



BenevolentAI: Complex biology, unlocked

J.P Morgan Healthcare Conference

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Benevolent^{AI}

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.

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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

Generating a 360° view of disease biology

Experiments

Assay Data (Binding, Omics Comparison, CRISPR Screens)
Clinical Trial

OMICS

Genes
Proteins
Isoforms
Transcripts & Variants

Biological Systems

Cellular Component
Molecular Function
Biological Process
Mechanism
Pathways

Literature

Scientific Literature
Patent Literature
Regulatory Documents

Aetiology

Diseases
Symptoms

Molecules

Organic Compounds
Preclinical Candidates
Approved Drugs
Antibodies
Other Biologics
Pharmacology
Pharmacokinetics



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



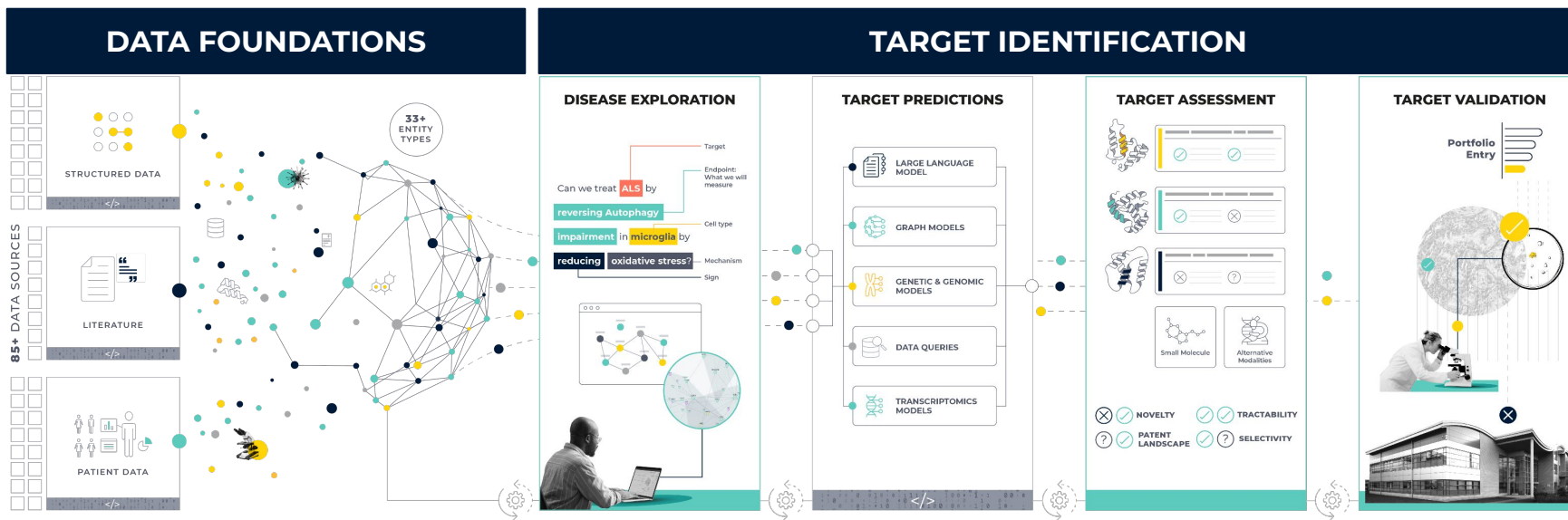
Provides a proprietary integrated view of biomedical data that supports discovery and decision-making

The Benevolent Platform™

✓ Comprehensive data foundations

✓ Biology first

✓ Hypothesis driven



DEMO

Disease Exploration

The screenshot displays the 'Entity Explorer' interface for 'amyotrophic lateral sclerosis'. On the left, a sidebar lists related entities: amyotrophic lateral sclerosis (530), astrocyte activation (155), and cellular response to oxidative stress (234). The main area features a Venn diagram showing the overlap between these three entities. A yellow callout box highlights the 'Mechanisms' tab, which shows 869 related mechanisms. Below this, a table provides detailed information for the top mechanism: RNA localization to nucleus.

Entity Explorer | Explore | Visualise | Saved Shortlists

ALS Demo
Disease program: ALS demo
Data release: 142 (latest)
Number of entities: 3
Number of unique benchmark genes: 853

amyotrophic lateral sclerosis (530)
Disease

Entity definition
Amyotrophic lateral sclerosis (ALS) is a neurodegenerative disease characterized by degeneration of motor neurons in the primary motor cortex, corticospinal tracts, brainstem, and spinal cord.

