combination, and set to reduce beyond 2022.

Non-cash listing service expenses reflects cost of share issuance to Odyssey SPAC as part of Business Combination net of assets acquired (before PIPE and backstop).

<table>
<thead>
<tr>
<th></th>
<th>31 December 2022</th>
<th>31 December 2021</th>
</tr>
</thead>
<tbody>
<tr>
<td>Operating loss</td>
<td>(197,034)</td>
<td>(121,322)</td>
</tr>
<tr>
<td>Adjustments for:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>G&amp;A - Direct Transaction costs</td>
<td>11,255</td>
<td>2,911</td>
</tr>
<tr>
<td>G&amp;A - Transaction-related listing service SBP expense</td>
<td>83,067</td>
<td>-</td>
</tr>
<tr>
<td>G&amp;A - Transaction-related employee-related SBP expense</td>
<td>3,883</td>
<td>-</td>
</tr>
<tr>
<td>G&amp;A - Impairment of assets</td>
<td>-</td>
<td>10,700</td>
</tr>
<tr>
<td>G&amp;A - Transaction-related stamp duty</td>
<td>3,740</td>
<td>-</td>
</tr>
<tr>
<td>Revaluation of investments</td>
<td>491</td>
<td>-</td>
</tr>
<tr>
<td>Normalised¹ group operating loss</td>
<td>(94,958)</td>
<td>(107,711)</td>
</tr>
</tbody>
</table>

¹) Excludes exceptional costs related to the Business Combination
Cash flows focused upon drug and platform development

<table>
<thead>
<tr>
<th>31 December</th>
<th>2022</th>
<th>£'000</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normalised¹ operating loss</td>
<td>(94,598)</td>
<td></td>
</tr>
<tr>
<td>Depreciation &amp; amortisation</td>
<td>3,058</td>
<td></td>
</tr>
<tr>
<td>Foreign exchange</td>
<td>(3,141)</td>
<td></td>
</tr>
<tr>
<td>Other employee-related SBP expense</td>
<td>29,935</td>
<td></td>
</tr>
<tr>
<td>Cash flows from changes in working capital</td>
<td>(13,094)</td>
<td></td>
</tr>
<tr>
<td><strong>Cash expended from underlying operating activities</strong></td>
<td><strong>(77,840)</strong></td>
<td></td>
</tr>
<tr>
<td>Opening cash, cash equivalents and short-term deposits</td>
<td>40,553</td>
<td></td>
</tr>
<tr>
<td>Closing cash, cash equivalents and short-term deposits</td>
<td>130,182</td>
<td></td>
</tr>
</tbody>
</table>

£1.7m property-related leases.

£3.2m gain from EUR holdings; £0.3m gain from USD holdings; £0.4m charge from operational.

Non-Transaction-related equity awards removed from the P&L (no cash impact)

Largely driven by increase in R&D tax credit receivable (£4.0m), as well as decrease in SBP employer-related tax provision (£6.2m).

Year end cash position of £130.2m at the top end of our stated guidance.

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¹) Excludes exceptional costs related to the Business Combination
Cash runway to Q4-2024 providing sufficient capital for key value inflection points

**Cash Runway**

- **Cash¹ at 31 December 2022**: £130.2m
- 2022 cash burn of £64.7m before working capital movements
- Cash runway guidance assumes no future capital from licensing or collaboration agreements
- Multiple assets at, or close to, key value inflection points

**Capital allocation**

1. Fund Phase I trial for BEN-8744 in Ulcerative Colitis and commencement of Phase II trial in 2024
2. Fund CTA enabling work for BEN-28010 and begin Phase I trial in GBM in 2024
3. Progress balance of pipeline as well as fund CTA enabling work of novel ALS asset to complete in 2024
4. Continuous enhancement of the Benevolent Platform™ to support further collaborations
5. Business Operations to support Group activities

¹) Includes cash, cash equivalents and short-term deposits (maturity between 3 and 12 months).
Pipeline review

