A fully integrated next generation modular systemic AAV gene therapy company

High quality potent liver targeted platform
- Rationally designed next generation capsid
- Cutting edge proprietary CMC platform (Quality, Scale, COGS)
- Clinical and Commercial GMP supply

Functional cures and broad pipeline enabled by high protein expression
- Lead program in Hemophilia B completing pivotal dose selection
- Second program in Fabry Disease in the clinic
- Gaucher and Hemophilia A in IND-enabling studies
- Cutting edge research enabling reach outside monogenic diseases

Strong Executive Team with depth and breadth of expertise
- Spanning from Research to Clinical Translation and Approvals
- Deep CMC and Manufacturing experience
- Strong financial position with $200 mm raised to date and $70 mm on hand
Current systemic AAV platforms cannot access high protein levels

Estimated therapeutic levels

- Inflammatory disorders and beyond
- LSDs – Fabry, Gaucher, others
- Consistent cures in Haemophilia

40% FIX activity level

Protein produced (pmol/ml/hr)
Freeline’s proprietary AAVS3 capsid delivers next generation performance

**Estimated therapeutic levels**

- **Inflammatory disorders and beyond**
- **LSDs – Fabry, Gaucher, others**
- **Consistent cures in Haemophilia**

**Protein produced (pmol/ml/hr)**

- **40% FIX activity level**

- **AAV8**
  - 4.3% % GFP positive human cells

- **AAVS3**
  - 24.3% % GFP positive human cells

**AAVS3 high tropism for the human liver verified in preclinical studies**

Dane A et al; abstract 2197, ASH 2018

40% activity assumes Padua

Estimates of therapeutic levels for different endogenous proteins are shown
## Proprietary pipeline with two programs in the clinic and two more entering within 24 months

<table>
<thead>
<tr>
<th>Programme</th>
<th>Research</th>
<th>IND enabling studies</th>
<th>Phase 1/2</th>
<th>Next Milestone</th>
<th>Patient No (US &amp; EUS)</th>
<th>Worldwide rights</th>
</tr>
</thead>
<tbody>
<tr>
<td>Haemophilia B FLT180a</td>
<td></td>
<td></td>
<td></td>
<td>Dose Selection</td>
<td>9,000</td>
<td>FREELINE</td>
</tr>
<tr>
<td>Fabry FLT190 and FLT191</td>
<td></td>
<td></td>
<td></td>
<td>Results from dose escalation</td>
<td>9,000</td>
<td>FREELINE</td>
</tr>
<tr>
<td>Gaucher FLT200 and FLT201</td>
<td></td>
<td></td>
<td></td>
<td>CTA/IND</td>
<td>6,000</td>
<td>FREELINE</td>
</tr>
<tr>
<td>Haemophilia A FLT210</td>
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<td></td>
<td></td>
<td>CTA/IND</td>
<td>38,000</td>
<td>FREELINE</td>
</tr>
<tr>
<td>Undisclosed inflammatory disorders</td>
<td></td>
<td></td>
<td></td>
<td>Candidate Selection</td>
<td>50,000 – 200,000</td>
<td>FREELINE</td>
</tr>
</tbody>
</table>


Fabry Disease epidemiology sources: Metchler et al 2012; Spada et al 2016; Fabry Register; Fabry Outcome Survey; Waldek et al 2009; Desguin et al 2006.

Management team of experienced leaders in gene therapy, manufacturing and rare disease development

**Freeline Management Team**

- **Chris Hollowood**
  - Executive Chairman
  - Nightstar
  - Syncroma
  - Gyroscope

- **Amit Nathwani**
  - Founder and Chief Scientific Adviser

- **Markus Hörer**
  - Founder and Chief Technology Officer

- **Romuald Corbau**
  - SVP Research

- **Natalia Misciattelli**
  - SVP Strategy

- **Ged Short**
  - SVP Clinical & Regulatory

- **Jan Thirkettle**
  - Chief Development Officer

- **Brian Silver**
  - Chief Financial Officer & Corporate Development

- **Duncan Whitaker**
  - VP Intellectual Property

- **Julia P Gregory**
  - Non-Executive Director

**Board of Directors**

- **Chris Hollowood**
  - Executive Chairman

- **Amit Nathwani**
  - Founder & Chief Scientific Adviser

- **Martin Andrews**
  - Non-Executive Director

- **Jeffrey Chodakewitz**
  - Non-Executive Director

- **Julia P Gregory**
  - Non-Executive Director
Transatlantic organization with footprint in major biotech centres

