Transforming Medicine through Synthetic Biology

Corporate Presentation

June 2022
Forward Looking Statements

This presentation contains "forward-looking statements" that involve substantial risks and uncertainties for purposes of the safe harbor provided by the Private Securities Litigation Reform Act of 1995. All statements, other than statements of historical facts, included in this press release regarding strategy, future operations, clinical development plans, future financial position, future revenue, projected expenses, prospects, plans and objectives of management are forward-looking statements. In addition, when or if used in this press release, the words "may," "could," "should," "anticipate," "believe," "estimate," "expect," "intend," "plan," "predict" and similar expressions and their variants, as they relate to Synlogic may identify forward-looking statements. Examples of forward-looking statements, include, but are not limited to, statements regarding the potential of Synlogic's approach to Synthetic Biotics to develop therapeutics to address a wide range of diseases including: inborn errors of metabolism, and inflammatory and immune disorders; our expectations about sufficiency of our existing cash balance; the future clinical development of Synthetic Biotics; the approach Synlogic is taking to discover and develop novel therapeutics using synthetic biology; and the expected timing of Synlogic's clinical trials of SYNB1618, SYNB1934, SYNB1353 and SYNB8802 and availability of clinical trial data. Actual results could differ materially from those contained in any forward-looking statement as a result of various factors, including: the uncertainties inherent in the clinical and preclinical development process; the ability of Synlogic to protect its intellectual property rights; and legislative, regulatory, political and economic developments, as well as those risks identified under the heading "Risk Factors" in Synlogic's filings with the SEC. The forward-looking statements contained in this press release reflect Synlogic's current views with respect to future events. Synlogic anticipates that subsequent events and developments will cause its views to change. However, while Synlogic may elect to update these forward-looking statements in the future, Synlogic specifically disclaims any obligation to do so. These forward-looking statements should not be relied upon as representing Synlogic's view as of any date subsequent to the date hereof.
Advancing a New Class of Biotherapeutics

<table>
<thead>
<tr>
<th>Lead Program: Opportunity to Transform PKU Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Relatively large rare disease market: with ~25% penetration, generate $500mm in global revenue</td>
</tr>
<tr>
<td>• ~75% of patients remain untreated due to limitations of today’s options</td>
</tr>
<tr>
<td>• Synlogic candidate has potential as effective, safe and convenient oral treatment to address needs across PKU</td>
</tr>
</tbody>
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<table>
<thead>
<tr>
<th>Wholly-Owned Pipeline from Validated Product Engine</th>
</tr>
</thead>
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<tr>
<td>• Rare Metabolic Diseases</td>
</tr>
<tr>
<td>• Phenylketonuria (PKU): Proof of concept from interim analysis of Phase 2 study, Phase 3 initiation activities underway</td>
</tr>
<tr>
<td>• Homocystinuria (HCU): IND-enabling studies</td>
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<td>• Enteric Hyperoxaluria: Phase 1b study in patients</td>
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<td>• Preclinical Research Programs: Targeting additional metabolic and immunological diseases</td>
</tr>
<tr>
<td>• Research partnerships with Gingko (synthetic biology technology) and Roche (IBD research target)</td>
</tr>
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<th>Multiple Expected Near-Term Milestones Ahead</th>
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<td>• PKU Full Phase 2 data readout ➤ H2 2022</td>
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<td>• HCU Phase 1 data from healthy volunteers ➤ H2 2022</td>
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<td>• PKU Phase 3 initiation ➤ H1 2023</td>
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<td>• Enteric hyperoxaluria proof of concept ➤ H2 2022</td>
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</table>

Strong balance sheet: $120.5m* with projected runway into 2024

PKU = phenylketonuria; IND = Investigational New Drug; IBD = Inflammatory Bowel Disease
* As of March 31, 2022

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Synthetic Biotics
A New Paradigm of Biotherapeutics – Based on Synthetic Biology

Reproducible, Proprietary Engine for Drug Design

Programable, precision genetic engineering + Well-characterized probiotic chassis

Differentiated Drug Candidates

- Target metabolites from validated biological pathways
- Orally-administered convenience
- Probiotic chassis that avoids systemic absorption (restricted to GI tract)
- Non-colonizing, non-integrating, and reversible via rapid GI clearance
- Addressing rare and common, metabolic and immunological diseases

GI = gastrointestinal

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Synthetic Biotics: Potential to Transform Treatment Paradigms

- Founded in 2014 at MIT by world-leading experts in synthetic biology, James J. Collins and Tim Lu