Anne Phelan, CSO
Robust pipeline entirely generated by the Benevolent Platform™

<table>
<thead>
<tr>
<th>Target ID</th>
<th>Chemistry &amp; Lead Opt</th>
<th>Preclinical</th>
<th>Phase I</th>
<th>Phase II</th>
</tr>
</thead>
<tbody>
<tr>
<td>BEN-2293</td>
<td>Atopic Dermatitis</td>
<td>Yellow</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BEN-8744</td>
<td>Ulcerative Colitis</td>
<td>Red</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BEN-28010</td>
<td>Glioblastoma Multiforme</td>
<td>Green</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BEN-9160</td>
<td>Amyotrophic Lateral Sclerosis</td>
<td>Green</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- BEN-2293: Phase IIa read out Q1-2023
- BEN-8744: Novel target with zero prior linkage to UC. Delivered drug candidate within 2 years from programme initiation, starting Phase I H1-2023
- AstraZeneca: multi-year Target-ID collaboration expanded in Jan 2022 to include systemic lupus erythematosus & heart failure.

Highlights

- All pipeline programmes generated using the Benevolent Platform™
- BEN-2293: Phase IIa read out Q1-2023
- BEN-8744: Novel target with zero prior linkage to UC. Delivered drug candidate within 2 years from programme initiation, starting Phase I H1-2023
- AstraZeneca: multi-year Target-ID collaboration expanded in Jan 2022 to include systemic lupus erythematosus & heart failure.

BAI pipeline as at end-December 2022

+10 Exploratory stage programmes
BEN-2293 for Atopic Dermatitis

- Atopic dermatitis (AD) is the **most common chronic inflammatory skin disease**, characterized by intensely itchy, red, and swollen skin\(^1\)
  - Affects **10-20% of children** and up to **3% of adults**\(^2\)
  - Approximately **60-70% of all cases** present with mild-moderate disease severity\(^3\)
  - Prevalence is rising\(^3\), with market value in 7MM **forecast to exceed $16.7 billion** by 2030\(^4\)

- BEN-2293 is expected to **treat atopic dermatitis** by:
  - Inhibiting **itch signaling** and blocking nerve sensitization (TrkA) in addition to inhibiting Th1/Th2-mediated **dermal inflammation** (TrkB, TrkC).
  - Using our Molecular Design expertise we were able to design a PanTrk inhibitor, equipotent against the 3 receptors.

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**BEN-2293** will target **Mild, Moderate and Severe AD patients**, addressing unmet need as a steroid sparing alternative and in more severe patients undergoing treatment with systemics (e.g. dupilumab) that require add-on treatment.
BEN-2293 Phase IIa clinical study designed to demonstrate efficacy in mild-moderate Atopic Dermatitis

**STUDY DESIGN: SAFETY & EFFICACY**

*Recruitment completed end of 2022*

91 patients randomised 1:1 for BEN-2293:Vehicle

*Patients (Inclusion Criteria)*

- Mild-Moderate AD
  - Baseline vIGA 2-3
  - Baseline Itch NRS ≥4
  - Atopic dermatitis affecting 1-30% BSA of treatable skin

- 18-65 years

*Dosing*

- 7 day medication washout followed by 3 day placebo run-in prior to dosing
- 1% w/w BEN-2293, or placebo/vehicle applied twice daily to treatable lesioned skin up to 30% BSA
- 28 days on treatment

= Powered endpoints

**STUDY EFFICACY OUTCOMES**

*Itch*

- Change from baseline in the **Pruritus NRS** (Worst itch over 24 hours and Current itch)
- Time to itch reduction
- Fraction of patients achieving itch reduction

*Inflammation*

- Change from baseline in **EASI** score
- Fraction of patients achieving improvement in **EASI** score
- Change from baseline in BSA affected by AD in treated area(s)
- Change from baseline in **vIGA**

*Quality of life*

- Change from baseline in **POEM**
- Change from baseline in **DLQI**
- Change from baseline in **EQ-5D**
- Change from baseline in **PROMIS** (sleep subscale)
BEN-2293 - Phase IIa study recruitment completed

