Corporate presentation

July 2019
Freeline is a leading clinical stage gene therapy company focused on liver expression for chronic systemic diseases

<table>
<thead>
<tr>
<th>Proprietary capsid with best-in-class liver transduction profile, allowing for high protein expression levels</th>
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</thead>
<tbody>
<tr>
<td>Haemophilia B program in phase 1/2 demonstrating activity levels allowing for normalisation of FIX activity levels</td>
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<td>Robust pipeline with goal of filing a new IND every year</td>
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<td>- Fabry Disease program to start dosing 2019</td>
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<td>- Gaucher and 4th program (undisclosed) to initiate IND enabling studies in 2019</td>
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<td>- Good progress on research programs for chronic inflammatory diseases</td>
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<tr>
<td>Industry leading CMC platform at commercial quality and scale, supported by advanced analytics and in-house manufacturing capabilities</td>
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<td>£120m+ raised to date in Series A and B predominantly from Syncona</td>
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<tr>
<td>World leading founder and executive team with extensive track record in gene therapy, clinical translation, early and late stage development and global drug approvals</td>
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</table>
Executive team includes experienced leaders in gene therapy, manufacturing and clinical development
Successful expansion of global footprint and organisation

130 FTEs covering research, clinical development, process development, analytics and GMP manufacturing

- **United Kingdom**
  - HQ & Research Labs
  - Stevenage, UK
  - Manufacturing & QC
  - Stevenage, UK
  - Animal Labs
  - London, UK

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

- **United States**
  - Corporate Offices, New York, USA
Our technology builds upon the pioneering liver expressing gene therapy in Haemophilia B

First to prove long-term sustainable expression of systemic AAV gene therapy in humans

Prof. Amit Nathwani

First generation FIX gene therapy (NEJM 2011 and 2014)
Our technology builds upon pioneering liver expressing gene therapy in Haemophilia B

Limitations of First Generation constructs

Field set out to replicate the results of Prof. Nathwani with constructs very similar to his original construct:

- No change in protein level compared to original construct
- Not extendable to pipeline across indications due to low protein levels achieved

Next Generation

Improve construct with the aim of achieving higher protein expression
Aim for functional cure/normalisation
Create foundation for broad pipeline
Our best in class capsid is the foundation of our pipeline

Expression = Cassette x Gene x Capsid

- AAVS3 is a novel, human-selective liver tropic capsid with a high transduction efficiency of human hepatocytes
- Best in class liver specific promoter
- Optimised intron
- Codon-optimised gene
- Utilise gain-of-function mutations, when feasible
AAVS3 high tropism for the human liver verified in animal studies

FRG xenograft mouse model, chimeric human mouse liver model

Dose: 4e12 vg/kg

Source: Poster presented at ASH 2018 – “Preclinical Evaluation of an Engineered AAV Capsid in Non-Human Primates for the Treatment of Haemophilia B”
The strength of our proprietary capsid allows continuous development of broad pipeline.

- Proprietary capsid
  - Liver directed protein replacement for monogenic disorders
  - Other diseases treatable by protein replacement or enhancement
- Haemophilia
- Lysosomal storage disorders
- Chronic inflammatory diseases
Proprietary and balanced pipeline with two programs in the clinic by 2019

<table>
<thead>
<tr>
<th>Program</th>
<th>Research</th>
<th>IND enabling studies</th>
<th>Phase 1/2</th>
<th>Next Milestone</th>
<th>WW Rights</th>
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<tbody>
<tr>
<td>Haemophilia B</td>
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<td>Results from next dose cohort H2 2019</td>
<td>FREELINE</td>
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<tr>
<td>FLT180a</td>
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<td>Fabry Disease</td>
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<td>First human dose 2019</td>
<td>FREELINE</td>
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<tr>
<td>FLT190</td>
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<tr>
<td>Gaucher Disease</td>
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<td>Initiation of IND enabling studies</td>
<td>FREELINE</td>
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<tr>
<td>FLT200</td>
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<tr>
<td>Undisclosed Haematology</td>
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<td></td>
<td>Initiation of IND enabling studies</td>
<td>FREELINE</td>
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<tr>
<td>Undisclosed Inflammation</td>
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<td>Lead candidate selection</td>
<td>FREELINE</td>
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</table>
Normal blood coagulation occurs in people with FIX activity between 50 and 150%