- Since founding, within eight years, this product engine has:
  - Progressed to clinical-stage pipeline of therapeutic candidates
  - Achieved Proof of Concept in PKU, with Phase 3 readiness activities underway
  - Established fully-integrated discovery, manufacturing and clinical development capabilities
  - 5 INDs opened to date
  - Dosed >350 individuals with Synthetic Biotics
Pipeline Targets Metabolic, Immunological Diseases

<table>
<thead>
<tr>
<th>Metabolic Diseases</th>
<th>Exploratory</th>
<th>Preclinical</th>
<th>IND-Enabling Studies</th>
<th>Phase 1</th>
<th>Phase 2</th>
<th>Phase 3</th>
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</thead>
<tbody>
<tr>
<td>Phenylketonuria (PKU)</td>
<td>SYN1618</td>
<td></td>
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<tr>
<td>Homocystinuria (HCU)</td>
<td>SYN1934</td>
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<tr>
<td>Enteric Hyperoxaluria</td>
<td>SYN1353</td>
<td>Phase 1 HV Data H2 2022</td>
<td>Proof of Concept H2 2022</td>
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<tr>
<td>Undisclosed Metabolic Program</td>
<td>SYN8802</td>
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<th>Phase 3</th>
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<tr>
<td>Inflammatory Bowel Disease (IBD)</td>
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</tbody>
</table>
| IBD Program – Single Target | | | | | | Roche

GI = Gastrointestinal; HV = Healthy Volunteers

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Rare Metabolic Diseases

SYNB1618 and SYNB1934 for Phenylketonuria (PKU)
PKU: Unique Opportunity for Value Creation

**Significant unmet medical need** - 75% of patients remain untreated

**De-risked path** to registration

**Well-connected patient population** at concentrated sites of care

**Differentiated profile** established in POC

**Phase 3 initiation in H1 2023** expected
PKU Burden Includes Extreme Diet Restrictions & Neurocognitive Risks

With a global population of ~55,000, PKU is caused by defects in PAH, the enzyme that metabolizes phenylalanine (Phe), found in dietary protein.

Phe build-up can cause neurological damage and neurocognitive defects.

Risk of intellectual disabilities, deficits in mental processing and social engagement, and emotional problems\textsuperscript{1,2,3}.

Lifelong metabolic control of Phe is the key to risk reduction\textsuperscript{3}.

PKU Can Be Devastating for Patients and Families

“Adding **10g of protein per day** would be a **game changer** for my family”
— Parent of PKU Patient

“If my boys could **just eat a slice of normal bread or a serving of regular pasta it would be huge**”
— Parent of PKU Patient

People think this isn’t too bad, I look okay. But this is a **lifelong burden**. It’s a challenge to think straight, to plan my day.
— Adult PKU Patient
Current Treatment Limitations Create Need for New Approach in PKU

PKU Patients, US
(n=17,000)

75% Untreated

On sapropterin

~3,200 on sapropterin
- Use limited to BH4-responsive segment
- ~$500 million revenues pre-genericization
- Potential for adjunctive treatment

~1,200 on pegvaliase injection
- “Anaphylaxis at any time” warning, restrictive REMS, requiring autoinjectable epinephrine “at all times”

~12,600 untreated
- Nonresponsive to sapropterin*
- Potential for monotherapy

*Responsive to BH4 (tetrahydrobiopterin) = molecule that the body produces to act as a cofactor with PAH, the enzyme that is impaired in PKU. Sapropterin is a synthetic form of BH4.


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Targeting Pent-Up Demand: Two Opportunities to Meet Needs in PKU

**Clinical Positioning – Initial Launch**
PKU Patients, US (n=17,000)¹

1) **Monotherapy**

- ~75% currently untreated² (BH4 nonresponsive)
- ~2,400 in US
- Discontinued, declined or averse to Palynziq²

2) **Adjunctive (Add-On)**

- ~15% taking sapropterin (Kuvan)² (BH4 responsive)
- ~1,200 in US
- Sapropterin (Kuvan)-treated, Phe >600 µmol/l³

>3,500 Patients: Estimated Addressable Launch Population (US)

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¹ Patient numbers for sapropterin, pegvaliase derived from Biomarin financials and disclosures YE 2021
Synlogic’s Approach: Targeted to Meet Needs in PKU

**Intuitive Design**

- Consumes **Phe in GI tract**
- *E. coli* Nissle chassis **avoids systemic absorption** and associated adverse events
- Converts Phe to harmless metabolite (TCA), **reducing plasma Phe levels**