Phase IIa clinical study design

- Baseline assessments: itch and AD score
- Re-baseline or exclude
- Continuous safety monitoring
- Study endpoints - itch and AD rating scales

Screening
- Wash out
- Run in

Wash out: 7 day
Wash out from any existing medication

Run in: 3 day
Placebo run in

28d BID dosing over affected skin area
- 28 day
BID dosing on affected skin up to a maximum of 30% BSA
Placebo: Active (1:1), Moderate: Mild patient ratio 70:30, Total of 91 patients (50% active:50% placebo)

Follow up
- 14 day
Final safety assessment

Current Status
- LPLV achieved end January 2023
- 91 patients randomised (65 moderate and 26 mild)
- DBL completed 1st March
- TLR anticipated end March

Our intention is to partner this asset with a pharmaceutical company that has a focus in dermatology for continued clinical development and, if approved, commercialisation.
BEN-8744

Ulcerative Colitis (UC)

Affects 0.4% US population\(^1\), 1.7 million patients in 7MM\(^1\), forecast $7.8bn market by 2026\(^2\)

- A chronic, lifelong disease that causes inflammation and ulceration of the inner lining of the colon and rectum
- 64% of patients are mild-moderate, 31% of patients are moderate-severe and 5% of patients are severe-fulminant
- Efficacy - 20-40% of Moderate-severe patients do not respond to anti-TNF (main treatment paradigm)\(^3\)
- Safety - Treatments have many side effects — from steroids to anti-TNF and JAK inhibitors (black box warnings)\(^4\)
- High unmet need for an alternative oral small molecule treatment option with improved safety profile and efficacy in treatment of refractory patients

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Phosphodiesterase 10 (PDE10) was identified by our TargetID platform as an entirely novel target for the treatment of UC/IBD

Using our Molecular Design expertise we optimally designed a best in class peripherally restricted PDE10 inhibitor: BEN-8744

BEN-8744 is expected to provide an efficacious disease modifying oral treatment for UC/IBD

BEN-8744 will target Moderate and Severe UC/IBD patients, meeting the unmet need left by existing therapies including:
- Patients refractory to anti-TNFs or other biologics
- Improved safety and tolerability profile compared to competitors
- Aiming to use a Precision Medicine approach to target key responder patient cohorts and avoid the safety risks associated with ineffective therapies

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BEN-8744: potent activity in UC colon biopsies

Cross donor response summary: % inhibition cytokine release (mean % inhibition from N=15 IBD donors)

Endoscopic Biopsy from UC patients → Colonic mucosa organ culture and compound treatment → Inflammatory cytokine measurement

Selective PDE10 inhibition showed comparable reduction of IL-6 and IL-8 to the positive controls in ex vivo UC biopsies
Novel target for UC
- Discovered using Benevolent TargetID tools
- PDE10 has **zero linkage to UC** in all available biomedical literature
- Experimentally **validated in ex-vivo** UC colon samples from patients refractory to SoC treatment

**CHEMISTRY**
- **Molecular Design tools** enabled rapid and efficient lead optimisation
- **Candidate nominated in Sep ‘21** Novel, potent, selective, peripherally restricted PDE10. Inhibitor, with low dose prediction
- Delivered drug candidate within **2 years** from programme initiation

**CLINICAL DEVELOPMENT**
- We will develop responder and progression endotypes, **adding molecular descriptors**
- These will inform our trial design, **patient selection** and further target identification in UC
- Augmenting a further loop of iteration on an enriched graph
Outlook

Joanna Shields, CEO
“With the world’s attention on AI applications that deliver real-world impact, we are strongly positioned to capitalise on this moment. With our substantial portfolio of platform-generated drugs, our work with big pharma and research collaborators, and our continued investment in state-of-the-art technology, we are showing every day how AI can be used to unlock the next wave of biopharma innovation.”