Benchmark Genes | Geneset Genes

There are 530 benchmark genes in your selection:
SLC18A3, LGALS4, MFN2, LHX3, SYNCRIP, LANCL1, KPNB1, SNCG, CLP1, MADD, SLC12A1, ZNF512B, SNCA, TSPPO, SOD1, SARM1

Show all 530 benchmark genes

+ Add as new custom list (530)

Mechanisms | Diseases | related to **amyotrophic lateral sclerosis**

There are 869 Mechanisms related to amyotrophic lateral sclerosis

Related cell: All | Mechanism ontology: All | Genetic Evidence: All

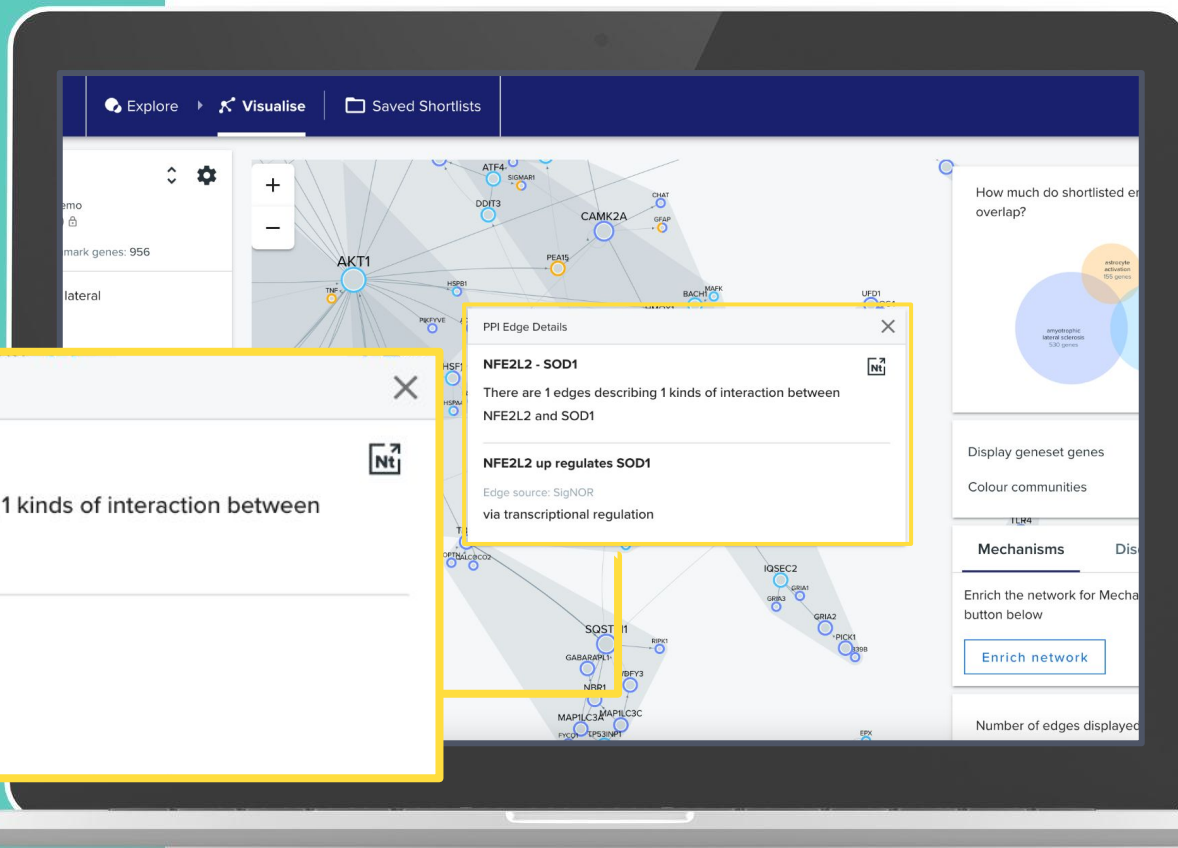
Number of benchmark genes	Number of geneset genes	Benchmark gene overlap	Genetic evidence
198	245	51	No

Cluster mechanisms Filter by: Related tissues: All | Related cell: All | Mechanism ontology: All | Genetic Evidence: All

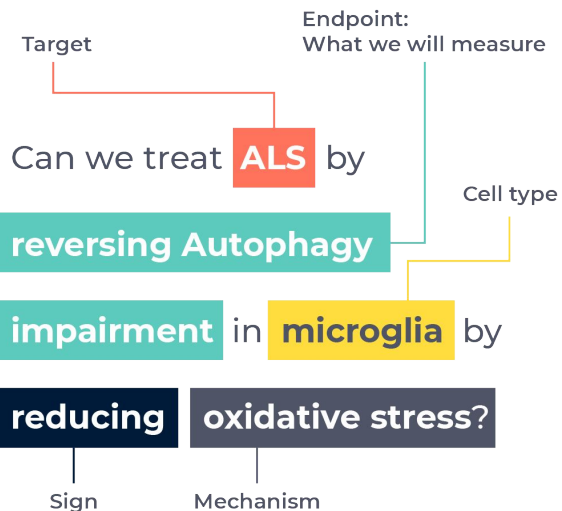
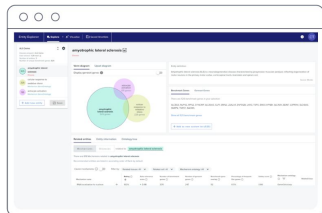
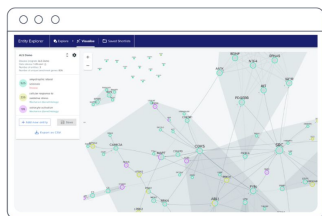
Mechanism name	Rating	Data relevance score	Number of benchmark genes	Number of geneset genes	Benchmark gene overlap	Genetic evidence
RNA localization to nucleus	+	100%	198	245	51	No

