PIPE Investor Presentation:
Supplementary Materials
December 2021
Forward-looking statements.

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- changes in market conditions;
- changes in the rate of exchange between foreign currencies and the U.S. dollar or any other foreign currency; and
- the Company's ability to implement its business plan.

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Any investment in Odyssey or the Company involves numerous risks and uncertainties related to the Company's business and the Proposed Transactions that may result for investors in a partial or total loss of their investment. The following is a non-exclusive selection of key risks that, alone or in combination with other events or circumstances, could have a material adverse effect on the Company's business, financial condition, results of operations and prospects as well as the Proposed Transactions. Investors should read, understand and carefully consider the risks and uncertainties described below. This summary is not comprehensive and the below key risks are subject to change. An additional discussion of the risks and uncertainties of the Company and the Proposed Transaction will be included in under the heading "Risk Factors" contained in the circular and prospectus in connection with the proposed business combination.

**Risk Factors**

1. **We have a history of significant operating losses, and we expect to incur losses over the next several years.**
2. **Our operating history and business model may make it difficult for you to evaluate the success of our business to date and to assess our future viability, which may depend on us obtaining additional capital, which might not be available on economically acceptable terms, or at all.**
3. **Our interim and annual results may fluctuate significantly, which could adversely impact the value of our shares.**
4. **We have no products approved for commercial sale, our revenues to date have been derived from a single source and it may take several years before we generate revenue from product sales, if at all.**
5. **If we and our present and future collaborators are unable to successfully develop and commercialise drug products, our revenues may be insufficient for us to achieve or maintain profitability.**
6. **All of our drug candidates are in early-stage preclinical development or in clinical development. If we are unable to advance our drug candidates through clinical development, to obtain regulatory approval and ultimately to market our drug candidates, or if we experience significant delays in our clinical development, results of operations and prospects will be materially harmed.**
7. **We are substantially dependent on our technology platform to identify promising drug targets to accelerate drug discovery and development. Our platform technology may fail to discover and design molecules with therapeutic potential or may not result in the discovery of commercially viable products for us or our collaborators.**
8. **If we cannot maintain existing partnerships, including data partnerships, and/or enter into new partnerships or similar business arrangements, our business could be adversely affected.**
9. **We face substantial competition, which may result in others discovering, developing or commercialising products more successfully than we do, requiring us to rapidly adapt our approach to significant technological change and respond to the introduction of new products and technologies to remain competitive.**
10. **We contract with third parties, including, but not limited to, a number of contract research organisations ("CROs"), site providers, laboratory testing service providers, and universities for assay and experimental work for all of our drug programmes, including where applicable the manufacture of our drug candidates for preclinical development and clinical testing, and expect to continue to do so for commercialisation. This reliance on third parties increases the risk of non-performance or delay to some or all of our drug programmes, or that we will not have sufficient quantities of our drug candidates or products or such quantities at an acceptable cost, which could delay, prevent or impair our development or commercialisation efforts.**
11. **Because we have multiple programmes and drug candidates in our development pipeline, we may expend our limited resources to pursue a particular drug candidate and fail to capitalise on development opportunities or drug candidates that may be more profitable or for which there is a greater likelihood of success.**
12. **Clinical development involves a lengthy and expensive process with uncertain outcomes. If our preclinical studies and clinical trials are not sufficient to support regulatory approval of any of our drug candidates, we may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development of such drug candidate.**
13. **If we are unable to obtain, maintain, enforce and protect patent or other intellectual property right protection for our technology and drug candidates or if the scope of such protection obtained is not sufficiently broad, our competitors could develop and commercialise technology and products similar or identical to ours, and our ability to successfully develop and commercialise our technology and drug candidates, as well as the value of our brand and our business, may be adversely affected.**
14. **Our internal information technology systems, or those of our third-party vendors (including providers of cloud-based infrastructure), contractors or consultants, may fail or suffer security breaches, loss or leakage of data and other disruptions, which could result in a material disruption of our services, compromise sensitive information related to our business, or prevent us from accessing critical information, potentially exposing us to liability or otherwise adversely affecting our business.**
15. **If we fail to comply with our obligations under any of our existing intellectual property licence agreements and data licensing agreements or under any future such agreements, or otherwise experience disruptions to our business relationships with our current or any future licensors, we could lose intellectual property rights (including access to data) that are important to our business.**
16. **We make use of the UK’s small and medium sized enterprises research and development tax relief regime, through which we have obtained cash tax credits from Her Majesty's Revenue & Customs ("HMRC"). HMRC could seek to challenge the historical cash tax credits paid, or a change of law or our circumstances could restrict our ability to claim additional such cash tax credits.**
17. **Current and future legislative and regulatory requirements may have a material adverse effect on our business and results of operations.**
18. **Regulatory authorities may implement additional regulations or restrictions on the development and commercialisation of our product candidates. Such changes can be difficult to predict, may require significant systems changes, divert the attention of our personnel, subject us to additional liabilities and may adversely affect our business.**
19. **Compliance with stringent and evolving global privacy and data security requirements could result in additional costs and liabilities to us or inhibit our ability to collect and process data globally, and the failure to comply with such requirements could subject us to significant fines and penalties, which may have a material adverse effect on our business, financial condition or results of operations.**
20. **The effects of health epidemics, including the ongoing COVID-19 pandemic, in regions where we, or the third parties on which we rely, have business operations could adversely affect our business, including our preclinical studies and clinical trials, as well as the business or operations of our CDOs or other third parties with whom we conduct business.**
21. **Our current and future clinical trials or those of our current or future collaborators may reveal significant adverse events not seen in our preclinical or nonclinical studies and may result in a safety profile that could inhibit regulatory approval or market acceptance of any of our future drug candidates.**
22. **Interim, "topline" and preliminary data from our clinical trials that we announce or publish from time to time may change as more patient data becomes available and are subject to audit or verification procedures that could result in material variations in our final data.**
23. **If we experience delays or difficulties in the enrolment of patients and/or provision of medical data in clinical trials, our receipt of necessary regulatory approvals could be delayed or prevented.**
Risks Related to the Proposed Transactions

1. Odyssey and the Company will be subject to business uncertainties and contractual restrictions while the proposed business combination is pending.
2. Odyssey and the Company will incur significant transaction and transition costs in connection with the proposed business combination.
3. Odyssey's sponsor and certain of its directors and officers have interests in the proposed business combination that are different from or in addition to other shareholders in recommending that shareholders vote in favor of approval of the proposed business combination.
4. Odyssey's sponsor holds a significant number of shares of Odyssey's securities, and their entire investment will be lost if the proposed business combination is not completed.
5. Odyssey's sponsor and its directors or officers or their affiliates may elect to purchase shares from public shareholders, which may influence a vote on the proposed business combination and reduce Odyssey's public float.
6. Odyssey does not have a specified maximum redemption threshold. The absence of such a redemption threshold may make it possible for Odyssey and the Company to complete the proposed business combination with which a substantial majority of Odyssey's shareholders do not agree.
7. Warrants will become exercisable for Odyssey's ordinary shares, which would increase the number of shares eligible for future resale in the public market and result in dilution to Odyssey's shareholders.
8. The ability of Odyssey's ordinary shareholders to exercise redemption rights with respect to a large number of shares could deplete Odyssey's trust account prior to the proposed business combination and thereby diminish the amount of working capital of the combined entity.
9. Goldman Sachs International and J.P. Morgan AG and its or their affiliates (the "Placement Agents") are engaged in a wide range of financial services and businesses (including investment management, financing, securities trading, corporate and investment banking and research) and there may be situations where the Placement Agents and/or its or their clients either now have or may in the future have interests, or take actions, that may conflict with Odyssey's or the Company's interests. For example, the Placement Agents have in the past and may, in the ordinary course of business, engage in trading in financial products or undertake other investments for their own account or on behalf of other clients, including, but not limited to, trading in or holding long, short or derivative positions in securities, loans or other financial products of Odyssey, or other entities connected with the Proposed Transactions.
10. Goldman Sachs International is both acting as a Placement Agent in this proposed private placement of securities and as financial advisor to the Company in connection with the proposed business combination, and a potential conflicts of interest, or a perception thereof, may arise as a result of such relationships.
11. Odyssey has not obtained a third-party valuation or fairness opinion in determining whether or not to proceed with the proposed business combination.
12. As Odyssey may migrate its tax residence to the UK prior to closing the proposed business combination, Odyssey may be subject to both the Luxembourg and UK corporate and tax regimes over the coming accounting periods, which could create a conflict in approach to cross-border and domestic compliance. Odyssey may be adversely affected by amendments to the corporate laws, tax laws or accounting policies of either or both of these jurisdictions, which may also have retrospective effect and be implemented unexpectedly. Future tax audits and other investigations conducted by the competent tax authorities in Luxembourg or the UK in respect of Odyssey's residence could result in the assessment of additional taxes, including corporate income taxes and withholding taxes. Odyssey's entitlement to treaty benefits under the 1967 Luxembourg-UK Double Taxation Convention (as modified by the Multilateral Instrument) (the "Treaty") may be withdrawn or the Treaty may be amended. The materialization of any of these risks could have a material adverse effect on our business, net assets, financial condition, cash flows or results of operations.
The Benevolent Platform™ Overview
Benevolent’s Product & Tech Team