Joanna Shields, CEO

Poised for growth: multiple value inflection points expected

**BEN-2293**
- Top-line results of the Phase IIa clinical trial expected in Q1 2023
- Out-license in H2 2023 subject to results

**BEN-8744**
- Initiate the Phase I study in H1 2023

**BEN-28010**
- Submit the CTA in H2 2023

**2023**
- Continued investment in state-of-the-art technology
- Aim to sign additional commercial collaboration
- Commence IND-enabling studies for at least one additional asset
- Continue to progress pipeline assets to value inflection points
Thank you
Appendix
World-class team

We “build tech in the service of science”

Board of Industry Luminaries

Combines deep expertise across AI, pharma, & drug discovery & development

[Diagram showing the composition of the team, with 350+ World Class Scientists & Technologists (48%), Drug Discovery (37%), and Bus Ops (15%)]

Baroness Joanna Shields
CEO & Executive Director

François Nader
Chairman

Susan Liautaud
Non-Executive Director

Olivier Brandicourt
Non-Executive Director

Jean Raby
Non-Executive Director

Jackie Hunter
Non-Executive Director

Nigel Shadbolt
Non-Executive Director

John Orloff
Non-Executive Director

As of December 2022
Proven to enhance drug discovery

**DISEASE-AGNOSTIC**

We can work on any therapeutic area due to the breadth and diversity of our data foundations.

**MODALITY-AGNOSTIC**

The Benevolent Platform™ can be applied to antibody and biologic targets, in addition to small molecule targets.

**BUILT FOR SCALE**

Our scalable and versatile Platform can support multiple in-house drug programmes and commercial collaborations.

**ACCELERATES DISCOVERY**

By combining our AI Platform, scientific expertise and wet lab facilities, we accelerate discovery and reduce discovery and development timelines.

**IDENTIFIES NOVEL TARGETS**

Our predictive tools can surface targets that have never been considered for a disease before.

**POTENTIAL TO INCREASE PROBABILITY OF SUCCESS**

By building higher confidence hypotheses in the earliest stages of drug discovery, we aim to reduce costly failures down the line.
Poised for growth: multiple value inflection points

**H1 2023**
- **BEN-2293: AD** Data expected Q1 2023
- **BEN-8744: UC** Begin Phase I study H1 2023

**H2 2023**
- **BEN-2293: AD** Out-licensing
- **BEN-28010: GBM** Submit Clinical Trial Application (CTA)

**2024**
- **BEN-8744: UC** Phase I data package 2024, Phase II to follow shortly after
- **BEN-28010: GBM** Initiate Phase I study

Internal pipeline depth and progression
- Expect to add 4-6 names drug programmes to portfolio
- Aim to progress 1-2 CTA/IND stage drug candidates every year

AZ Collaboration
- Potential new targets added for SLE and Heart Failure - prior targets (3 for IPF and 2 for CKD) advancing

Other Platform Collaborations
- Discussions with a number of parties ongoing
Atopic Dermatitis – BEN-2293, pan-Trk inhibition rationale

**TrkA**
- TrkA levels in skin dramatically increase in response to inflammatory stimuli
- NGF produced by AD keratinocytes, is a major mediator of cutaneous hyperinnervation
- Increased NGF in the skin sensitizes primary afferents contributing to peripheral itch sensitization and chronic pruritus
- Involved in the inflammatory activation of mast cells and basophils

**TrkC**
- NT3/TrkC potentiates stimulated Th2 T-cell inflammatory responses and synergistically enhances T-cell receptor induced IL-4 production by Th2 cells
- *Mast cells* within AD skin lesions express high levels of NT3 compared to normal controls

**TrkB**
- AD Skin-resident eosinophils express elevated levels of TrkB (together with TrkA and C) and functionally respond to BDNF
- BDNF/TrkB inhibit eosinophil apoptosis and increase chemotactic index

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**TrkA**
- TrkA levels in skin dramatically increase in response to inflammatory stimuli
- NGF produced by AD keratinocytes, is a major mediator of cutaneous hyperinnervation
- Increased NGF in the skin sensitizes primary afferents contributing to peripheral itch sensitization and chronic pruritus
- Involved in the inflammatory activation of mast cells and basophils
BEN-2293: Excellent skin penetration