DEMO

Disease Exploration Network View



Understanding disease biology to build robust hypotheses



Provides an **unprecedented view** of the **disease landscape**



Accelerates discovery of novel biology

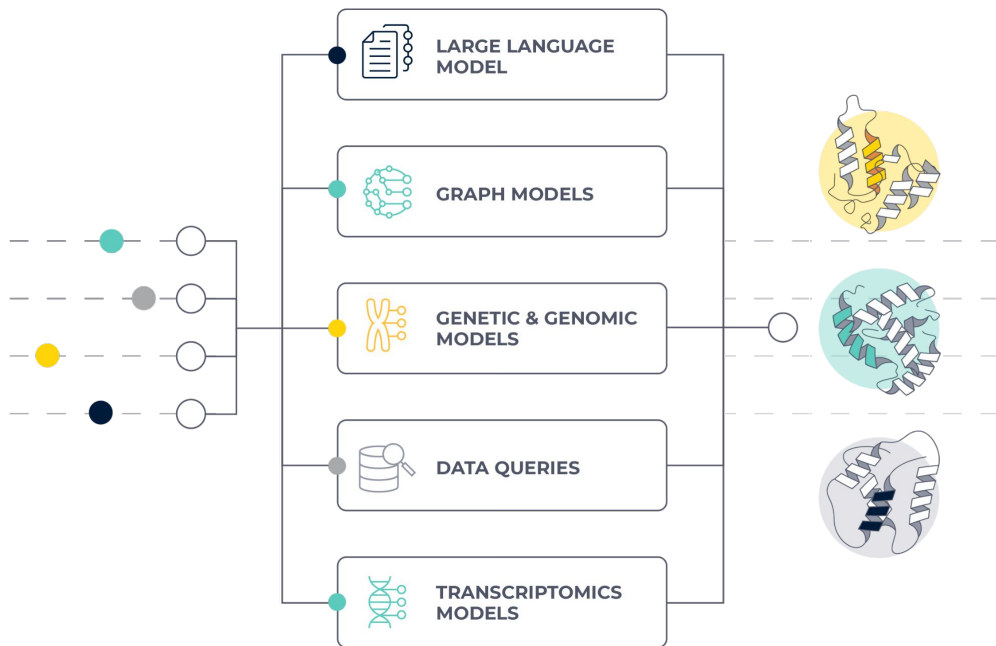


Surfaces potential targets and mechanisms that **may not have otherwise been found**

[T] *Your biological question ...*



Multiple machine learning models expand the target universe

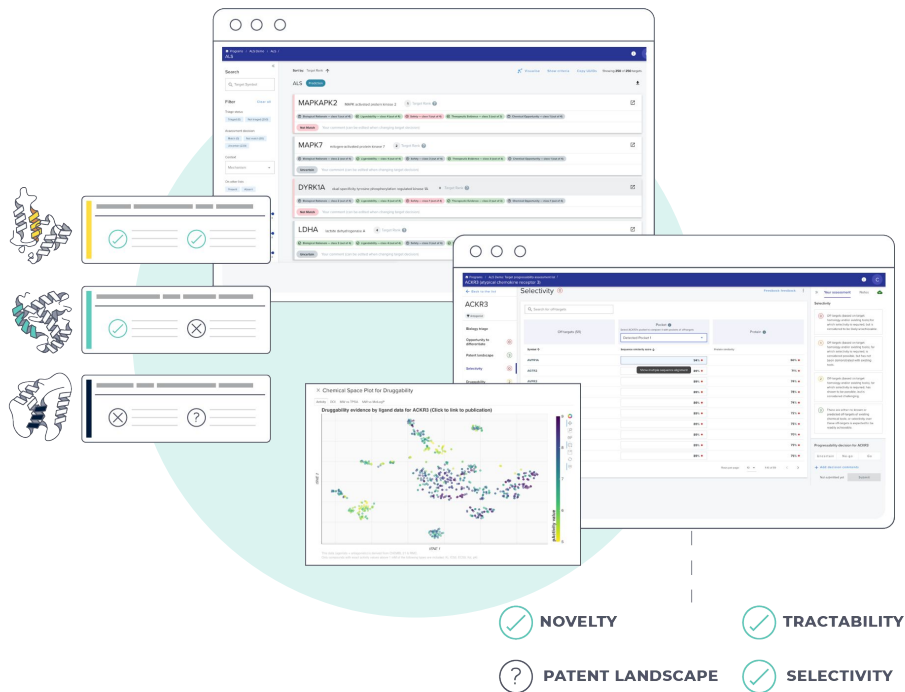


✓ **Expands pool of possible targets** by approaching target identification from different angles: some models can rank the entire human genome, others provide promising targets that answer biological questions