- **End-to-end AI enabled drug discovery** capabilities - from Knowledge and Data integration through to application in Precision Medicine, TargetID and Chemistry
- Team of approx **130 technologists** across London and NYC
- **Expertise** in AI & Machine Learning, Data Science, Bioinformatics, Genetics, Cheminformatics, Software & Hardware engineering, Product Management, Project Management, Design/UX
- Experience drawn from **Big Tech, Biotech, academic research and healthtech startups**
- Team fully integrated with:
  - Biologists
  - Chemists
  - Informatics and BD
The Benevolent Platform™ is our scientifically-validated computational R&D platform. At its core sits a proprietary knowledge graph, which captures the interconnectivity of scientific literature and relevant, available biomedical data.

Our suite of exploratory and predictive AI tools allow scientists to identify novel insights, interrogate data within disease networks, ask biological questions, refine hypotheses and interpret results.

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1 [https://www.labiotech.eu/trends-news/exscientia-drug-discovery-ai/]
The Benevolent Platform™
Knowledge Foundations
Proprietary Knowledge Graph, purpose-built for drug discovery

The data engine that powers the Benevolent Platform™

**COMPREHENSIVE DATA**
- 400m NLP derived relationships
- 30m structured relationships

**DIVERSITY OF DATA**
- 85+ data sources used
- 1bn relationship edges

**GROWTH OF DATA**
- 22m additional mechanism connections
- 14x growth over 12 months

**Proprietary Knowledge Graph, purpose-built for drug discovery**

The data engine that powers the Benevolent Platform™

- **Uniquely combines** public, proprietary & inferred knowledge
  - ✔️ 60%+ of the most important information used by our models is AI-derived, proprietary knowledge
  - ✔️ Therapeutic area and drug modality agnostic
  - ✔️ Can be deployed with partners in secure cloud environment

**Literature**
- Scientific Literature
- Patent Literature
- Regulatory Documents

**Pathology**
- Diseases
- Symptoms

**Biological Systems**
- Cellular Component
- Molecular Function
- Biological Process
- Mechanism
- Pathways

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

**OMICS**
- Genes
- Proteins
- Isoforms
- Transcripts & Variants

**Molecules**
- Organic Compounds
- Preclinical Candidates
- Approved Drugs
- Antibodies
- Other Biologics
- Pharmacology
- Pharmacokinetics

Benevolent Knowledge Graph

400m NLP derived relationships
30m structured relationships
85+ data sources used
1bn relationship edges
22m additional mechanism connections
14x growth over 12 months
Domain-specific data processing pipelines support integration of a broad range of data modalities for drug discovery.
Data Fabric

The Data Fabric engineering framework orchestrates the ingestion of data from multiple processing pipelines, providing access to versioned and tracked data releases.

Input Data Layer
- Dataset downloaders and importers
- DBs
- APIs
- Files

Managed Data Layer
- UUID Builder (versioned)
- Entity Builder (versioned)
- Synonym Builder (versioned)
- Relationship Builder (versioned)

Extract-Transform-Load

Data View Layer
- UUID Avro (versioned)
- Entity Avro (versioned)
- Syn Avro (versioned)
- Rel Avro (versioned)

Use Case
- Excavator
- OP

DBs
- Files
- APIs
AI used to extract meaningful information from biomedical literature at scale

Automated Data Ingestion
Source documents (e.g. Scientific Literature, Patents), extracted and normalised for into format optimised for BenevolentAI Natural Language Processing pipeline.

Named Entity Recognition
Entities mentioned in unstructured text are identified, normalised and grounded to BenevolentAI entities.

Relationship Extraction
NLP models extract meaningful relationships between identified entities using contextual information.

<table>
<thead>
<tr>
<th>NAME</th>
<th>RELATIONSHIP</th>
<th>INFERRED FROM (CHEMBL)</th>
<th>DISEASE CLASSIFICATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amyotrophic Lateral Sclerosis</td>
<td>SOD1 — is associated with,</td>
<td></td>
<td>Motor Neuron Disease</td>
</tr>
<tr>
<td></td>
<td>Syntactically-linked pairs (35k</td>
<td></td>
<td>Primary lateral sclerosis (PLS) is a rare neuromuscular disease characterized by</td>
</tr>
<tr>
<td></td>
<td>relations in 4.6k papers)</td>
<td></td>
<td>progressive muscle weakness in the voluntary muscles. PLS belongs to a group of</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>disorders known as motor neuron dise...</td>
</tr>
</tbody>
</table>

ALS example extract above taken from a readout from the Benevolent Platform™
The Benevolent Platform™
Target Identification
Data Preparation: Optimising the set-up

1. **Data Preparation**
   - Focus and curate a biological question

2. **Predictions Package**
   - Model fleet predictions
   - Prediction evaluation

3. **Hypothesis Package**
   - Equip experts with data
   - Triage predictions

4. **Validated Hypothesis Package**
   - Perform Assays
   - Analysis & retro

### Example Table

<table>
<thead>
<tr>
<th>Target</th>
<th>Safety</th>
<th>Drugs?</th>
<th>Metadata</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tgt1</td>
<td>Safe</td>
<td>Partial</td>
<td>OPC, GCNN</td>
<td>0.71</td>
</tr>
<tr>
<td>Tgt2</td>
<td>Unsafe</td>
<td>No</td>
<td>SQT</td>
<td>0.65</td>
</tr>
<tr>
<td>Tgt3</td>
<td>Safe</td>
<td>Yes</td>
<td>OPC, CROM</td>
<td>0.51</td>
</tr>
<tr>
<td>Tgt4</td>
<td>PhaseII</td>
<td>Offtgts</td>
<td>OPC</td>
<td>0.49</td>
</tr>
</tbody>
</table>
AI augmented workflows uncover insights from data

- We turn data into Knowledge by applying our **AI augmented** analysis workflows
- Data availability, genetic architecture, and mechanistic understanding varies between disease
- According to these factors we choose the **most appropriate workflows** to apply to the disease area
Biological mechanism selection expands nuance and data coverage, even for rare diseases

**Disease / Endotype**

**Result**

**Mechanism / Pathway**

**Tissue / Cell Type**

**Benevolent Platform**

**Example analysis from Benevolent Platform™:**

**Pulmonary Arterial Hypertension**
Associated with **32k** scientific articles and **33k** unique relationships from databases, ontologies, genetic data, etc.