**Transformative Profile**

**Efficacy**

- SYNB1618 **achieved target mean Phe change** in **Phase 2 interim analysis** of -20% \(^1\)
- Saproterin 'all comers' (ITT) Phe change of -10% \(^2\)
- SYNB1934 Ph 1 data confirmed greater potency \(^3\)

**Favorable safety profile, no SAEs to-date**

**Convenience:** Oral administration

**Monotherapy or Adjunct**
SYNB1934: Designed for Greater Phe Metabolizing Activity

**SYNB1618 / SYNB1934**

- **SYNB1618 PAL**: 5 amino acid changes (yellow)
- **SYNB1934 PAL**: 5 amino acid changes (yellow)

**SYNB1934 Overview**

- Developed from SYNB1618 with the goal of increasing PAL enzyme productivity\(^1\); >99% same genetic material
- Head-to-head Phase 1 study in healthy volunteers demonstrated potential for increased Phe lowering and dosing flexibility\(^2\)
- Added as 2\(^\text{nd}\) arm in Phase 2 Synpheny-1 study after healthy volunteer data confirmed greater potency than SYNB1618\(^2\)

PAL = phenylalanine ammonia lyase; LAAD = L-amino acid deaminase
\(^{2}\) Synlogic PKU Program Update September
Phase 2 Synphony-1 Study Design in Patients with PKU

**SynPheny-1 Trial Design**

<table>
<thead>
<tr>
<th>Diet Run-In</th>
<th>Treatment Period (monotherapy &amp; adjunctive to sapropterin)</th>
<th>Wash-Out</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Arm 1:</strong> SYNB1618</td>
<td>Dose Ramp</td>
<td>1e12 TID</td>
</tr>
<tr>
<td><strong>Arm 2:</strong> SYNB1934</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Trial Endpoints:**

- **D5-Phe Tracer Study**
- **Fasting Plasma Phe**
- **Biomarker Study**
- **Safety and Tolerability** (AE collection)

- After Phase 1 HV data confirmed greater potency vs. SYNB1618 in healthy volunteers, 2nd arm with SYNB1934 to Phase 2 to assess activity in PKU patients
- Study amended to include treatment as monotherapy and adjunctive treatment

1. Endpoints: % Change from baseline in D5 Phe: 24h AUC evaluated, d-1, 14 (at 2e12 dose); Fasting Phe: Evaluated in AM pre-dose on Days -1, 7, 14, 29; Biomarkers (TCA, HA): Evaluated d1, 7, 15; Safety & tolerability: AEs collected throughout treatment and at Day 29
Proof of Concept in PKU Patients Achieved in Phase 2 Interim Analysis

**Clinically Meaningful Efficacy**

- **Mean Reduction Met Target:** % change is ~2x that of sapropterin’s pivotal study
  
  ⬤ 50% response rate (4 of 8)

- **Response Rate Favorable:** Four of eight patients in analysis achieved the pre-specified responder definition (>20% reduction) in plasma Phe

- **Additional Biomarkers Support Effect:** A labeled Phe challenge and other biomarker assessments confirm Phe-lowering effect of drug candidate

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**Phe Reduction: Intent-to-Treat**

(ITT or “All Comers”, N=8)

- **Dose**
  - **Day 7**: $3 \times 10^{11}$
  - **Day 14**: $1 \times 10^{12}$

- **Percent Change from Baseline**
  - **Day 7**: -14%
  - **Day 14**: -20%
  - **Day 29**: 19%

**Treatment End**

*Result is statistically significant because the 95% CI does not cross zero.; $p<0.05$
PKU Programs Have Consistent Safety Profile: Generally Well-Tolerated with No Serious Adverse Events

Safety Findings Across PKU Programs to Date

- No Serious Adverse Events (SAEs) or systemic safety issues identified
- Tolerability profile in Phase 2 interim analysis consistent with experience in healthy volunteers
- Most adverse events were mild-to-moderate and GI in nature
- One discontinuation in Phase 2 interim analysis (anxiety due to PKU)
Connected Community Facilitates Development & Commercialization

Established Diagnosis

Regulatory, Payer Precedent

Networked Specialists and Clinics

Sites of Care

NPKUA = National PKU Alliance
Regulatory Considerations
Prior Approvals, the Synlogic Platform and the PKU Program

PKU: Two FDA-Approved Therapies
- Both approved products received full approval with:
  - A single, registrational study, using the primary endpoint of plasma Phe reduction
  - Efficacy analysis in both examples of registrational trials were based on responder population