✓ **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

Suite of AI tools enable data-driven decisions



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

DEMO

Target Triage

Triage criteria

Biological Rationale

1 ————— 4

Ligandability

1 ————— 4

Safety

1 ————— 4

Tissue Expression

1 ————— 4

Therapeutic Evidence

Programs / ALS demo / Oxidative stress in ALS / ALS demo

Filter Clear all

Triage status
Triaged (0) Not triaged (12)

Assessment decision
Match (5) Not match (2)
Uncertain (5)

Context
Mechanism

On other lists
Present Absent

Triage criteria
Biological Rationale
1 ————— 4
Ligandability
1 ————— 4
Safety
1 ————— 4
Tissue Expression
1 ————— 4
Therapeutic Evidence

Match Your comment (can be edited when changing target decision)

GRM5 glutamate metabotropic receptor 5 5 Target Rank ?

Biological Rationale — class 3 (out of 4) Ligandability — class 4 (out of 4) Safety — class 3 (out of 4) Tissue Expression — class 1 (out of 4) Therapeutic Evidence — class 1 (out of 3)
Tractability — class 3 (out of 4)

Uncertain Your comment (can be edited when changing target decision)

SLC7A11 solute carrier family 7 member 11 6 Target Rank ?

Biological Rationale — class 3 (out of 4) Ligandability — class 1 (out of 4) Safety — class 3 (out of 4) Tissue Expression — class 1 (out of 4) Therapeutic Evidence — class 1 (out of 3)
Tractability — class 2 (out of 4)

Uncertain Your comment (can be edited when changing target decision)

NFE2L2 NFE2 like bZIP transcription factor 2 7 Target Rank ?

Biological Rationale — class 4 (out of 4) Ligandability — class 1 (out of 4) Safety — class 1 (out of 4) Tissue Expression — class 1 (out of 4) Therapeutic Evidence — class 1 (out of 3)
Tractability — class 4 (out of 4)

Match Your comment (can be edited when changing target decision)

TRPV1 transient receptor potential cation channel subfamily V member 1 8 Target Rank ?

Biological Rationale — class 1 (out of 4) Ligandability — class 4 (out of 4) Safety — class 3 (out of 4) Tissue Expression — class 1 (out of 4) Therapeutic Evidence — class 3 (out of 3)

DEMO

Target Triage

Programs / ALS demo / Oxidative stress in ALS / ALS demo / prostaglandin-endoperoxide synthase 2

← Back to the list

PTGS2

3 Match

Absent on other lists

Overview

Literature

Biological Rationale

Literature

Enterprise Evidence

Literature evidence relevant to the biological question according to the Enterprise model. Enterprise uses the name of the target and the components of the biological question to form a set of sentence-like queries. The model then finds and scores sentences from publications that are similar to each query, based on its understanding of the literature.

Query 1

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**

Publication	Rank	Enterprise score	Where in publication	Sentence from publication
View paper September 2005	1	0.771	text	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.
View paper December 2021	2	0.726	text	Therefore, the role of Cox-2, which is upregulated by SP1, in the oxidative stress state of neurons and glial cells during the onset of ischemic stroke needs to be further explored.
View paper January 2021	3	0.698	text	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 expression promoted neuroprotective effects according to several experiments [25, 27, 28].

Overview

Literature

Biological Rationale

Ligandability

Safety

Tissue Expression

Therapeutic Evidence

Druggability

Query 1

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Advanced in-house lab capabilities move programmes faster



Cutting-edge technologies

including invitro / in vico 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.