**Mechanism Expansion**
- **Smooth muscle cell proliferation:** 14k publications 6.9k relationships
- **Estrogen metabolism:** 3.8k publications 2.4k relationships
- **Vasoconstriction:** 107k publications 26k relationships

**Asking the biological question**

**Biological process curation expands data coverage and reveals novel associations. Relationships from similar biology can be leveraged in predictive models.**

**Algorithms recommend important aspects of biology in the context of a disease. Metrics are computed to evaluate mechanism relevance, novelty, and specificity.**

**Scientists select concepts to form the biological question they wish to ask at the target inference stage.**

**Biologists and data scientists collaborate to guide data buildout predictions**
Target prediction

1. Disease Data Package
   - Focus and curate a biological question

2. Target Prediction
   - Graph Completion
   - Human Queries
   - Reinforcement Learning
   - 'omics
   - Model fleet predictions
   - Prediction evaluation

3. Target Triage
   - Equip experts with data
   - Triage predictions
   - Target Safety
   - Drugs?
   - Metadata
   - Score
   - Tgt1 Safe 0.71
   - Tgt2 Unsafe 0.65
   - Tgt3 Safe 0.51
   - Tgt4 PhaseII 0.49

4. Target Validation
   - Perform Assays
   - Analysis & retro
Many strands of AI are used to generate target predictions

Knowledge Graph

- Path-based
- Tensor Factorization
- Human Queries
- Genetic Basis

Interpretability

Accuracy

Augmentation

Hypotheses

Learned Weighted Rank Aggregation

Data-modality specific

Multi-prediction Aggregation

Specialized models are designed to best produce complementary predictions from the Benevolent Knowledge Graph.

Smart aggregation combines predictions by examining which models have been successful in the past, learning what combination of features - and which kinds of evidence - identify a successful target.

AI-derived assistance provides support for predictions, for example, from Graph Convolutional Neural Networks\(^1\).

Results in a list of potential therapeutic targets for expert triage

Diverse training data yields high-quality AI inferences

**Literature and Knowledge Graph Training Data**

- Gene inhibitor attenuates Disease
- Gene regulates Biological Process
- Targeted inhibition of Gene limits Disease

Algorithms **identify sentence forms that suggest strong links** by expanding on small curated ground-truth datasets.

Internal experts define a subset of **key relationships** that model biomedical knowledge from the scientific literature.

Our large scientific text corpus results in **very high recall** across diseases and mechanisms.

**High-Quality Assay Data**

- CD-8 T Cell Activation
- Endothelial LDL regulation
- B Cell CD40 Positive Regulation

Internal **experts curate** public and private high-quality transcriptomics datasets.

Datasets are grounded to diseases, mechanisms, and proteins in the knowledge graph, allowing **prediction and evaluation** from the knowledge graph representation.

**Previous Disease Programs**

Prior **disease programs** provide results for **training** subsequent models.

Three kinds of information are routinely captured and available for training:

- Hit / no-hit
- Ranked assay results
- Triage annotations and reasoning (safety, efficacy, novelty, etc.)

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1 By volume of high-quality target associations
Target Triage: Prioritising insights and hypotheses

1. Disease Data Package
   - Focus and curate a biological question

2. Predictions Package
   - Model fleet predictions
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3. Hypothesis Package
   - Equip experts with data
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<td>No</td>
<td>SQT</td>
<td>0.65</td>
</tr>
<tr>
<td>Tgt3</td>
<td>Safe</td>
<td>Yes</td>
<td>OPC, CROM</td>
<td>0.51</td>
</tr>
<tr>
<td>Tgt4</td>
<td>PhaseII</td>
<td>Offgtts</td>
<td>OPC</td>
<td>0.49</td>
</tr>
</tbody>
</table>

4. Validated Hypothesis Package
   - Perform Assays
   - Analysis & retro
The Benevolent Platform™ provides a systematic process for target triage sharing insights and context for each prediction.

Target hypotheses undergo **expert review** with criteria that are tailored to the programme.

**Recommended classifications** are made to guide triage decisions using the Knowledge Graph and information presented in the **triage tool**.

**Decisions are captured** in a structured and unstructured manner to both ensure an audit trail and allow the system to learn over time.

Targets that pass triage are **progressed into validation**.

In a recent deployment\(^1\), 39% of targets were progressed into experimental testing.

Of those not progressed; 22% were already known to our program experts, 24% were deemed to have safety concerns and 15% did not have sufficient supporting evidence.

---

\(^1\) Company internal drug programme statistics
Target Validation: Confirming the hypotheses

1. Disease Data Package
   - Focus and curate a biological question

2. Predictions Package
   - Model fleet predictions
   - Prediction evaluation

3. Hypothesis Package
   - Equip experts with data
   - Triage predictions

4. Target Validation
   - Perform Assays
   - Analysis & retro

<table>
<thead>
<tr>
<th>Target</th>
<th>Safety</th>
<th>Drugs?</th>
<th>Metadata</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tgt1</td>
<td>Safe</td>
<td>Partial</td>
<td>OPC, GCNN</td>
<td>0.71</td>
</tr>
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<td>Tgt2</td>
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<td>Offgtts</td>
<td>OPC</td>
<td>0.49</td>
</tr>
</tbody>
</table>
Target Validation and Progressability Assessment (TPA)

Opportunity to differentiate
- Can a new therapeutic against this target compete relative to the current and future standard of care?

Freedom to Operate
- Exploitable chemistry/biologics space from an intellectual property perspective

Selectivity
- Are there selectivity challenges with off-targets that are expected to cause tolerability issues?

Druggability
- To what extent is the target amenable to small molecules, siRNA or mAb therapeutics?

Assayability
- Can suitable assays be accessed or developed to support medicinal chemistry?

Safety Assessment
- Are there anticipated safety issues that could be problematic for onward development?
The Benevolent Platform™
Precision Medicine
Molecularly defined clinical sub-phenotypes

At BenevolentAI, we detect subgroups of patients by analysing EHR\(^1\) and other clinical data. By using our genetic tooling, we infer genetic signatures for both entire disease cohorts and more refined subsets of the patient population.

Including:
- UK Biobank
- Bespoke cohorts
- Partner Cohorts

GWAS Pipeline
Spark-enabled engineering framework

Variant-to-Gene Annotation
(Coloc, VEP, MR, scoping AI/ML methods currently)

QTL datasets\(^2\)

Chromatin Features

Target Prediction

Target Triage

Biomarker ID

\(^1\) pseudonymised or anonymised Electronic Health Records data. \(^2\) QTL = quantitative trait loci genetics data. \(^3\) Whole Exome/Genome sequencing
Ulcerative Colitis Example: molecular-signature detection linked to outcomes

Generative ML models

Transcriptomes organised into latent structure

PATIENT SAMPLES CLUSTERED

Inflammatory marker response from suite of models

Data-derived mechanism entities are integrated into the Knowledge Graph and connected to enriched biological pathways and relevant biomedical entities (e.g. diseases, tissues, targets)

ML models recapture specific subgroups with key inflammatory markers (IL1 and TNFα signalling) and immune cells (M1 macrophages and neutrophils) and uncover mechanistic areas to explore further
The Benevolent Platform™
Chemistry
We combine deep expertise in Drug Discovery with innovative techniques in structure-based design, virtual screening and machine learning

✔ **Highly experienced Drug Discovery team** with a proven track record of taking nascent programme ideas and delivering drugs to the clinic.

✔ **Chemoinformatic and AI tools impacting all stages of a drug programme** from target selection through to candidate selection, by:

✔ **Identifying differentiated opportunities** through novel binding sites and prioritising previously undrugged targets for exploitation.

✔ **Maximising the use of available data** to derive new knowledge, at scale, for objective molecular design.

✔ **Empowering chemists to design better drugs in fewer cycles** – Candidate drugs delivered in as little as 2 years\(^1\) from programme inception, compared to a 3-5 year industry standard\(^2\).

\(^1\) Based on BEN-8744 timelines - see Portfolio Overview deck November 2021 for more information\(^7\)
Molecular Design - Expertise in structure-based design, virtual screening and machine learning

We combine deep expertise in drug discovery with innovative techniques in structure-based design, virtual screening and machine learning.

