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Clinical-stage, fully integrated, next generation, systemic AAV gene therapy company dedicated to transforming the lives of patients suffering from systemic debilitating diseases

1. Proprietary capsid with significantly higher transduction efficiency in the liver

2. High protein levels at low doses allows us to target diseases perceived as beyond the reach of AAV GT

3. Potential for a functional cure for Haem B* with FIX expression levels in the normal range

4. Fabry clinical program demonstrating initial evidence of sustained αGLA activity levels

5. Proprietary analytics and CMC capabilities that can deliver high quality at commercial scale

6. Leadership Team with deep CMC, development & commercial expertise in GT and rare diseases

* Certain adult Haem B patients
Haemophilia B data validates AAVS3 capsid and platform

Our rationally designed AAVS3 capsid enables:
- Potent liver transduction
- High protein expression
- Low dose levels and improved safety margin

<table>
<thead>
<tr>
<th>Capsid</th>
<th>Dose (vg/kg)</th>
<th>FIX Activity Level (% Mean)</th>
<th>Study 1</th>
<th>Study 2</th>
</tr>
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<tbody>
<tr>
<td>AAV8</td>
<td>2T</td>
<td>73%</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>AMT061</td>
<td>5T</td>
<td>136%</td>
<td>15</td>
<td>2</td>
</tr>
<tr>
<td>SPK-9001</td>
<td>0.5T</td>
<td>92%</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>FLT180a</td>
<td>0.45T</td>
<td>99% **</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>FLT180a</td>
<td>0.975T</td>
<td>130%***</td>
<td></td>
<td></td>
</tr>
<tr>
<td>FLT180a</td>
<td>1.5T</td>
<td>168%</td>
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</tbody>
</table>

Steady state: 38% *  
Mean: 99% **  
Mean: 130%***

AAVS3 enables FIX activity levels in normal range

Normal Range

Mean: 5%  
Mean: 6%  
Mean: 41%  
Mean: 22%  
Mean: 38% *

T-values:
- Stable FIX activity levels at 38% at 52 weeks, and following an additional 52 weeks, or two years after infusion, we have continued to observe a durable response of 38% mean FIX activity in this cohort.
- Mean value calculated based on following FIX levels: patient 7 136% (d 21 +/-1), patient 8 82% (d 21 +/-1), patient 9 73% (d 21 +/-1), patient 10 105% (d 21 +/-1).
- Mean value calculated based on following FIX levels: patient 3 92% (d 21 +/-1), patient 6 168% (d 21 +/-1).

2. Poster presented at The 13th Annual Congress of the European Association for Haemophilia and Allied Disorders, EAHAD 2020
3. Miesbach et al; Blood 2018 131:1022-1031
Robust pipeline with retained global rights

<table>
<thead>
<tr>
<th>Programme</th>
<th>Research</th>
<th>IND enabling studies</th>
<th>Phase 1/2</th>
<th>Phase 3</th>
<th>Patient No. US &amp; EU</th>
<th>Development &amp; WW Commercial rights</th>
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</thead>
<tbody>
<tr>
<td>Haemophilia B</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>~ 9,000</td>
<td>FREELINE</td>
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<tr>
<td>FLT180a (RMAT designation)</td>
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<tr>
<td>Fabry</td>
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<td></td>
<td></td>
<td></td>
<td>~ 9,000</td>
<td>FREELINE</td>
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<tr>
<td>FLT190 (Orphan designations)</td>
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<td></td>
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<tr>
<td>Gaucher</td>
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<td></td>
<td></td>
<td></td>
<td>~ 6,000</td>
<td>FREELINE</td>
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<tr>
<td>FLT201</td>
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</tr>
<tr>
<td>Haemophilia A</td>
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<td></td>
<td></td>
<td></td>
<td>~ 38,000</td>
<td>FREELINE</td>
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<tr>
<td>FLT210</td>
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</tbody>
</table>

1. In the research stage, we conduct in vitro and in vivo preclinical studies to evaluate different product candidates to select those with the best tolerability and potency profiles.

2. In the IND enabling studies stage, we conduct preclinical in vivo studies in disease-specific mouse models and good laboratory practice, or GLP, toxicity studies in non-human primates and generate the CMC information and analytical data required for an investigational new drug, or IND, submission to the FDA for a clinical trial authorization, or CTA, submission to the EMA.

3. These figures represent the total approximate diagnosed population for each indication. The seroprevalence of antibodies against the AAV capsid renders approximately 30-50% of patients ineligible for gene therapy.

4. Owned and in-licensed intellectual property rights.

Fabry Disease epidemiology: Metchler et al 2012; Spada et al 2016; Fabry Registry; Fabry Outcome Survey; Waldeyer et al 2009; Oexen et al 2008.
The Freeline mission: To be life changers

Haemophilia B & A
Adaptive B-AMAZE trial in Haemophilia B designed to establish a dose that demonstrates normal range of FIX activity

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

Adaptive dose escalation design:
Aim is to establish effective dose (50 – 150% FIX)

Results to date have informed our optimised immune management strategy with the potential to prevent loss of factor IX expression during the critical period of 4 to 16 weeks

Immune management includes initiation of Prednisolone and Tacrolimus at week 3 with rapid taper of steroids until discontinuation at month 3; continue tacrolimus until discontinuation up to month 5. Immune management treatment includes patient monitoring for 9 months, followed by annual monitoring of FIX activity levels.