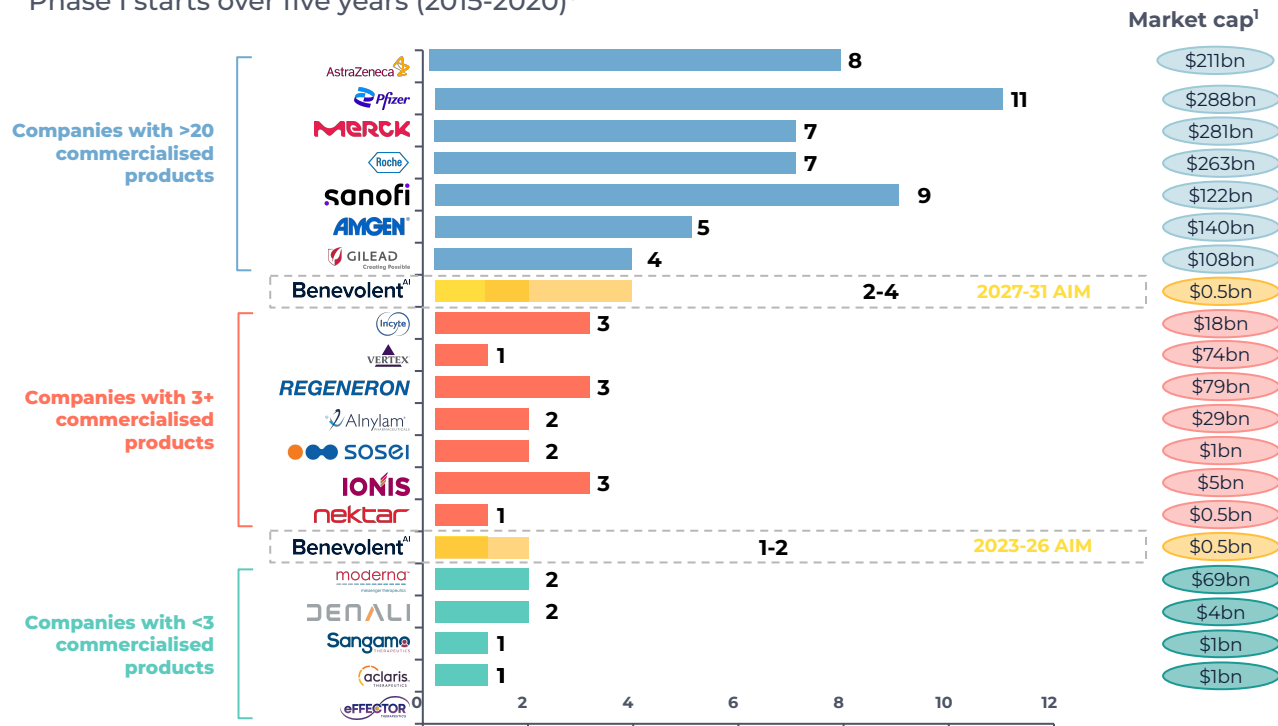


POTENTIAL TO INCREASE PROBABILITY OF SUCCESS

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

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

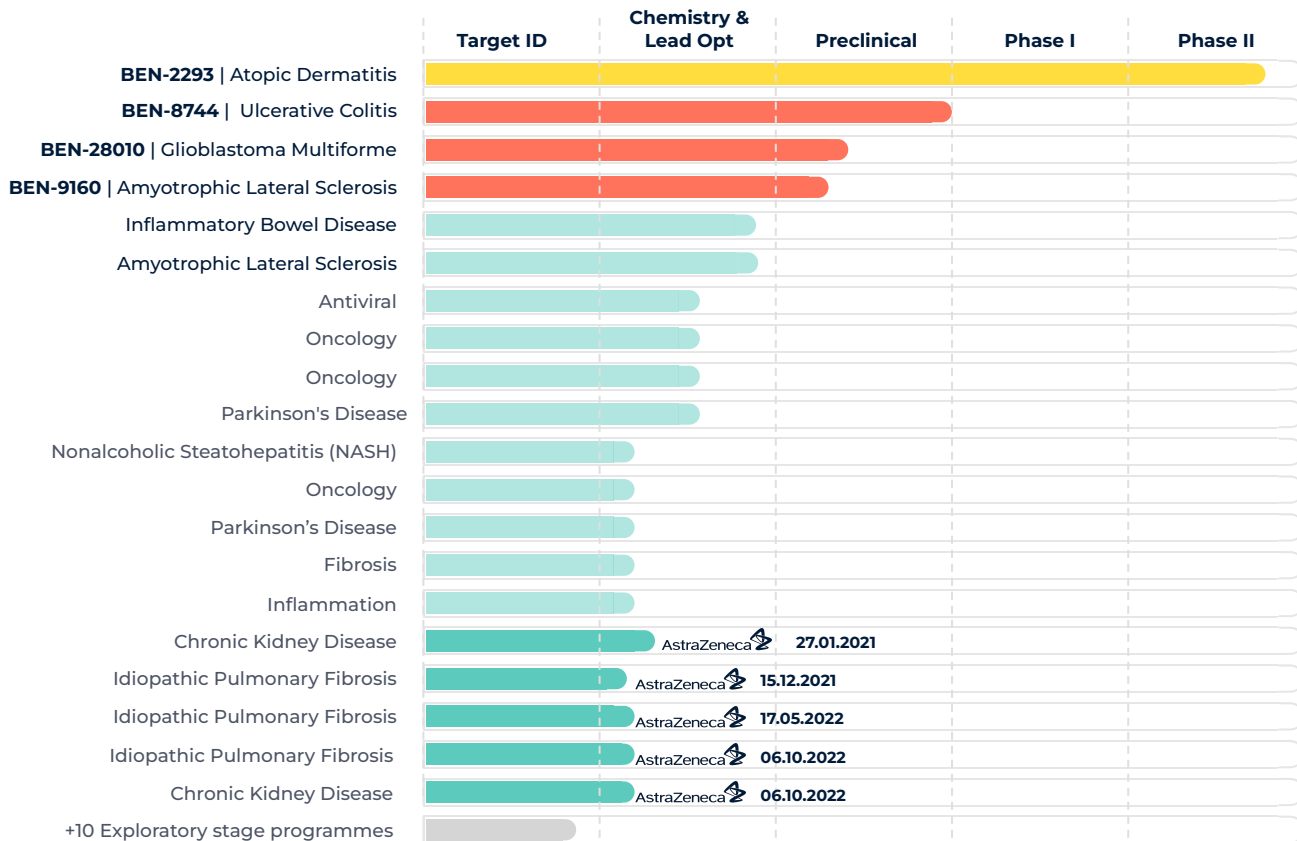
Note *IND filing rate is based on Phase I trial starts with the company as the lead sponsor. Average adjusted for companies which started clinical development during time period; ¹ Market cap as of 30/12/2022 (USD M)