Platform: Advantages of Synthetic Biotics
- Fit within existing FDA framework for Live Biotherapeutic Products
- Familiarity with chassis E. coli Nissle probiotic, which has been studied in humans for >100 years
- Manufacturing based on well-established technologies of fermentation and lyophilization

Program: Drug Candidates SYNB1618 and SYNB1934
- Safety and tolerability profile consistent across studies; No treatment-related serious adverse events
- Most common adverse events were mild to moderate and GI-related
- Proof of Concept established for SYNB1618; Greater potency confirmed in healthy volunteers for SYNB1934

GI = gastrointestinal;
With POC Established, PKU Program Has Clear Path to Phase 3

September 2021
- SYNB1618: POC established
- SYNB1934: Greater potency confirmed
- Phase 3: Committed based on strength of POC

H2 2022*
- SYNB1618: Complete Phase 2 dataset
- SYNB1934: PKU patient data
- Monotherapy and adjunctive use data

H1 2023*
- Phase 3 initiation

* Anticipated Milestones
Rare Metabolic Diseases

SYNB1353 for Homocystinuria (HCU)
**Clinical Candidate SYNB1353**

- **HCU:** mutations in CBS gene result in accumulation of homocysteine, with significant risks: thromboembolism, lens dislocation, skeletal abnormalities, intellectual disability

- **SYNB1353:** orally administered, non-systemically absorbed, designed to lower homocysteine levels by consuming methionine in the GI tract

- **Synergies with PKU:**
  - Research, manufacturing, regulatory, development
  - Commercialization (shared call point, connected patient communities)

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**Validated Preclinically\(^1\) - Phase 1 Data in 2022**

![Graph showing plasma homocysteine levels](image)

- **Methionine Load:**
  - 100 mg/kg
  - 300 mg/kg

![Graph showing urinary 3MTP](image)

- **Biomarker production:**
  - SYNB1353 vs Vehicle

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**CBS = cystathionine beta-synthase**


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Enteric Hyperoxaluria

SYNB8802
Enteric Hyperoxaluria

Acute Crises with Long-Term Damage

Excess dietary oxalate: absorbed from GI tract into circulation

Causes crystal formation and chronic, recurrent kidney stones

- Oxalate crystals damage kidneys, impair renal function
- Leading to severe pain, CKD, ESRD, nephrocalcinosis, systemic oxalosis

“I would rather experience the pain of childbirth every year for the rest of my life than ever have one more stone.”

— C., Female, 53 yrs. old, 7 stones

“Our current ‘treatment’ options are very arbitrary... the dietary control of things is very difficult for 99% of people.”

— US Urologist

GI = gastrointestinal, CKD = chronic kidney disease, ESRD = end stage renal disease
Enteric Hyperoxaluria: Treatment and Unmet Medical Need

**Diagnosis**

Typical **presentation**: severe pain associated with kidney stones  
**Diagnosis based on urine oxalate** levels

**Standard of Care**

Patients primarily managed by urologists, nephrologists; gastroenterologists if underlying GI disease  
**No FDA-approved treatments**; diet, nutritional support only (low fat, increased calcium, hydration)

**Unmet Need**

Painful, recurrent calcium oxalate kidney stones, risk of kidney failure  
Significant, **negative impact on quality of life**

**Healthcare System Impact**

~10% or people in U.S. experience kidney stones  
($2.5-$4.5 billion in direct healthcare costs)  
Longer-term risks include **CKD** ($82 billion cost to Medicare) and **ESRD** ($37 billion cost to Medicare)

GI = gastrointestinal, CKD = chronic kidney disease, ESRD = end stage renal disease
SYNB8802: Genetically Engineered to Consume Excess Oxalate

Genetically Engineered Probiotic Medicine
Able to Consume Excess Oxalate

- SYNB8802 consumes oxalate throughout GI tract
- Metabolizes excess oxalate into formate for excretion

Gut lumen
Intestinal epithelium

SYNB8802

oxalate
formate

GI = gastrointestinal
### Oxalate Absorption

<table>
<thead>
<tr>
<th>Dietary Oxalate</th>
<th>ABSORPTION</th>
<th>SITES OF ACTION</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Healthy State</td>
<td>Disease State</td>
</tr>
<tr>
<td>Stomach</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Small Intestine</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Colon</td>
<td>✓</td>
<td>✓</td>
</tr>
</tbody>
</table>

- SYN8802 consumes oxalate throughout the GI tract
- Extends duration of action, increasing oxalate-lowering efficacy potential
SYNB8802 Phase 1 Findings: Robust Dose-Related Oxalate Reductions