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✔ Empowering chemists to design better drugs in fewer cycles – candidate drugs delivered in as little as 2 years from programme inception compared to 3-5 year industry standard

Druggability scoring to prioritise targets

Binding site comparison to identify Hit matter and evaluate selectivity

Proprietary pharmacophore building methodology

ML models of activity and ADMET endpoints

<table>
<thead>
<tr>
<th>Target ID</th>
<th>Hit Identification</th>
<th>Hit Expansion</th>
<th>Lead Optimisation</th>
<th>Candidate Seeking</th>
</tr>
</thead>
<tbody>
<tr>
<td>Binding site detection to identify differentiating chemistry opportunities</td>
<td>Customisable virtual screening pipeline now on &gt;10 billion compound scale</td>
<td>Protein-Ligand interaction mining to surface protein-centric bioisosteres</td>
<td>Programme visualisation</td>
<td></td>
</tr>
</tbody>
</table>
Project ‘Y’¹ - a Benevolent tech-augmented programme

Novel target identified in Target ID
- No prior literature association with disease of interest

One main chemotype reported in the literature
- Covered extensively by >20 patents
- Multiple closely-related cores also claimed - challenge to identify novel chemical space
- Close family members with known safety risks so selectivity important

Hit ID & Hit Expansion completed in 7 months
- Employed both Virtual Screening and focused Fragment Screening approaches

Project now in late Lead Optimisation
- 13 months, 380 compounds
- Low nM potency
- 200 fold selectivity over all family members
- Low metabolic clearance in microsomes and hepatocytes (Eh <0.4)
- Good aqueous solubility (>200uM)
- Clean in Ames, hERG and Cyp inhibition assays

¹Internal Company programme - target confidential, no prior literature detected by Benevolent Platform™. Lead Optimisation stats from internal Company experimental data.
The Benevolent Platform™
Apps, Infrastructure, Research
Apps & Infrastructure

Make the Benevolent Platform™ cheaper, easier to develop, easier to use, and more reliable for running deployments and collaborations.

Apps

✔ Engineering & UX
✔ Primary focus on development of the platform interfaces used by our drug discoverers
✔ Works across the Delivery Areas

Infrastructure

✔ Shared Engineering
✔ Site Reliability Engineering
✔ Security
✔ IT

Cross-organization delivery

✔ Accessible, reusable, and scalable infrastructure for training models and serving predictions
✔ Shared and accessible development and deployment platform for all Delivery Areas
✔ Common protocols that align product development with drug discovery process

1 Based on internal Company statistics covering time taken to complete insilico steps (data build out, model running, triaging)
Some of our recent publications

<table>
<thead>
<tr>
<th>Knowledge</th>
<th>Target Identification</th>
<th>Precision Medicine</th>
<th>Chemistry</th>
</tr>
</thead>
</table>
| ● Wiatrak et al. (2021)
  Zero-Shot Metric Learning Entity Linking submitted to Transactions of ACL. | ● Dunbar et al. (2021)
  Molecular representation learning with language models and domain-relevant auxiliary tasks, in NeurIPS 2020, Machine Learning for Molecules Workshop. |
| ● Shah and Fauqueur (2020)
  Preclinical validation of therapeutic targets predicted by tensor factorization on heterogeneous graphs in Nature Scientific Reports. | ● Sim et al. (2021) **Directed Graph Embeddings in Pseudo-Riemannian Manifolds** in ICML 2021. | Simonovsky and Meyers (2020)
  **DeeplyTough: Learning Structural Comparison of Protein Binding Sites**, in Journal of Chemical Information and Modeling. |
| Wiatrak and Iso-Sipila (2020)
  Applications of machine learning to diagnosis and treatment of neurodegenerative diseases, in Nature Reviews Neurology. | ● Schneider and Tomlinson (2020)
  **Artificial Intelligence in Drug Discovery**, in Royal Society of Chemistry |

Richardson et al. (2020) **Baricitinib as potential treatment for 2019-nCoV acute respiratory disease**, in The Lancet

BenevolentAI
Discovery Portfolio Overview
Portfolio program examples illustrate the Benevolent Platform™ in action

- Inflammatory Bowel Disease - IND-enabling program
- Amyotrophic Lateral Sclerosis - Candidate seeking program
- Glioblastoma multiforme - Lead optimisation program
- NASH - Hit expansion program
- NASH - Hit Identification program for currently undrugged target
- Atopic Dermatitis - Phase I/II clinical program
Growing number of platform-generated programmes moving into clinical phases

<table>
<thead>
<tr>
<th>Disease Area</th>
<th>Target ID</th>
<th>Hit to Lead</th>
<th>Lead Opt</th>
<th>Preclinical</th>
<th>Clinical</th>
<th>Commercial</th>
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<tbody>
<tr>
<td>Atopic Dermatitis (PanTrk inhibitor)</td>
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<td>Phased</td>
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<tr>
<td>Ulcerative Colitis (PDE10 inhibitor)</td>
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<tr>
<td>Amyotrophic Lateral Sclerosis</td>
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<tr>
<td>Inflammatory Bowel Disease</td>
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<tr>
<td>Glioblastoma Multiforme</td>
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<tr>
<td>CNS Diseases</td>
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<tr>
<td>Nonalcoholic Steatohepatitis (NASH)</td>
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<tr>
<td>Oncology</td>
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<tr>
<td>Antiviral</td>
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<tr>
<td>Chronic Kidney Disease</td>
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<td>Idiopathic Pulmonary Fibrosis</td>
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<tr>
<td>10+ Early Discovery Programmes</td>
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</tbody>
</table>

(Multiple indications & targets in therapy areas such as Oncology, Immunology, CNS, GI, Metabolic Disorders and Others)

Source: (1) GlobalData, Epidemiology forecasts 2021, Atopic Dermatitis (7MM), IBD (8MM), ALS (8MM), GBM (7MM), NASH (7MM), CKD (7MM), IPF (7MM); 7MM = 7 major markets (US, JP, EUS); 8MM = US, JP, EUS + Canada; (2) Evaluate Pharma, Current Worldwide Market Size (data pull 22nd Sept 2021) Atopic Dermatitis, IBD, ALS, GBM, NASH, CKD, IPF

- All Pipeline assets generated from Benevolent Platform™
- Broad therapy area coverage given disease agnostic approach
- Mix of Best in class, First in class and novel indications
- Potential for rapid scaling and expansion into new modalities

Existing pipeline alone addresses prevalent patient base* of >263m(1) and current market opportunity >$30bn(2)
Inflammatory Bowel Disease (IBD) 
Ulcerative Colitis (UC) and Crohn’s Disease (CD)
Both the Ulcerative Colitis and Crohn’s Disease markets are large, and expected to experience sizable growth

- Taken together, the 2019 UC and CD market sizes were valued at approx. $14B across the 7 major markets, expected to increase to approx $24B in total by 2029, growing at a ~6% CAGR

- Growth in the UC and CD markets is driven by:
  - Improved diagnosis and increasing prevalence
  - Approval of numerous pipeline drugs (both small molecules and biologics)
  - High treatment rates
  - High unmet need for safe & efficacious therapies

- Despite a competitive pipeline, there is opportunity to differentiate BEN-8744 as an oral small molecule with a novel MoA based on safety, efficacy and through pursuing a precision medicine approach

Source: (1) GlobalData, Ulcerative Colitis: Global Drug Forecast and Market Analysis to 2029; (2) GlobalData, Crohn’s Disease: Global Drug Forecast and Market Analysis to 2029. 7MM (7 Major Markets): EU5, US, Japan
# BEN-8744: IBD Asset Overview

Best-in-class, oral, peripherally restricted potent and selective Phosphodiesterase 10 (PDE10) inhibitor for the treatment of Moderate to Severe Ulcerative Colitis and Crohn’s Disease (IBD)

<table>
<thead>
<tr>
<th>Asset Overview</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mechanism of Action</strong></td>
</tr>
<tr>
<td>● Phosphodiesterase 10 (PDE10) inhibitor, immunomodulatory</td>
</tr>
<tr>
<td><strong>Formulation</strong></td>
</tr>
<tr>
<td>● Small molecule, oral, chronic treatment</td>
</tr>
<tr>
<td><strong>Competitive Advantage</strong></td>
</tr>
<tr>
<td>● New immunomodulatory mechanism of action, providing additional option to patients refractory to current treatments</td>
</tr>
<tr>
<td>● Disease modifying treatment targeting the disease mechanisms associated with IBD</td>
</tr>
<tr>
<td>● Targeting induction and maintenance of clinical remission, allowing for reduction in long-term corticosteroid use</td>
</tr>
<tr>
<td>● Peripherally restricted, devoid of on-target central side effects</td>
</tr>
<tr>
<td>● Clean safety profile compared to other oral small molecule competitors (e.g. JAK inhibitors, tofacitinib/Xeljanz – black box warning for infection risk)</td>
</tr>
<tr>
<td>● Precision Medicine approach for patient stratification</td>
</tr>
<tr>
<td><strong>IP Position</strong></td>
</tr>
<tr>
<td>● Second Medical Use &amp; Composition of Matter patent applications filed</td>
</tr>
<tr>
<td><strong>Current Status</strong></td>
</tr>
<tr>
<td>● Commenced preclinical development, with Candidate selection completed August 2021</td>
</tr>
</tbody>
</table>
PDE10 inhibition: potential to normalise dysregulated mechanisms in IBD

