BenevolentAI: Complex biology, unlocked

J.P Morgan Healthcare Conference
Joanna Shields, CEO, BenevolentAI
9 January 2023
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.
A clinical-stage AI-enabled drug discovery company

**SCIENTIFIC VALIDATION**

- 15 named **Platform-generated drug** programmes
- 3 assets in **pre-IND**
- 1 asset in **Phase II**
- 10+ **exploratory stage** programmes

**COMMERCIAL VALIDATION**

- 5 **novel targets** selected for AstraZeneca’s portfolio

**REGULATORY VALIDATION**

- **FDA** approval of COVID-19 treatment identified by BenevolentAI
We are drowning in a sea of data and starving for knowledge

Sydney Brenner
The Nobel Prize winner in Physiology of Medicine 2002
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™

Comprehensive data foundations

Biology first

Hypothesis driven

DATA FOUNDATIONS

TARGET IDENTIFICATION
Disease Exploration

DEMO

The image shows a user interface for exploring disease mechanisms, specifically focusing on amyotrophic lateral sclerosis (ALS). The interface allows users to explore related mechanisms and diseases, with options to filter by related tissues, cell types, and ontology categories. The page also includes visual representations of gene overlaps and mechanisms associated with ALS.
**DEMO**

**Disease Exploration**

**Network View**

**PPI Edge Details**

**NFE2L2 - SOD1**

There are 1 edges describing 1 kinds of interaction between NFE2L2 and SOD1

**NFE2L2 up regulates SOD1**

Edge source: SigNOR
via transcriptional regulation
DISEASE EXPLORATION

Understanding disease biology to build robust hypotheses

- Provides an unprecedented view of the disease landscape
- Accelerates discovery of novel biology
- Surfaces potential targets and mechanisms that may not have otherwise been found

Can we treat ALS by reversing Autophagy

impairment in microglia by reducing oxidative stress?

Target

Endpoint: What we will measure

Cell type

Sign

Mechanism

Your biological question ...
TARGET PREDICTIONS

Multiple machine learning models expand the target universe

- **Expands pool of possible targets** by approaching target identification from different angles: some models can rank the entire human genome, others provide promising targets that answer biological questions.

- **Reveals novel drug targets** that have never been considered for a disease before.

- **Modality agnostic**: the Benevolent Platform™ can be applied to antibodies and other biologic agents, in addition to small molecules.
Empowers scientists to make data-driven decisions on which targets to take into experimental validation.

Scientists can assess key aspects for progressability including optimal modality, patent and competitive landscape and the druggability and selectivity potential.

Select targets that are most likely to succeed.
PTGS2 is a promising novel therapeutic target to **decrease response to oxidative stress** in amyotrophic lateral sclerosis.

Top 100 sentences found in 70 unique publications. Top Enterprise score is **0.771**

<table>
<thead>
<tr>
<th>Publication</th>
<th>Rank</th>
<th>Enterprise score</th>
<th>Where in publication</th>
<th>Sentence from publication</th>
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<tr>
<td>View paper</td>
<td>1</td>
<td>0.771</td>
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<td>Thus, COX-2 could play a partial role in neuronal damage, as suppression of its activity offers an incomplete neuroprotective effect in a mouse model of SOD1 related ALS.</td>
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<td>December 2021</td>
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<td>Therefore, the role of Cox-2, which is upregulated by SPl, in the oxidative stress state of neurons and glial cells during the onset of ischemic stroke needs to be further explored.</td>
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<td>Neurotoxicity via elevating COX-2 expression was noted in neurodegenerative diseases, such as multiple sclerosis, amyotrophic lateral sclerosis, and Parkinson and Alzheimer diseases; meanwhile, the inhibition of COX-2 appears to produce neuroprotective effects in some neurodegenerative disorders [53–55].</td>
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Advanced in-house lab capabilities move programmes faster

Cutting-edge technologies including invitro / in vivo Biology, Chemistry, CMC, DMPK with in-house investment in CRISPR, RNA seq and human iPSC

Work progresses rapidly from in-silico to in-vitro experimental test

The more we do, the more we learn; experimental insights enrich our Knowledge Graph and enhance future target predictions
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.
Our prolific drug discovery engine drives higher productivity

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<th>Market cap¹</th>
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<td>AstraZeneca</td>
<td>$211bn</td>
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<td>Pfizer</td>
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<td>Merck</td>
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<td>Vertex</td>
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**Number of new INDs filed by year by pharma and biotech companies.** Median number of Phase I starts over five years (2015-2020)*

BenevolentAI potential productivity is in line with medium and large companies, but at a fraction of the total cost.

BenevolentAI will aim to increase the number of INDs from its Platform with incremental cost largely from development through to the clinic only.