**Normal coagulation**
- >60% needed to ensure coverage during surgery or trauma

**Normal**
- 50 – 150%

**Mild haemophilia**
- 5 – 40%

**Prolonged bleeds**
- >15% needed to prevent joint bleeds

**Mod/Sev Haemophilia**
- <5%

**Frequent spontaneous bleeds**
Normal blood coagulation occurs in people with FIX activity between 50 and 150%.

**FIX activity %**

- **Normal**
  - 50 – 150%

- **Mild haemophilia**
  - 5 – 40%

- **Mod/Sev Haemophilia** ≤ 5%

**Freeline has the potential to deliver the first and only AAV gene therapy capable of normalising FIX levels.**

**Prolonged bleeds**

- >15% needed to prevent joint bleeds

**Frequent spontaneous bleeds**

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Uijl et al. 2011. Analysis of low frequency bleeding data: the association of joint bleeds according to baseline FVIII activity level. Haemophilia (2011), 17, 41–4

WFH Guidelines on the management of haemophilia table 7.1 and 7.2
Patients and physicians want normal factor activity levels

Cowen physician panel October 2018 reported **60% of specialists** would like to see gene therapy leading to Factor IX levels within the normal range (50%-150%)

<table>
<thead>
<tr>
<th>Haemorrhage type</th>
<th>WFH Min. FIX level</th>
<th>Best practice</th>
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<tbody>
<tr>
<td>CNS</td>
<td>60 %</td>
<td>100% FIX level by bolus injection followed by continuous infusion maintained at 100% for a week after surgery</td>
</tr>
<tr>
<td>Throat and neck</td>
<td>60 %</td>
<td>Maintain the level over 80% for a further period until discharge.</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>60 %</td>
<td></td>
</tr>
<tr>
<td>Joint</td>
<td>40 %</td>
<td></td>
</tr>
<tr>
<td>Surgery</td>
<td>60 %</td>
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B-AMAZE is an open label Phase 1/2 study of FLT180a in Haemophilia B

**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 $\geq 18$ 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 trial design**

<table>
<thead>
<tr>
<th>Dose</th>
<th>Description</th>
<th>Concentration</th>
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<tbody>
<tr>
<td>Low dose</td>
<td>4.5e11 vg/kg (N=2)</td>
<td></td>
</tr>
<tr>
<td>Mid dose</td>
<td>1.5e12 vg/kg</td>
<td></td>
</tr>
<tr>
<td>Lower dose</td>
<td>7.5e11 vg/kg</td>
<td></td>
</tr>
<tr>
<td>Higher dose</td>
<td>3e12 vg/kg</td>
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</table>

**Sponsor:** UCL

1 hour infusion
6 months follow up
Long term follow-up in separate protocol
Dose 6e11 equals 4.5e11 with Ph3 standard
Dose 2e12 equals 1.5e12 with Ph3 standard
Prophylactic steroids from week 6 (1st cohort) or week 4 (2nd cohort)
With FLT180a at a low dose of $4.5 \times 10^{11}$ stable expression levels of 42-49% were achieved from week 14.

Source: ASH 2018 Oral Presentation by Prof. Nathwani: “A Single Intravenous Infusion of FLT180a Results in Factor IX Activity Levels of More Than 40% and Has the Potential to Provide a Functional Cure for Patients with Haemophilia B”
No spontaneous bleeding episodes during 9 and 6 months, respectively, of observation.

**Patient 1**

- **Prophylactic infusion Day 2**
- FIX Conc Usage IU/9 months
  - pre-GT: 0
  - post-GT: 50000

**Patient 2**

- FIX Conc Usage IU/6 months
  - pre-GT: 0
  - post-GT: 150000

**Number of bleeds**

- **Bleed rates No/9 months**
  - pre-GT: 0
  - post-GT: 3

- **Cut finger, no FIX infusion**

**Dose 6e11 vg/kg equals 4.5e11 vg/kg with Ph3 standard**

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

**Source**: ASH 2018 Oral Presentation by Prof. Nathwani: “A Single Intravenous Infusion of FLT180a Results in Factor IX Activity Levels of More Than 40% and Has the Potential to Provide a Functional Cure for Patients with Haemophilia B”
FLT180a has the potential to be the first Haemophilia B gene therapy to provide normalisation of FIX levels

- **Clinical superiority**: B-AMAZE Phase 1/2 data points to first gene therapy providing normalisation in haemophilia B
- **Rapid progression**: Optimised development plan with ongoing natural history study and use of surrogate endpoint allows for rapid progression to market
- **Clear regulatory pathway**: Potential qualification for accelerated regulatory review