- Reduced inflammatory cytokine release from intestinal epithelia via ↓NFκb\(^{(1)}\)
- Reduced tissue-resident macrophage activation

**Reduced intestinal inflammation**

**Improved TJ assembly via** PKG/PKA-mediated ↓pMLC\(^{(2)}\)

**Improved fluid/mucus homeostasis via** PKG phosphorylation of intestinal CFTR\(^{(3)}\)

**Improved barrier integrity**

Source: \(^{(1)}\) doi:10.1371/journal.pone.0079180; \(^{(2)}\) doi:10.1371/journal.pone.0016139; \(^{(3)}\) doi:10.3109/00365521.2015.1038849
BEN-8744 is a highly potent and selective PDE10 inhibitor

<table>
<thead>
<tr>
<th>Primary Pharmacology¹</th>
<th>Safety Pharmacology¹</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Human PDE10 IC50 (biochem &amp; cell-based assays)</strong></td>
<td><strong>hERG IC50</strong></td>
</tr>
<tr>
<td>&lt;1nM</td>
<td>13uM</td>
</tr>
<tr>
<td><strong>Mouse PDE10 IC50</strong></td>
<td><strong>CaV1.2 IC50</strong></td>
</tr>
<tr>
<td>&lt;1nM</td>
<td>&gt;30uM</td>
</tr>
<tr>
<td><strong>IC50 in IBD biopsy inflammatory cytokine release assay (UC &amp; Crohn's)</strong></td>
<td><strong>Nav1.5 Ic50</strong></td>
</tr>
<tr>
<td>&lt; 1nM</td>
<td>&gt;30uM</td>
</tr>
<tr>
<td><strong>Selectivity vs other PDE family members</strong></td>
<td><strong>Human iPSC-derived cardiomyocyte toxicity</strong></td>
</tr>
<tr>
<td>≥1000 fold</td>
<td>No flags</td>
</tr>
<tr>
<td></td>
<td><strong>Selectivity vs broad panel of safety targets (Cerep87)</strong></td>
</tr>
<tr>
<td></td>
<td>≥1000 fold</td>
</tr>
<tr>
<td></td>
<td><strong>Ames (5 strain, +/- S9)</strong></td>
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<tr>
<td></td>
<td>Negative</td>
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<td></td>
<td><strong>IVMN</strong></td>
</tr>
<tr>
<td></td>
<td>Negative</td>
</tr>
<tr>
<td></td>
<td><strong>Hepatic toxicity (hepatocyte cytotoxicity; DILI panel, 14 day 3D liver organoid assay)</strong></td>
</tr>
<tr>
<td></td>
<td>Negative</td>
</tr>
<tr>
<td></td>
<td><strong>7 day rat toxicology study</strong></td>
</tr>
<tr>
<td></td>
<td>No overt toxicity or clinical observations &gt;100x predicted hAUC</td>
</tr>
</tbody>
</table>

- Highly potent
- Good selectivity
- No safety flags

¹ Company internal drug programme data
BEN-8744: Potent activity demonstrated in both UC & CD patient ex-vivo colon biopsies²

- Demonstrated inhibition of proinflammatory cytokine release (IL-6/IL-8) from individual UC and CD patient biopsy samples, comparable to corticosteroids
  - Indicative of a robust anti-inflammatory response with BEN-8744
- BEN-8744 has now progressed into preclinical development and a Clinical Trial Application (CTA) is scheduled Q4 2022
- First-in-Human (SAD/MAD¹) clinical studies will commence early 2023
- Subsequently supporting a Ph2a clinical study in Ulcerative Colitis, together with a follow-on clinical study in Crohn’s Disease

¹SAD/MAD - Single Ascending Dose, Multiple Ascending Dose
²Company internal drug programme data
Amyotrophic Lateral Sclerosis (ALS)
Amyotrophic Lateral Sclerosis (ALS)

Affects 0.02% US population over age 40 years\(^{(1)}\), ~75 thousand patients in 8MM\(^{(2)}\), forecast $1.04bn market by 2029\(^{(3)}\)

- ALS is a rare and devastating fatal neurodegenerative disease in which the motor neurons degenerate or die, and stop sending messages to the muscles. Fewer than 50% of patients survive 30 months from symptom on-set\(^{5}\)

- Efficacy and Safety - Current treatments (riluzole and radicava) are largely ineffective and only extend patient survival by ~6 months. Patients are largely treated with oral riluzole, however radicava is an intense intravenous treatment placing significant burden on patient quality of life

- New, safe and effective disease-modifying therapies are urgently needed

BEN-9160: CNS-Penetrant c-Abl inhibitor for the Treatment of Sporadic and Familial ALS Subtypes, with potential to expand to Parkinson’s Disease

- Deployment of the Benevolent Platform\(^{TM}\) led to the discovery of c-Abl - a target with demonstrated capacity to modulate pathways critical to ALS pathology

- Our Molecular Design expertise resulted in a potent, brain-penetrant small molecule c-Abl inhibitor BEN-9160 with a pharmacokinetic profile enabling significant target engagement\(^{4}\)

- BEN-9160 is expected to provide an efficacious oral treatment for ALS, targeting key disease-relevant mechanisms
  - Disease modifying treatment for the benefit of both the Sporadic and Familial ALS patient populations
  - Delay of disease progression with extension of life significantly better than Standard of Care
  - Clean safety profile (no relevant drug-drug interactions, hepatotoxicity, CV liability, CNS effects on memory or cognition or myelosuppresion)

Source: (1) GlobalData: Amyotrophic Lateral Sclerosis: Epidemiology Forecast to 2029; (2) and (3) GlobalData,Amyotrophic Lateral Sclerosis (ALS): Opportunity Analysis and Forecasts to 2029; (4) Company internal drug programme data; (5) https://www.sciencedirect.com/science/article/pii/S0140673610611567
https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(10)61156-7/fulltext

ALS

<table>
<thead>
<tr>
<th>Familial</th>
<th>Sporadic</th>
</tr>
</thead>
<tbody>
<tr>
<td>10%</td>
<td>90%</td>
</tr>
</tbody>
</table>
ALS: Hypothesis Generation with a focus on key mechanisms and Precision Medicine based approaches

1. Targets associated with key mechanisms in neurodegeneration identified using knowledge graph based relational inference models using a “Fleet” of algorithmic models
   ○ **Key mechanisms**: Autophagy, mitochondrial health, proteosome function, and lysosomal function

   ![Graph Inference](image)

   **Target Triage**
   Hypotheses prioritised based on relevance to ALS, neurodegeneration mechanisms, druggability

2. Omics/Precision medicine based approach using Target ALS collaboration dataset
   ○ 612 RNA-Seq samples from 149 individuals identify subgroups of ALS patients (endotypes) with distinct molecular disease mechanisms/targets

<table>
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<tr>
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<td>PhaseII</td>
<td>Offtgts OPC</td>
<td>0.49</td>
<td></td>
</tr>
</tbody>
</table>
Multiple assays used for target validation in ALS, similar approaches being employed for Parkinson’s disease

1. Autophagy assay in Hela cells
- TR-FRET between LC3-Tb and LC3-D2 or p62-D2 and p62-Tb
- LC3 is found in the cytoplasm and is conjugated to the lipid phosphatidylethanolamine to form LC3II
- LC3II binds to the autophagic vacuoles’ membrane → marker of autophagic vacuoles
- SOSTM1 (p62)
  - selective autophagy receptor
  - sequesters ubiquitinated proteins into AIs by interacting with LC3
  - p62 is a substrate for autophagic degradation → its degradation can be used as a marker of autophagic clearance