Source: clinicaltrials.gov ; Company websites: L.E.K. research & analysis

Our flexible business model unlocks multiple routes to value creation



Robust pipeline entirely generated by the Benevolent Platform™



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)

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

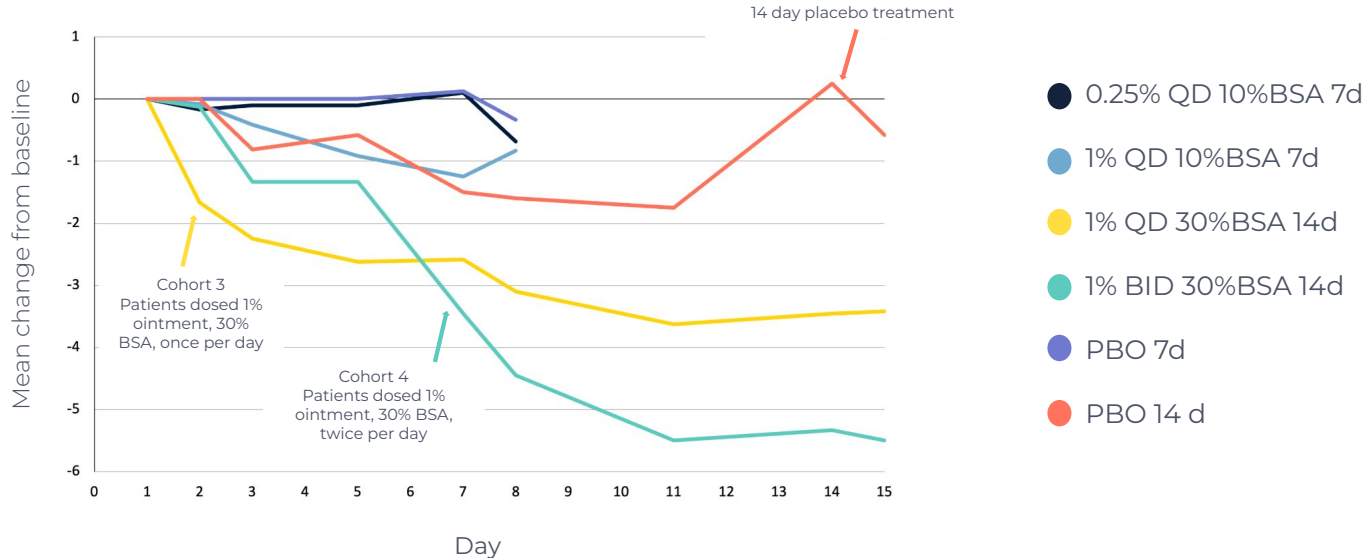
- **BEN-2293** is a **PanTrk inhibitor** targeting TrkA,B and C receptors. The Trk receptors were identified as part of an effort to find **mediators of both itch and inflammation in AD**. Using our Molecular Design expertise we were able to design a PanTrk inhibitor, equipotent against the 3 receptors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

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



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**

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

Target validation in colon tissue from ulcerative colitis patients

Inflamed colonic mucosa biopsies from UC patients

- Disease phenotype retained with high basal cytokine release
- Readouts: IL6 and IL8 - key mediators of UC pathology

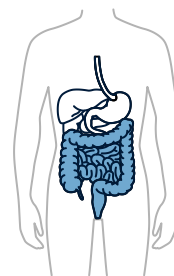
Tissue samples treated with:

- Target-selective tool compound (BEN-3218)
- Positive controls – prednisolone and tofacitinib

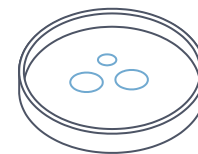
Selective target inhibition showed comparable reduction of IL-6 and IL-8 to the positive controls