**United Kingdom**
- Headquarters & Research Labs
  - Stevenage Bioscience Catalyst
  - Stevenage, UK
- Catapult Manufacturing & QC Labs
  - Stevenage, UK
- In Vivo Labs
  - London Bioscience Innovation Centre
  - London, UK

**Germany**
- CMC Development & Analytics Labs
  - Munich, Germany

**United States**
- Corporate Office
  - New York City, NY
- Manufacturing
  - Boston, MA

~170 FTEs covering Research, Clinical Development, Process Development, Analytics and GMP Manufacturing
Clinical programs
Patients, physicians and payers all want the most effective gene therapy for Haemophilia B

**Patient aspiration:** Parity with general population
- Confidence in a lifetime cure
- No need for ERT top up in any circumstances

**HCP aspiration:** Reduction in disease burden
- Complete relief of clinical symptoms

**Payer aspiration:** Improved treatment at lower cost
- Completely eliminate need for expensive and burdensome ERT
Our Haemophilia B adaptive design has allowed us to escalate to the therapeutic window

**Objective:** To assess the safety and efficacy of systemic administration of FLT180a in adult patients with severe Haemophilia B

**Enrolment criteria:** Haemophilia B patients aged >=18 years with FIX activity levels <2%; Lack of neutralising antibodies to AAVS3; >50 exposure days to FIX and no history of inhibitors; Normal liver function; No evidence of active Hepatitis B, C, or HIV infection

**Assessments:** Safety; FIX activity level (one stage clotting assay); Exogenous FIX concentrate usage; Bleeding frequency

**Adaptive study design:** Allowing titrating to target range between 50 – 150 % FIX

<table>
<thead>
<tr>
<th>Dose</th>
<th>FIX Concentrate (vg/kg)</th>
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<tbody>
<tr>
<td>Low dose</td>
<td>4.5e11</td>
</tr>
<tr>
<td>Mid dose</td>
<td>1.5e12</td>
</tr>
<tr>
<td>High dose</td>
<td>3e12</td>
</tr>
</tbody>
</table>
Haem B Low Dose cohort (4.5e11) patients 1 and 2 have shown stable expression over time at 66 and 74 weeks.

Patient 1 (low dose)

Steady state mean 40% +/- 5.5 for cohort 1

Steroid Prophylaxis
Prophylactic prednisolone from week 6-12, 60 mg tapered

Patient 2 (low dose)
Patients, physicians and payers all want the most effective gene therapy for Fabry Disease

**Patient aspiration:** Freedom from disease progression

- Confidence in a lifetime cure
- No need for ERT top up

**HCP aspiration:** Reduction in disease burden

- Effective treatment of clinical manifestations through high GLA levels
- **Opportunity for earlier intervention**
- Potential for tolerization

**Payer aspiration:** Improved treatment at lower cost

- Completely eliminate need for expensive and burdensome ERT
- Confidence in a lifetime cure
- No need for ERT top up
The MARVEL1 design allows rapid escalation to the therapeutic dose.

**Objective:** To assess the safety and efficacy of systemic administration of FLT190 in adult patients.

- **Low dose:** 0.75e12 vg/kg
- **Mid dose:** 1.5e12 vg/kg
- **High dose:** 4.5e12 vg/kg

**Assessments:** Safety and GLA Level Response – 2 week

- Initially 1-3 patients per cohort
- Patients previously treated with ERT

**Adaptive Study Design**

- Initially 1-3 patients per cohort
- Patients previously treated with ERT

- **Low dose** 0.75e12 vg/kg
- **Mid dose** 1.5e12 vg/kg
- **High dose** 4.5e12 vg/kg