2. Glutamate induced excitotoxicity in sporadic ALS patient iPSC MNs

3. SITraN ALS iAstrocyte mouse motor neuron co-culture assay

4. Tunicamycin induced motor neuron toxicity
Abl target hypothesis has been validated using complex cell-based systems

The SiTraN assay: a humanised cell model of ALS

- Working in collaboration with academic experts at SiTraN who have developed a patient cell derived assay system

- iAstrocytes (via induced progenitors) obtained from genetically-diverse ALS patients cause motor neuron toxicity in a co-culture assay

- Can test biological hypotheses by measuring the rescue of motor neuron survival

- Benevolent proprietary CNS penetrant Abl inhibitors are neuroprotective in this assay
Abl inhibitor is neuroprotective in *in vitro* Parkinson’s disease and ALS models

**MMP+ induced TH neuron toxicity and a-synuclein aggregation in mouse primary dopaminergic neuron cultures**

**Tunicamycin induced apoptosis of sporadic ALS patient iPSC derived motor neurons**

**Glutamate induced apoptosis of sporadic ALS patient iPSC derived motor neurons**

---

1 Data from Neurosys. 2 Data from iXcell (both CROs are engaged by the Company to provide services for this programme)
Current Status: Programme in candidate seeking with candidate selection due to complete Q4 2021

**Efficacy**
- Demonstrated with humanised ALS cellular models using motor neurons and motor neuron astrocyte co-cultures
- Multi-donor screens in these cell types currently ongoing, to provide evidence of effects in sporadic and defined genetic ALS subtypes (including TDP-43 mutants)
- In vivo efficacy models initiated

**Safety**
- In-vitro toxicity and safety assays showing better or equivalent safety to clinical comparators
- Panel of cellular toxicity screen including cardiomyocytes, hepatocytes, kidney and HUVEC cells complete
- In-vivo rat tox study (7 days) complete

**DMPK**
- Demonstrable target engagement in the mouse CNS
- PK/PD using target engagement biomarkers in mouse CNS
- Comprehensive human dose predictions
- Dose projections commensurate with BID dosing
- Cyp inhibition/induction/TDI

**IP/Chemistry**
- Composition of matter patent applications filed

---

- At the end of candidate seeking (Q4 2021), we will have completed our efficacy, safety/in-vivo toxicity and DMPK studies for BAI-5002
- Planning for preclinical and future clinical studies now ongoing

---

1 Internal Company drug programme data using SITraN assay. 2 Combined internal Company drug programme data and CRO specific safety assays
Glioblastoma Multiforme (GBM)
Glioblastoma Multiforme (GBM)

One of the most lethal and aggressive brain tumours
  ● Extremely poor prognosis and high unmet need

Prevalence
  ● Incidence of GBM ranges from 0.59 to 5 per 100,000 (1)
  ● Mean age at presentation 53y, 5 year survival rate - 5%

Standard of Care (SoC)
  ● Surgery, Radio- & Chemotherapy, Temozolomide (TMZ)
  ● Current therapy rarely curative

Glioblastoma Stem Cells - key component
  ● Self renewal
  ● Resistant to radio & Chemotherapy
  ● Highly infiltrative and heterogeneous
    ○ MES-Aggressive; Poor survival
    ○ PN- Favourable outcome
    ○ CL- Best response to therapy

Reasons why GBM has high unmet need
  ● Tumour intrinsic
    ○ Glioblastoma Stem Cells (GSC)
    ○ High level of Tumour heterogeneity
    ○ Tumour Micro environment (TME)
    ○ Rapid evolution of the tumour and its transition into aggressive phenotype

KOL most cited reason for therapy failure
  ● Lack of effective BBB penetrant molecules

Source (1) 1- Grech et al. 2020, DOI: 10.7759/cureus.8195
GBM: Hypothesis Generation and Validation

A therapeutic target which functions as a radiosensitiser identified for Glioblastoma (GBM) using knowledge-graph-based relational inference models.

Benevolent Knowledge Graph enriched and customised to identify targets modulating viability of Glioblastoma Stem Cells (GSCs) or radiosensitisers.

Predictions enriched with disease relevance by use of Patient datasets (combination of ‘Omics platforms).

**Target ID**
Entity selection and data build out around GBM stem cells (GSC) and radiosensitisers. Predictions for GBM using relation inference models on the Benevolent Knowledge Graph.

**Target Triage**
Hypotheses prioritised based on relevance to GSC modulation, suitable safety profile, “druggability”

**‘Omics**
Target expression GBM vs normal brain tissue (Patient dataset; Single Seq), mapped across diverse pathways & mechanisms for GSC.

**Target selection**
- Novel MoA for GBM
- Expression in GBM tumours
- Subtype preference
- Radiosensitiser

---

**Graph Inference**

<table>
<thead>
<tr>
<th>Target</th>
<th>Safety</th>
<th>Drugs?</th>
<th>Metadata</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tgt1</td>
<td>Safe</td>
<td>Partial</td>
<td>OPC, GCNN</td>
<td>0.71</td>
</tr>
<tr>
<td>Tgt2</td>
<td>Unsafe</td>
<td>No</td>
<td>SQT</td>
<td>0.65</td>
</tr>
<tr>
<td>Tgt3</td>
<td>Safe</td>
<td>Yes</td>
<td>OPC, CROM</td>
<td>0.51</td>
</tr>
<tr>
<td>Tgt4</td>
<td>PhaseII</td>
<td>Offtgts</td>
<td>OPC</td>
<td>0.49</td>
</tr>
</tbody>
</table>

---

**Experimental testing**

---
Target R identified as a therapeutic target for GBM

Target R was predicted by the Benevolent Platform™ as a potential therapeutic target to:

- Modulate viability of glioblastoma stem cells (GSC)
- Sensitise with radiotherapy (Radiosensitiser)

Data from the **“stem cell enriched” neurosphere assay** indicated that Target R had ‘on-target’, single agent activity across majority of GBM patient cells but was less sensitive to MES GPCs.

Data from the **3D clonogenic assay** indicated that Target R had both ‘on-target’, single agent activity and sensitised with ionising radiation.
### BAI-5028: Target Product Profile

<table>
<thead>
<tr>
<th>Product Properties</th>
<th>Profile</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mechanism of action</td>
<td>CNS penetrate, potent and selective inhibitor with Single Agent &amp; Radiosensitising activity</td>
</tr>
<tr>
<td>Modality</td>
<td>Small molecule</td>
</tr>
<tr>
<td>Primary indication</td>
<td>Glioblastoma Multiforme (GBM)</td>
</tr>
<tr>
<td>Patient population</td>
<td>Newly Diagnosed (MGMT methylated and MGMT unmethylated); Recurrent if RT approved</td>
</tr>
<tr>
<td>Treatment route/duration</td>
<td>Oral, concurrent with RT</td>
</tr>
<tr>
<td><strong>Target Efficacy</strong></td>
<td><strong>For recurrent GBM patients: improvement in PFS at 6 months to &gt;40% (based on RANO criteria) compared to 25% typical for SOC. For unmethylated GBM patients at first diagnosis: improvement in overall survival of &gt; 3 months</strong></td>
</tr>
<tr>
<td><strong>Differentiation from other Target R inhibitors in development</strong></td>
<td>None in development for GBM or other neurological indications CNS penetrant</td>
</tr>
<tr>
<td>Other factors for differentiation</td>
<td>Potential for use in combination with RT and Chemotherapy (CT) in other cancer patients: cancers where RT is established treatment (examples such as lung, breast, head and neck cancers).</td>
</tr>
</tbody>
</table>
Target R: Chemistry progressed to deliver a potent, selective and highly brain penetrant molecule

**Hit ID**

<table>
<thead>
<tr>
<th>BEN-9677</th>
<th>pIC50 (LLE)</th>
<th>Pfizer CNS MPO</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>6.1 (5.2)</td>
<td>5.4</td>
</tr>
</tbody>
</table>