Note *IND filing rate is based on Phase I trial starts with the company as the lead sponsor. Average adjusted for companies which started clinical development during time period;¹ Market cap as of 30/12/2022 (USD M)

Source: clinicaltrials.gov ; Company websites: L.E.K. research & analysis
Our flexible business model unlocks multiple routes to value creation

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

A. OWNED PIPELINE
- Platform-generated assets
- In-house development

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

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

D. NON-COMMERCIAL COLLABORATIONS
- ESG
- Platform Validation
- Data generated enriches the Benevolent Platform™
Robust pipeline entirely generated by the Benevolent Platform™

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Highlights

- **BEN-2293** - Phase Ib complete, Phase IIa ongoing
- **BEN-8744** - Novel target with zero prior linkage to UC. Delivered drug candidate within 2 years from programme initiation
- All pipeline programmes generated using the Benevolent Platform™
BEN-2293
Atopic Dermatitis (AD)

- Atopic dermatitis 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 $14 billion**\(^2,4\)

- Skin inflammation and chronic pruritus associated with atopic dermatitis negatively impact quality of life and psychosocial well-being\(^1\)

- Clear unmet need in **mild to moderate patient segment** for treatment addressing itch and inflammation, without side effects of steroids

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Topical best-in-class PanTrk inhibitor to relieve inflammation and rapidly resolve itch in patients with AD

- BEN-2293 is a **PanTrk inhibitor** targeting TrkA, B and C receptors. The Trk receptors were identified as part of an effort to find **mediators of both itch and inflammation in AD**. Using our Molecular Design expertise we were able to design a PanTrk inhibitor, equipotent against the 3 receptors

- BEN-2293 is expected to **treat atopic dermatitis** by: inhibiting **itch signaling** and blocking nerve sensitization (TrkA) in addition to inhibiting Th1 and Th2-mediated **dermal inflammation** (TrkB, TrkC)

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

Sources: (1) Weidinger et al. Nat Rev Dis Primers 2018; (2) GlobalData Report 2018: Atopic Dermatitis: Global Drug Forecast and Market Analysis to 2027; (3) GlobalData Report 2018: Atopic Dermatitis: Epidemiology Forecast to 2027; (4) Evaluate Pharma
**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).

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**Mean Change from Baseline %BSA affected in treated areas**

- **Cohort 3:** Patients dosed 1% ointment, 30% BSA, once per day.
- **Cohort 4:** Patients dosed 1% ointment, 30% BSA, twice per day.

---

**Day**

- Mean change from baseline
- 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

---

EASI: Eczema Area and Severity Index
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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**BEN-8744: Oral, peripherally-restricted, PDE10 inhibitor under development as a first-in-class treatment for refractory UC**

- 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

---

Validated as a target with a novel mechanism of action for ulcerative colitis

Inflamed colonic mucosa biopsies from UC patients
- Disease phenotype retained with high basal cytokine release
- Readouts: IL6 and IL8 - key mediators of UC pathology

Tissue samples treated with:
- Target-selective tool compound (BEN-3218)
- Positive controls – prednisolone and tofacitinib

Selective target inhibition showed comparable reduction of IL-6 and IL-8 to the positive controls
BEN-8744 results and progress to date

**TARGET IDENTIFICATION**
- 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**
- Rapid and efficient lead optimisation
  - 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**
- Developing responder and progression endotypes
  - 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

---

**Timeline**
- 2019: Target validation
- 2020: Novel, potent advanced lead molecule developed within 2 years
- 2021: Preclinical development
- 2022: Candidate nominated
- 2023: Preclinical development

**Key Milestones**
- Candidate nominated in Sep ‘21
- Drug candidate delivered within 2 years from programme initiation

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*Note: Benevolent*
Robust pipeline entirely generated by the Benevolent Platform™

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**Highlights**

- **Focus on complex multifactorial diseases**
- **Broad therapy area coverage** enabled by disease-agnostic Platform, with future investment to focus on three therapeutic indications
- **Balance of risk** between “best in class” and “first in class” drug candidates
- **Potential for rapid scaling** and expansion into new modalities
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 focussed 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**\(^1\)

EFFECTIVE
COV-BARRIER trial showed baricitinib reduces mortality by 38% in hospitalised patients\(^2\), and by **46% in ventilated or ECMO patients**\(^3\)

FDA approved the baricitinib to treat COVID-19 in **May 2022**\(^4\) after first granting EUA in **Nov 2020**\(^5\)

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
World-class team

We “build tech in the service of science”

Board of Industry Luminaries

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

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

350+ World Class Scientists & Technologists

37%

30%

15%

Tech

Drug Discovery

Bus Ops

48%
Subject to positive date the asset will then be ready for Phase I studies in [2024].

**AZ Collaboration**

**Other Platform Collaborations**

- **BEN-2293: AD**
  - Data expected Q1 2023

- **BEN-8744: UC**
  - Begin Phase I study H1 2023

**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

**Discussions with a number of parties ongoing**