- Dose completion with 3 patient from chosen dose

- 3 previously ERT untreated patients (PUPs) evaluated
FLT190 leads to reversal of kidney and heart disease in GLA KO male mice

WORLD symposia 2019: Jey Jeyakumar et al. Liver-directed gene therapy corrects Fabry disease in mice

FLT190 vector genome pseudo-typed with AAV8 in GLA KO mice; Dose: 2e12 vg/kg. Error bars: mean ± SD

Time point: 16-week disease development prior to treatment; analysis 14 weeks post-treatment. Gb3/Lyso-Gb3 data (n=4, 2 males and 2 females)

freeline.life
Freeline’s iCellis based manufacturing platform delivers highest quality and potency at competitive cost

**Upstream in AAV is paramount**
- Downstream processing (DSP) cannot eliminate unwanted packaged DNA

**Maximised purity**
- Adherent cells have higher cell specific productivity than suspension

**Freeline’s know-how adds to quality**
- Proprietary split plasmid system drives quality and safety

**Purity and Quality at scale**
- iCellis is a commercial platform that allows adherent systems at scale

E1A % impurity / vg

<table>
<thead>
<tr>
<th>Mammalian adherent</th>
<th>Mammalian suspension</th>
</tr>
</thead>
<tbody>
<tr>
<td>3x</td>
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**Unwanted DNA**

1. Rep & helper genes
2. Cap & expression cassette
Capacity secured for pipeline from tox through commercialisation.

**FREELINE**
Munich, Germany

**Analytics & Process Development**

**FREELINE**
Stevenage, UK

**BRAMMER**
Cambridge, MA, US

**novasep**
Seneffe, Belgium

**PALL**
Portsmouth, UK

GMP manufacture (iCELLis® 500)

**Toxicology**

**Engineering**

**Clinical Supply**

**Commercial Supply**
Within 24 months Freeline will have 4 programs in the clinic

<table>
<thead>
<tr>
<th>PROGRAM</th>
<th>2020</th>
<th>2021</th>
<th>2022</th>
</tr>
</thead>
</table>
| Haemophilia B FLT180a| • B-AMAZE dose selection  
• Type B meeting  
• ECLIPSE enrolment | • Phase 3 started  
• Process validation  
• Antibody removal study | • Phase 3 complete |
| Fabry Disease FLT190/191| • Dose escalation  
• RMAT & PRIME submissions  
• ODD (US & EU) | • 1 year data  
• Regulatory path to market  
• Dose selection | • Phase 3 started |
| Gaucher FLT200/201   | • GLP Tox  
• Manufacturing  
• CTA Submission | • Phase 1/2 start  
• Initial results  
• Dose selection | • Phase 3 started |
| Haemophilia A FLT210| • GLP Tox  
• Process Development | • CTA / IND  
• Phase 1/2 start | • Dose selection |

EOP2: End of Phase 2  
RMAT: Regenerative Medicine Advanced Therapy Designation  

Within 24 months Freeline will have 4 programs in the clinic.
Freeline’s platform creates value across all key strategic domains

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<tr>
<th>Domain</th>
<th>Value</th>
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<tr>
<td><strong>Efficacy</strong></td>
<td>Highest safe protein levels</td>
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<tr>
<td><strong>Addressable market</strong></td>
<td>Lowest dose, lowest COGS, broadest market opportunities, largest market sizes</td>
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<tr>
<td><strong>Pipeline</strong></td>
<td>Rich set of potential targets to develop</td>
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<td><strong>Durability</strong></td>
<td>Best long term coverage</td>
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<td><strong>Safety</strong></td>
<td>Lowest dose for necessary expression =&gt; low level unwanted DNA</td>
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Freeline’s platform creates value across all key strategic domains

- **Efficacy**: Highest safe proteins levels
- **Addressable market**: Lowest dose, lowest COGS, broadest market opportunities, largest market sizes
- **Pipeline**: Rich set of potential targets to develop
- **Durability**: Best long term coverage
- **Safety**: Lowest dose for necessary expression => low level unwanted DNA

~1,800 Secreted Proteins in the genome
~1,200 are within the Packaging limit of AAV
Thank you