- Experimental evidence supports high exposure in human skin at >IC90 free, and low exposure in blood with proposed clinical 1% ointment strength.<sup>1</sup>
- 1% BEN-2293 ointment BID exceeds the exposure needed for PanTrk inhibition in both epidermis/upper dermis and lower dermis even at IC<sub>90</sub>.<sup>1</sup>

- **Human in vitro** >>IC90 √
- **Minipig in vitro** >> IC90 √
- **Minipig in vivo** >IC90 √
- **Minipig in vivo** √
- Free plasma levels <<400 below IC50

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CTA-enabling 28d Tox Package: Rat (IV) and Mini-pig (topical) = Safety margins > 20 fold for AUC and > 269 fold for Cmax to dose limited NOAELs<sup>1</sup>

<sup>1</sup>[Internal Company drug programme data]
We expect BEN-2293 to provide both symptomatic relief and to reverse disease progression in atopic dermatitis

- **BEN-2293 is highly selective for Trk receptors**, with IC50 potencies in the low nM range for TrkA, B, and C
- **BEN-2293 dose dependently inhibits release of inflammatory Th1 and Th2 cytokines** TNFα, IFNγ, IL-13, and IL-4 in human peripheral blood mononuclear cells (PBMCs) stimulated with an inflammatory T-cell stimulus (anti-CD3/CD28)
- **BEN-2293 inhibits the release of Calcitonin Gene-Related Peptide (CGRP)**, a mediator of itch, sensory nerve hypersensitisation and neurogenic inflammation, in dorsal root ganglion (DRG) isolated from adult rats and stimulated with NGF
- **BEN-2293 series significantly (p<0.05) reduced mouse ear inflammation** following administration of PMA, significantly reducing expression of cytokines IL-1β, IL-4, IL-6, CXCL1, MCP-1, and Tarc
- **BEN-2293 demonstrates excellent tolerability and safety margins** in IND/CTA-enabling toxicology studies

![BEN-2293 Inhibition of human primary T-cell activation](image)

![Inhibition of sensory neuron activation](image)

![Reduction in mouse ear inflammation](image)

Key: Tropomyosin-related kinase (Trk) receptor tyrosine kinase family, namely TrkA, TrkB, and TrkC; Nerve Growth Factor (NGF); Brain Derived Neurotrophic Factor (BDNF); Neurotrophin-3 (NTF-3)/NT3
**BEN-2293 - Phase Ib safety and tolerability study successfully completed**

**Phase Ib/IIa double-blind, placebo-controlled, first-in-patient, two-part clinical study**

**Phase Ib**

1. **First-in-human dose escalation**

**Phase Ib completed Dec 2021**

8 Mild-Moderate AD patients (18-65 years) per cohort, randomised 3:1 BEN-2293:Placebo

**Safety, Tolerability, PK**
- Adaptive multiple ascending dose cohort design
- Includes efficacy endpoints
- MALDI imaging
  - To evaluate human skin PK

**Phase Ib: ✔ Successfully completed Safety and Tolerability arm**

BSA = Body surface area, QD = once per day dosing, BID = twice per day dosing
BEN-2293 - indicative data from Phase Ib

Caveats:

- Phase Ib was **NOT** powered to meaningfully assess efficacy - only 6 patients dosed with active per group
- Maximum duration of dosing 14 days (EASI score changes typically measured at 28 days)

Mean Change from Baseline %BSA affected in treated areas

0.25% QD 10%BSA 7d
1% QD 10%BSA 7d
1% QD 30%BSA 14d
1% BID 30%BSA 14d
PBO 7d
PBO 14 d

Cohort 3
Patients dosed 1% ointment, 30% BSA, once per day

Cohort 4
Patients dosed 1% ointment, 30% BSA, twice per day

Mean change from baseline

Day
BEN-8744 - Phosphodiesterase 10 (PDE10) - a novel target for UC

Transcriptomics data support the rationale for PDE10 as a novel target for UC

- PDE10 regulates signal transduction by hydrolysing cGMP
- PDE10 is significantly upregulated in UC-derived colon and colonic mucosa samples, whilst guanylyl cyclase, which makes cGMP, is down-regulated