FDA Draft guidance for industry. Human Gene Therapy For Haemophilia – July 2018
FLT190 – Fabry disease
The manifestations of Fabry Disease are broad and debilitating with significant unmet needs

**Disease characteristics**

- X-linked – men and women
- Alpha-galactosidase A (GLA) deficiency
- Accumulation of globotriaosylceramide (Gb3) primarily in vascular wall
- Affects a range of organs
- Renal and cardiac failure most common cause of morbidity
- Stroke is a common feature
Continuous high expression gene therapy holds potential for better treatment outcomes than ERTs

<table>
<thead>
<tr>
<th>Unmet needs</th>
<th>Role of high expressing gene therapy</th>
</tr>
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<tbody>
<tr>
<td>ERTs may stop progression but do not heal organ damage</td>
<td>Prevent disease progression</td>
</tr>
<tr>
<td></td>
<td>Rapid Gb3 clearance -&gt; improved renal function</td>
</tr>
<tr>
<td>High use of pain medicines due to peaks and troughs in ERT</td>
<td>Elimination of pain and GI symptoms</td>
</tr>
<tr>
<td>Ab development limiting treatment response</td>
<td>High expression level expected to lead to tolerization</td>
</tr>
<tr>
<td>Treatment barrier high leading to advanced disease</td>
<td>Earlier and simple intervention before organ damage</td>
</tr>
<tr>
<td>ERTs do not prevent stroke</td>
<td>Stroke risk likely to be reduced</td>
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</table>
FLT190 leads to reversal of kidney disease in GLA KO mice

Jeyakumar et al. Liver-directed gene therapy corrects Fabry disease in mice. Molecular Genetics and Metabolism 2019 Feb;126(2): Page S1, Poster #180

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)
...as well as reversal of heart disease in GLA KO mice

Jeyakumar et al. Liver-directed gene therapy corrects Fabry disease in mice. Molecular Genetics and Metabolism 2019 Feb;126(2): Page S1, Poster #180

FLT190 vector genome pseudo-typed with AAV8 in GLA KO mice; Dose: 2e12 vg/kg. Error bars represent 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)
FLT190 ready for first human dose in H1 2019

- Strong preclinical data
  - In-vitro and in-vivo data support achievement of therapeutic levels in humans
- High performing manufacturing process
  - CMC building on learnings from Haemophilia B programme
- Phase 1/2 ready for FHD 2019
  - MARVEL1 Phase 1/2 ready for dosing 2019
Platform technologies
Freeline has addressed the multiple steps to building a gene therapy platform delivering high systemic expression.
Our differentiated AAV manufacturing platform provides flexibility in readiness for commercial demands

**MAXIMISED POTENCY**
High product potency achieved through optimised cell line, plasmids and transfection system

**AGILE SUPPLY**
Single manufacturing platform meets demand from tox to commercial with low cost of goods

**HIGHEST QUALITY**
Quality built-in to product using proprietary technology and supported by world class analytics

**SPEED TO GMP**
Class-leading pipeline progression from candidate selection to GMP manufacture and commercialisation
Multiple value creating milestones with two programs in the clinic in 2019

<table>
<thead>
<tr>
<th>PROGRAM</th>
<th>2018</th>
<th>2019</th>
<th>2020</th>
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<tbody>
<tr>
<td>Haemophilia B</td>
<td>FLT180a - B-AMAZE cohort 1 results at ASH 2018</td>
<td>FLT180a - ASGCT: CMC platform presentations</td>
<td>FLT180a - B-AMAZE results</td>
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<td></td>
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<td>EOP2 meetings</td>
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<td></td>
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<td>Ph 3 enrolment</td>
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<tr>
<td>Fabry Disease</td>
<td>FLT190 - CTA approved for MARVEL1 (Ph 1/2)</td>
<td>FLT190 - Preclinical data WORLD 2019 FPFV MARVEL1</td>
<td>FLT190 - MARVEL1 initial clinical results</td>
</tr>
<tr>
<td>Gaucher</td>
<td>FLT200 - Generation of multiple candidates</td>
<td>FLT200 - Lead candidate selection</td>
<td>FLT200 - FHD Ph 1/2</td>
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<td>FLT200 - IND enabling studies initiated</td>
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EOP2: End of Phase 2  
FHD: First Human Dose  
PTPs: Previously Treated Patients