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

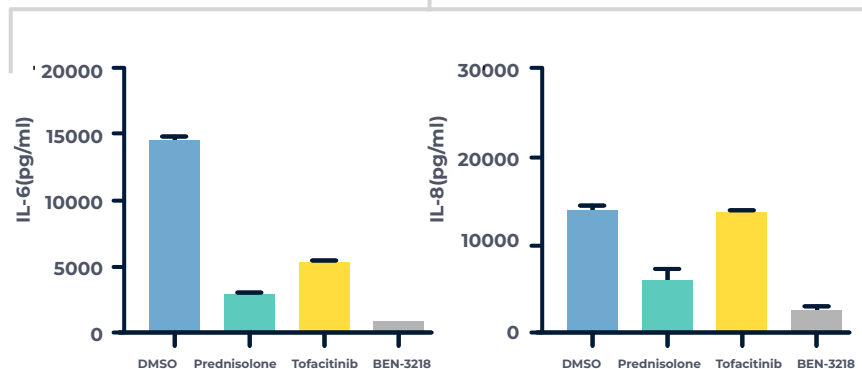
Endoscopic Biopsy from UC patients



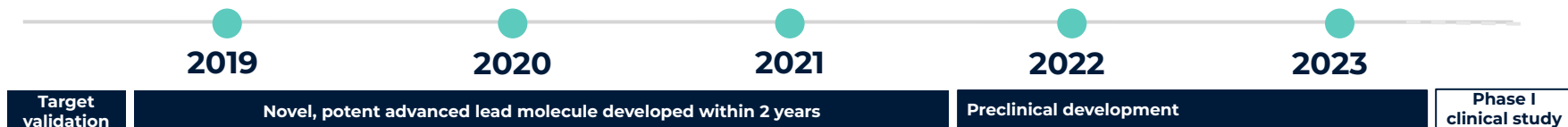
Colonic mucosa organ culture and compound treatment



Inflammatory cytokine measurement



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

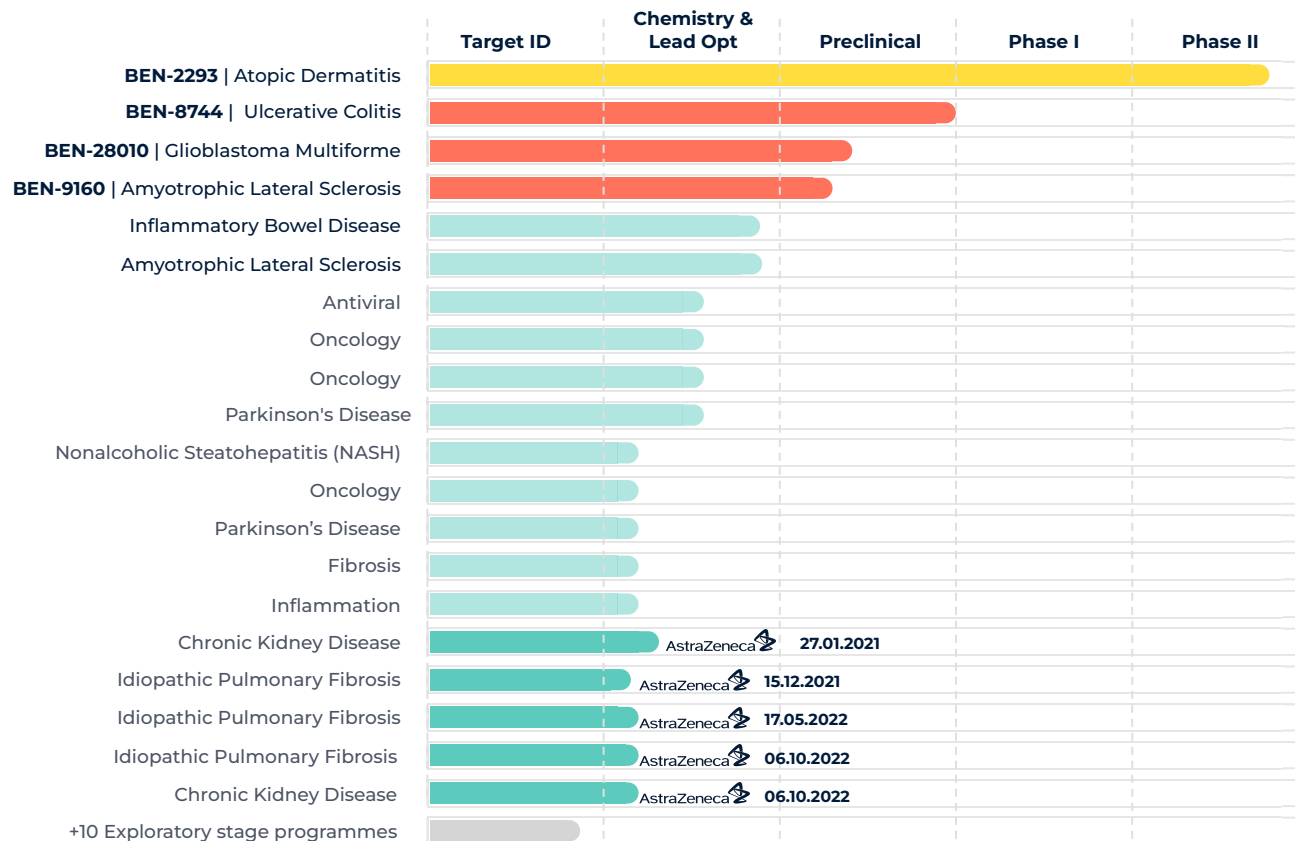
- ✓ **Molecular Design tools** enabled rapid and efficient lead optimisation
- ✓ **Candidate nominated in Sep '21**
Novel, potent, selective, peripherally restricted PDE10. Inhibitor, with low dose prediction
- ✓ Delivered drug candidate within **2 years** from programme initiation