Reduced levels of guanylyl cyclase correlate with increased TNF-α in UC colonic mucosa

- cGMP is downregulated in UC and its expression inversely correlates to disease severity
- PDE10 is well-studied in CNS disorders but not in inflammation with zero linkage to UC

PDE10 demonstrates restricted expression in peripheral tissue

- Reduces the safety liability of targeted inhibition

PDE10 degrades cGMP

Differential RNA expression of PDE10A and GUCY2C: normal vs UC

Low basal PDE10 expression, highest levels in brain. Low basal soluble guanylate cyclase (GUCY2C) levels except in colon and sm intestine
PDE10 inhibition: potential to normalise dysregulated mechanisms in IBD

- Reduced inflammatory cytokine release from intestinal epithelia via $\downarrow$NFkB$^{(1)}$
- Reduced tissue-resident macrophage activation$^{(1)}$
- Improved TJ assembly via PKG/PKA-mediated $\downarrow$pMLC$^{(2)}$
- Improved fluid/mucus homeostasis via PKG phosphorylation of intestinal CFTR$^{(3)}$


Images: Nettleford and Prabhu, Antioxidants 2018 (left); He et al. Int J Mol Sci 2020 (right)
Strategic validation: successful collaboration with AstraZeneca

Multi-year Target-ID collaboration is delivering multiple, novel targets for complex diseases with high unmet need

Separate data environment established to integrate AstraZeneca’s data into a bespoke Knowledge Graph

BenevolentAI and AstraZeneca teams working in close collaboration to explore, identify and validate targets

Deal structure of upfront license fee, milestone payments and downstream royalties

Data generated via the collaboration enriches the Benevolent Platform™

AstraZeneca

Five novel targets selected for AstraZeneca’s portfolio to date

2019

Initial deal focused on Chronic Kidney Disease & Idiopathic Pulmonary Fibrosis

2022

3-year collaboration expansion to include Heart Failure & Systemic lupus erythematosus
Using our platform for wider societal benefit

Identified a COVID-19 treatment now approved for use by the FDA

RAPID
Identified baricitinib as a treatment in just 48 hours, published research in The Lancet in Feb 2020

NOVEL
Our technology and AI workflows identified a previously unknown antiviral mechanism

EFFECTIVE
COV-BARRIER trial showed baricitinib reduces mortality by 38% in hospitalised patients, and by 46% in ventilated or ECMO patients

FDA approved the baricitinib to treat COVID-19 in May 2022 after first granting EUA in Nov 2020

Led to equity investment from Eli Lilly

Non-commercial collaboration

→ Focused on Dengue fever - a major healthcare burden

→ Aims to deliver biological targets and drug repurposing candidates

→ Experimental validation in progress - 6 assays
Categorisation of AI/ML companies in biotech, hit & target-ID

Companies can be characterized across two key dimensions: **Original technology focus** and **drug discovery approach**

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**Target-ID**

WHAT TARGET DO WE NEED TO HIT TO BE EFFECTIVE AND SAFE IN A SPECIFIC DISEASE (pathways, cellular processes)?

HIGH COMPLEXITY THROUGH BIOLOGY
Many layers of knowledge needed, and many areas where research is not yet complete

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**Hit-ID**

HOW DO WE NEED TO HIT THE TARGET WE HAVE IDENTIFIED (specific drug characteristics)?

HIGH COMPUTATIONAL COMPLEXITY
Atom-to-atom interaction is relatively well known, but requires many calculations and simulations

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**Company archetypes**

- **Hypothesis driven**
  - Involves a **data-driven hypothesis-led** approach to therapeutic target identification

- **Non hypothesis driven**
  - Leverages technology to identify solutions without specific conditions to target specified at the outset

Figure: Oliver Wyman Analysis (listed companies only)

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Source: Company Websites, Oliver Wyman Analysis

Pharma companies also active in the space, through internal development and/or collaborations