- Robust, dose-dependent reductions in oxalate in urinary and fecal analysis\(^1\)
- Well-tolerated in healthy volunteers with no serious or systemic adverse events
- Findings support 3e\(^{11}\) dose for further development

GI = gastrointestinal; LS mean change over Placebo, +/- 90% CI, all days baseline and treated

Synlogic Enteric Hyperoxaluria (EH) Development Program

2021:
Results in Healthy Volunteers
✓ Positive safety profile
✓ Proof of mechanism for reduction in urinary oxalate

2022:
Establish PoC in Patients
Urinary oxalate lowering in patients with Roux-en-Y gastric bypass

Future Development:
Multiple Paths to Market:
• EH patients with existing renal disease (<50,000 in US¹)
• Recurrent kidney stones due to EH (~100,000 in US²)
• Secondary prevention in kidney stone patients (>250,000 in US³)

Preclinical Programs & Research Opportunities
Focusing on Gut-Accessible Targets with Validated Biology

- **PKU (POC 2021)**
  - **SYNB1618**
    - Phe metabolism
  - **SYNB1934**
    - Phe metabolism
  - **SYNB8802**
    - Oxalate metabolism
  - **SYNB1353**
    - Methionine metabolism

- **Metabolic disease**
  - Uric acid metabolism for gout
  - Met metabolism for broader indications

- **Immunological disease**
  - Metabolism of pro-inflammatory metabolites

- **Non-metabolic / non-immunologic diseases**
Industry-Leading Partners Reflect Synlogic Expertise, Progress to Date

- Established 2019
- Five-year, $30 million strategic research collaboration
- Accelerates expansion and development of Synlogic’s pipeline, based on Synlogic’s product engine and Ginkgo’s discovery capabilities
- Synlogic retains exclusive marketing rights
- Results to date include SYNB1353 for HCU, with Phase 1 data expected in 2022

- Established June 2021
- Research collaboration for discovery of novel Synthetic Biotic addressing novel single target for the treatment of inflammatory bowel disease (IBD)
- Roche has exclusive option to enter a licensing and collaboration agreement for further development and commercialization
- Synlogic achieved a prespecified research milestone and payment in Q3 2021

IND = Investigational New Drug
Summary
Experienced Leadership Team and Board of Directors

**Leadership Team**

- **Aoife Brennan, MB ChB**
  President & CEO
- **Dave Hava, PhD**
  Chief Scientific Officer
- **Caroline Kurtz, PhD**
  Chief Development Officer
- **Antoine Awad**
  Chief Operating Officer
- **Molly Harper**
  Chief Business Officer
- **Michael Jensen**
  Chief Financial Officer

**Board of Directors**

- **Peter Barrett, Chair**
  Atlas Venture
- **Lisa Kelly-Croswell**
  Boston Medical Center Health System
- **Mike Burgess**
  Turnstone Biologics
- **Nick Leschly**
  2seventy bio
- **Michael Heffernan**
  Collegium
- **Ed Mathers**
  NEA
- **Patricia Hurter**
  Lyndra Therapeutics
- **Richard Shea**
  Independent
## Financial Results for First Quarter 2022

### Summary Results

<table>
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<th>Balance Sheet (unaudited)</th>
<th>31 March 2022</th>
<th>31 December 2021</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cash, Cash Equivalents, and Marketable Securities</td>
<td>$120.5 M</td>
<td>$136.6 M</td>
</tr>
</tbody>
</table>

### Financial Performance (unaudited)

<table>
<thead>
<tr>
<th>Financial Performance (unaudited)</th>
<th>31 Mar 2022</th>
<th>31 Mar 2021</th>
</tr>
</thead>
<tbody>
<tr>
<td>Revenue</td>
<td>$0.2 M</td>
<td>-</td>
</tr>
<tr>
<td>R&amp;D Expenses</td>
<td>$11.7 M</td>
<td>$11.2 M</td>
</tr>
<tr>
<td>G&amp;A Expenses</td>
<td>$4.3 M</td>
<td>$3.9 M</td>
</tr>
<tr>
<td>Net Loss</td>
<td>$(15.7 M)</td>
<td>$(15.0 M)</td>
</tr>
<tr>
<td>Net Loss per share – basic and diluted*</td>
<td>$(0.22)</td>
<td>$(0.36)</td>
</tr>
</tbody>
</table>

*Weighted Average Shares Outstanding* | 72.0 M | 41.5 M |

* weighted average shares used in computing net loss per shares - basic and diluted
## Multiple Expected Near-Term Milestones

<table>
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**Strong balance sheet:** $120.5m* with projected runway into 2024

* As of December 31, 2021

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Thank You