Novel kinase hinge binder  
Retained key motif for selectivity

- From BAI virtual screen  
- Patent ID and data extraction  
- Controlled substance checker

**Hit-to-Lead**

<table>
<thead>
<tr>
<th>BEN-11156</th>
<th>pIC50 (LLE)</th>
<th>Kinases IC50 &lt;1 µM</th>
<th>Cerep &gt;50% @ 1 µM</th>
<th>hERG IC50 (µM)</th>
<th>Efflux ratio MDR1/BCRP</th>
<th>Kpuu (rat)</th>
<th>Oral bioavailability (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>7.9 (6.7)</td>
<td>6 / 372</td>
<td>1 / 87</td>
<td>&gt;30</td>
<td>1.7 / 3.7</td>
<td>0.44</td>
<td>51</td>
</tr>
</tbody>
</table>

- On-/off-target docking models  
- Reaction enumeration  
- Predictive model suite  
  - Activity, metabolism, efflux  
- Generative chemistry

**Lead Optimisation**

- Advanced profiling underway  
- Upcoming milestone: GBM xenograft TE study  
- Potent backup series with low efflux also in development

Our lead series represents a potent, selective and highly brain-penetrant ‘Target R’ kinase inhibitor
BAI-5028 is approaching Candidate seeking

Key programme points:

- Therapeutic target for GBM which functions as a radiosensitiser identified using Benevolent Knowledge Graph-based relational inference models
- An attractive tech-derived virtual screening hit led to a potent, selective, and highly brain-penetrant series of “Target R” kinase inhibitors
- “Target R” sensitive GBM patient cohort identified using our Precision Medicine workflows for patient stratification
- Program on track to deliver within company timelines
Non-Alcoholic Steatohepatitis (NASH)
Non-Alcoholic SteatoHepatitis (NASH)

Affects 11% US population\(^\text{(1)}\), 63 million patients in 7MM\(^\text{(2)}\), forecast $27.2bn market by 2029\(^\text{(3)}\)

- Non-alcoholic fatty liver disease (NAFLD) is a metabolic disorder characterised by accumulation of fatty deposits in the liver; **non-alcoholic steatohepatitis (NASH) occurs when NAFLD progresses**, and is associated with liver inflammation, fatty deposits, and fibrosis

- **High unmet need** - NAFLD and NASH pose a high economic burden, driven by costs to provide chronic care for patients (including liver transplants) in the absence of any disease modifying therapy; currently hard to detect meaning NASH is often diagnosed later in the disease course

<table>
<thead>
<tr>
<th>Fibrosis Staging</th>
<th>NASH Prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-1</td>
<td>30%</td>
</tr>
<tr>
<td>2</td>
<td>27%</td>
</tr>
<tr>
<td>3</td>
<td>25%</td>
</tr>
<tr>
<td>4 (Cirrhosis)</td>
<td>17%</td>
</tr>
</tbody>
</table>

**BAI-5030**: (Target A) Best-in-class, potent and selective drug for the treatment of NASH. (Target B) First-in-class programme

- Targets A and B were identified by our TargetID platform as **entirely novel targets for the treatment of NASH** - representing mechanistically distinct approaches
- We are currently applying our **Hit Identification** (Target B) and **Hit expansion** (Target A) capabilities to support the identification of potent and selective inhibitors
- **BAI-5030** is expected to provide efficacious, mechanistically differentiated, disease modifying treatments for NASH, with the potential to reduce fibrosis in both early and late stages of disease
- **BAI-5030 will target fibrosis** (and potentially steatosis) in NASH, meeting the unmet need for patients including:
  - Lack of currently approved therapies
  - High mortality and prevalence of NASH
  - Severe disease progression in absence of disease modifying therapy, including development of cirrhosis and hepatocellular carcinoma

Source: (1), (2), (3) and (4): GlobalData, Non-Alcoholic Steatohepatitis (NASH): Opportunity Analysis and Forecasts to 2029
Prediction strategy geared for identification of fibrotic regulators driven through oxidative stress

Target identification and hypothesis validation strategies were aligned to identify targets that could impact:

- **Fibrosis** (hepatic stellate cell activation assay)
- **Steatosis** (hepatocyte lipid accumulation assay)

Models were trained using datasets focussed on:

- **NAFLD** disease biology
- **Oxidative stress** mechanism
Inhibition of Target A has antifibrotic effect in TGF-β activated primary human hepatic stellate cells

Fibroblast to myofibroblast transition

**Tool compound**

- **Target A SPR K<sub>d</sub> 17nM**
- **Cell-based TE assay IC<sub>50</sub> 5.4nM**
- WLP >30-fold selectivity
- Kinome profiling >200-fold selectivity
- No effect on cell viability

### Source: Company internal drug programme
Target A: Scheduled to transition into Lead Op 4Q21

Key programme points:

- **Best-in-class programme** with **no clear literature** associating Target A as a potential therapeutic option in NASH
- Compelling anti-fibrotic *in vitro* target **validation** data packing to support utility in treatment of NASH
- **Rapid progress** to identify inhibitors of **Target A**: biophysical screening data and co-crystal structure in-hand to enable identification of novel chemical matter and transition to Lead Optimisation
Target B - First in class programme targeting a previously undrugged target for the treatment of NASH

- Structure enabled hit identification strategy **commenced 3Q21**
- AI-enabled literature analysis was able to identify data showing target B is reported as being upregulated in NASH, with expression **correlating to the degree of fibrosis** in the liver
- **Mechanistically diverse from target A**, building depth to our NASH portfolio

![Graphs showing cSMA, Collagen I, and Cell count](image)

One way ANOVA with Dunnetts

**TGF-β activated immortalized human hepatic stellate cells**

- Fibrosis assay established in immortalised hepatic stellate cells
- Lentiviral delivery of shRNA constructs to knock down target expression
- Three separate shRNA constructs were run independently for the target
- Full target-story data package complete
Atopic Dermatitis
Atopic Dermatitis (AD)

- Atopic dermatitis is the most common chronic inflammatory skin disease, characterized by intensely itchy, red, and swollen skin
  - Affects \(10-20\%\) of children and up to \(3\%\) of adults \(^{(1)}\)
  - Approximately \(60-70\%\) of all cases present with mild-moderate disease severity \(^{(2)}\)
  - Prevalence is rising, with market value in 7MM forecast to exceed \(\$14\) billion by expected launch of BEN-2293 in 2028 \(^{(1)}\)
- Skin inflammation and chronic pruritus associated with atopic dermatitis negatively impact quality of life and psychosocial well-being
- Clear unmet need in mild to moderate patient segment for treatment addressing itch and inflammation, without side effects of steroids

BEN-2293: A potent PanTrk antagonist developed to relieve inflammation and provide rapid itch resolution 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 biologics (e.g. dupilumab) that require add-on treatment

Source: (1) GlobalData — Atopic Dermatitis: Global Drug Forecast and Market Analysis to 2027; EvaluatePharma - Eczema/Dermatitis: Worldwide Sales 2026 (2) GlobalData — Atopic Dermatitis: Epidemiology Forecast to 2027
Atopic Dermatitis – BEN-2293, pan-Trk inhibition rationale

**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

**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\(^1\).

- 1% BEN-2293 ointment BID exceeds the exposure needed for PanTrk inhibition in both epidermis/upper dermis and lower dermis even at IC\(_{90}\) \(^1\)

<table>
<thead>
<tr>
<th>Mode</th>
<th>Exposure Required</th>
<th>Exposure Achieved</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Human in vitro</strong></td>
<td>&gt;IC90</td>
<td>✓</td>
</tr>
<tr>
<td><strong>Minipig in vitro</strong></td>
<td>&gt; IC90</td>
<td>✓</td>
</tr>
<tr>
<td><strong>Minipig in vivo</strong></td>
<td>&gt; IC90</td>
<td>✓</td>
</tr>
<tr>
<td><strong>Minipig in vivo</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Free plasma levels</td>
<td>&lt;&lt;400 below IC50</td>
<td></td>
</tr>
</tbody>
</table>

\(^1\) Internal Company drug programme data

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\(^1\)
BEN-2293 is progressing in an adaptive Phase I/II clinical study, with full data expected in mid 2022

Part A

First in Human Dose Escalation

3/4 cohorts completed, data expected late 2021
8 Mild-Moderate AD patients (18-65 years) per cohort, randomised 3:1 BEN-2293:Placebo

Safety, Tolerability, PK
- Adaptive ascending dose cohort design
- Includes efficacy endpoints
- MALDI imaging (evaluate human skin PK)

Part B

Efficacy Cohort(s)

Full data expected by middle of 2022
30-45 Mild-Moderate AD patients (18-65 years) per arm, final design and sample size dependent on Part A outcome

Efficacy
- Outcome measures include itch (NRS) and inflammation (vIGA, EASI)
- Additional safety, tolerability and PK
- Biomarker panel (reflects PanTrk mechanism and AD effect)

Review

Late 2021

Part A efficacy readout variability and response
Statistical modelling
Finalise Part B design

Our intention is to out-licence development and commercialisation of BEN-2293 following completion of this trial, with good interest from key Big Pharma and Dermatology specialists as potential partners
Given the limitations of current available topical therapies, there is a large unmet need for an efficacious and safe alternative topical therapy for the treatment of patients with Atopic Dermatitis.