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

Robust pipeline entirely generated by the Benevolent Platform™



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™](#)



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

DNDi

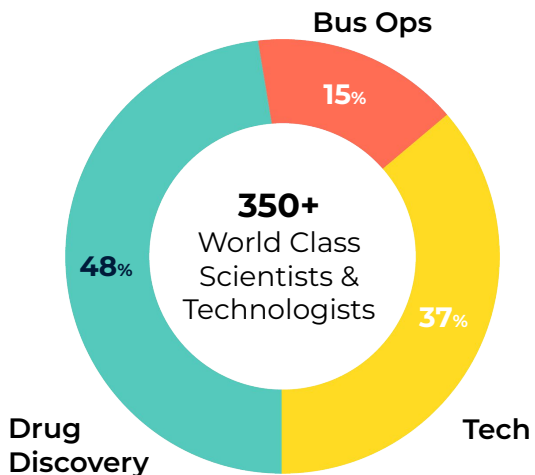
Drugs for Neglected Diseases *initiative*

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

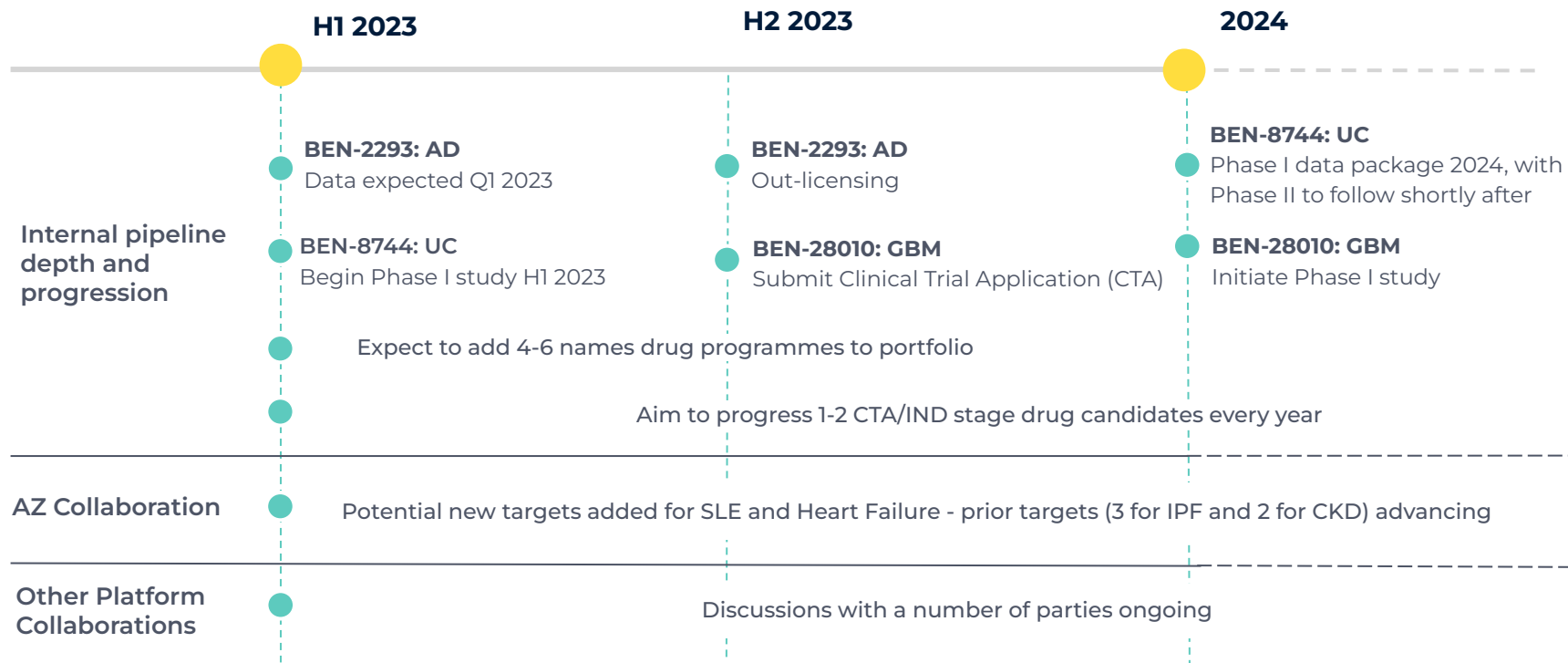


Nigel Shadbolt
Non-Executive Director



John Orloff
Non-Executive Director

Poised for growth: multiple value inflection points



Because it matters



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