Key Insights:

- **Topical Corticosteroids** (with increasing potency) - Poor side effect profile and concern of use by patients
- **Calcineurin inhibitors** (pimecrolimus or tacrolimus) - Poor side effect profile with associated black box warning
- **PDE4 inhibitors** - Issues with site application irritancy
- **Immunosuppressants** (azathioprine, ciclosporin and methotrexate) - Poor side effect profile
- **Topical JAKs** - ruxolitinib recently approved in the US, not yet approved in EU, but approval issued with a black box warning
- **Anti IL13/IL4 mAbs** (Dupilumab) - high cost treatment only indicated in moderate-severe.

**BEN-2293 (PanTrk)** - Combined solution addressing itch, inflammation and potential disease modifying effects, together with an improved safety profile and no irritancy on application.
- Potential to displace ineffective 2nd line treatment for chronic use in adults and paediatrics
- Potential use in a subset of 1st line patients where rapid itch resolution is key
- Potential for use in the severe patient population as an adjunct treatment option

**Atopic Dermatitis Treatment Paradigm**

<table>
<thead>
<tr>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Steroid Treatment</td>
<td>Calcineurin inhibitors</td>
<td>BEN-2293 (PanTrk)</td>
</tr>
<tr>
<td>Eucrisa/PDE4 Inhibitors</td>
<td>Topical JAKs</td>
<td>Immuno-suppressants</td>
</tr>
<tr>
<td>Dupilumab</td>
<td>Other anti-IL13/IL4 mAbs</td>
<td>Oral JAKs</td>
</tr>
</tbody>
</table>

Source: GlobalData and Company internal drug programmes
BenevolentAI Pipeline Market Opportunity
BenevolentAI pipeline assets target treatment of prevalent diseases with high unmet need

**BEN-2293 for the treatment of Atopic Dermatitis**
BEN-2293 is a first-in-class, topical, steroid sparing PanTrk antagonist to address itch and inflammation in mild-moderate atopic dermatitis

**Illustrative target patient population in 2020**
- All atopic dermatitis patients¹: 43.4M US | 33.9M EU5 | 5.1M JP
- Patients with mild-moderate disease¹: 82.6% US | 45.2% EU5 | 55.5% JP
- Treatable population: 35.8M US | 15.3M EU5 | 2.8M JP

**Illustrative approved therapies**
- Dupilumab (Dupixent, AD launch 2017)²
  - (Subcutaneous injection, mAb, anti IL4/IL13)
  - 2020 Net Revenue: $3.2B WW (Atopic Derm Only)²

**Illustrative pipeline / recently approved therapies**
- Ruxolitinib (Opzelura, AD launch 2021)³
  - (Topical cream, JAK inhibitor; expected cost ~$8,000 patient/year in US³)
  - Peak Sales Forecast: $1.1Bn WW (Atopic Derm Only)⁴

**BEN-8744 for the treatment of Ulcerative Colitis**
BEN-8744 is an oral, peripherally restricted, potent and selective PDE10 inhibitor for the treatment of moderate-to-severe Ulcerative Colitis

**Illustrative target patient population in 2020**
- All ulcerative colitis patients³: 0.62M US | 0.86M EU5 | 0.15M JP
- Patients with moderate-severe disease³: 42.6% US | 39.9% EU5 | 32.0% JP
- Treatable population: 0.26M US | 0.34M EU5 | 0.05M JP

**Illustrative approved therapies**
- Adalimumab (Humira, UC launch 2012)⁷
  - (Subcutaneous injection, mAb, anti TNF)
  - 2020 Net Revenue: $2.6B WW (UC Only)
- Vedolizumab (Entyvio, UC launch 2014)⁸
  - (Subcutaneous injection, mAb, anti α4β7 integrin)
  - Peak Sales Forecast: $2.0B WW (UC Only)

**Illustrative pipeline / recently approved therapies**
- Ozanimod (Zeposia, UC launch 2021)⁶
  - (oral, small molecule, S1P1/S1P5 modulator, $86,000 patient/year in US⁶)
  - Peak Sales Forecast: $3.0B WW (UC Only)⁶

Sources:
(1) GlobalData Atopic Dermatitis: Epidemiology Forecast to 2027; 28 November 2018
(3) GlobalData Ulcerative Colitis Drug Forecast and Market Analysis to 2029
(4) Endpoints/Andrew Berens at SVB Leerink
(5) Incyte Opzelura approval investor call 22 September 2021
(6) FiercePharma/Salim Syed at Mizuho Securities
BenevolentAI pipeline assets target treatment of prevalent diseases with high unmet need

**Illustrative Crohn's Disease target market**

| Mod- Sev Crohn's Disease patients 2020 | 239k US | 233k EUS | 17k JP |
| Global Crohn's Disease market value 2029 | $11.9B |
| Peak sales forecast Entyvio (2025) | $4.0B WW (Crohn's disease only) |

**Illustrative GBM target market**

| Treatable GBM patients 2020 | 10k US | 12k EUS | 1.5k JP |
| Global GBM market value 2026 | $1.57B |
| Peak sales forecast Tagrisso (2026) | $554M (GBM only) |

**Illustrative NASH target market**

| Treatable NASH patients 2020 | 13.9M US | 7.8M EUS | 4.6M JP |
| Global NASH market value 2029 | $27.2B |
| Peak sales forecast Resmetirom (2026) | $719M WW (NASH only) |

**Illustrative ALS target market**

| Treatable ALS patients 2020 | 21k US | 22k EUS | 11k JP |
| Global ALS market value 2029 | $1.04B |
| Peak sales forecast verdiperstat (2026) | $192M WW (ALS only) |

**Illustrative IPF target market**

| Treatable IPF patients 2020 | 115k US | 68.9k EUS | 21.5k JP |
| Global IPF market value 2026 | $3.74B |
| Peak sales forecast Ofev (2026) | $2.85B WW (IPF only) |

**Illustrative CKD target market**

| Treatable CKD patients 2020 | 3.7M US | 3.1M EUS | 1.8M JP |
| 7MM CKD market value 2026 | $10.5B |
| Peak sales forecast Farxiga (2024) | $639M WW (CKD only) |

BenevolentAI
Progress since mid-2020
Significant progress across all aspects of the business since mid-2020

**Pharma partnerships**
- Baricitinib; 38% reduction in mortality v SoC. Eli Lilly investment
- AstraZeneca; continued delivery, 1st target selected for CKD

**Pipeline Progress**
- Phase 1b for Atopic Dermatitis progressing well. Completion by mid-2022
- IND-enabling studies started for novel Ulcerative Colitis asset (PDE10)

**Platform Enhancements**
- Mechanism mapping to better represent disease
- Improved capacity to ingest human patient level data and genetics at scale

**Business Model**
- Ambition to take assets through to commercialisation ourselves including, PDE10 for UC

**People**
- Building a world-class Board (Dr. Francois Nader, Dr. John Orloff, Sir Nigel Shadbolt)
- Investing in people to support a scaling pipeline (>80 recruited in last year)