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

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

Oral treatment with Prednisolone and Tacrolimus at day 21 (post dosing) and continuing through month 3 for Prednisolone and up to month 5 for Tacrolimus*
Durable FIX activity achieved beyond 2 years

4.5e11 vg/kg - with short duration prophylactic steroid

Data as of 15th June 2020
Durable FIX activity levels in the normal range

Immune management includes initiation of Prednisolone and Tacrolimus at week 3 with rapid taper of steroids until discontinuation at month 3; continue tacrolimus until discontinuation up to month 5.

Immune management treatment includes patient monitoring for 9 months, followed by annual monitoring of FIX activity levels.

 FLT180a has demonstrated a favourable safety profile

No bleeds requiring supplemental FIX to date
Planning to file BLA in 2023

- **PHASE 1/2**: Patients 1 to 10 FIX activity at 6 months
  - Fully enrolled
- **EOP2 meeting**
- **PHASE 2b/3**: Run in study 6 months baseline
  - Enrolling

- **Long term safety study**
- **File BLA Accelerated Approval**

- **H2 2020**: PHASE 1/2
- **H1 2021**: EOP2 meeting
- **H1 2022**: Long term safety study
- **H1 2023**: PHASE 2b/3
- **H2 2023**: File BLA Accelerated Approval

**Legend**:
- S = Safety
- D = Durability
- E = Efficacy
The Freeline mission: To be life changers

Haemophilia A
Platform able to package shortened FVIII gene within the wild type AAV capacity

<table>
<thead>
<tr>
<th>Vector size comparison</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Standard</strong> 4.7 kbp</td>
</tr>
<tr>
<td><strong>AAV capacity</strong></td>
</tr>
<tr>
<td>SB-525 1</td>
</tr>
<tr>
<td>SPK-8011/SPK-8016 2</td>
</tr>
<tr>
<td>BMN270 3</td>
</tr>
<tr>
<td>FLT210</td>
</tr>
</tbody>
</table>

**Key attributes of FLT210:**

- **Smallest known** liver specific promoter
- **Shortened FVIII gene** to reduce expression cassette size
- **Allows expression cassette** to fit within the **natural capacity** of AAV capsid

**Delivery of more functional intact transgenes and predictable, less variable expression**

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**Sources of construct sizes:**

1. As presented at ASGCT (2016) and WFH (2020)
2. As documented in patent (int. patent number: WO 2016/025764 A2)

**Note:** Haem A candidate nomination reached. Toxicology, CMC and disease animal model confirmation work ongoing.
The Freeline mission: To be life changers

Fabry & Gaucher disease
Fabry mouse model demonstrates increased GLA expression and reduction in pathologic substrate

Kidney GLA activity levels

Heart GLA activity levels

Electron microscopy x5000

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 ± 5D
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)
Adaptive Phase I/II dose finding study in previously treated and naive patients with Fabry disease

**Dose finding plan**
*For patients with prior ERT therapy*

- 0.75e12 vg/kg
- 1.5e12 vg/kg
- 4.5e12 vg/kg
- 1.5e13 vg/kg

**Patient 1 results:** FLT190 demonstrated durable increases in plasma GLA in Patient 1 at lowest dose

- Baseline - Patient 1
- Steady state – Patient 1

*Normal range for GLA in plasma is 5-9 nmol/hr/ml*

Below 1 nmol/hr/ml is diagnostic for Fabry disease

Data as of 15th June 2020
The Freeline mission:
To be life changers
Low doses of longer acting FLT201 result in high uptake in tissues commonly affected by Gaucher Disease

**Conclusion**

- **Novel GCase variant FLT201** is more stable in serum than wild-type protein
- This leads to a greater than 20 fold increase in potency vs. wild type GCase and better substrate clearance in Gaucher mice
The Freeline mission: To be life changers
Platform built on deep AAV expertise enables supply of pipeline of products with the goal of maximising safety and efficacy

What we have

Proprietary promoters and construct designs

Why it’s important

✓ Product safety built into manufacturing design from the start
✓ High product potency enabling lower dose
✓ Increased predictability and longevity
✓ Enhanced production yield and low cost of goods
✓ Agile supply allowing fast response to changing business needs
<table>
<thead>
<tr>
<th>BRAMMER</th>
<th>GMP manufacture (iCELLis® 500)</th>
<th>novasep</th>
<th>FREELINE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cambridge, MA, US</td>
<td>Haem B</td>
<td>Seneffe, BE</td>
<td>Stevenage, UK</td>
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<tr>
<td></td>
<td>Fabry</td>
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<tr>
<td></td>
<td>Gaucher, Haem A, future pipeline</td>
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</tbody>
</table>

**FREELINE**

**Cambridge, MA, US**

- Haem B
- Fabry
- Gaucher, Haem A, future pipeline

**Seneffe, BE**

- Haem B
- Fabry

**Stevenage, UK**

- Haem B
- Fabry
- Pipeline

**Multiple supply chains running same commercial-scale production platform**

**Long term clinical/commercial facility planned**
The Freeline mission: To be life changers
Multiple near-term value-creating milestones expected

**2020**

- **Haem B** - Completed enrollment and dosing for Phase 1/2 study
- **Haem B** - Initiated baseline screening study
- **Haem B** - Present longer durability data from Phase 1/2 study
- **Fabry** - Submit IND
- **Fabry** - Resume dosing
- **Platform** - Secured Brammer capacity for potential Haem B product candidate commercialisation

**2021**

- **Haem B** - Initiate pivotal study
- **Haem B** - Present durability data up to 3 years
- **Haem A** - Complete preclinical proof of concept study
- **Fabry** - Complete dose escalation in Part 1 of Phase 1/2 study
- **Gaucher** - Initiate Phase 1/2 study
- **Platform** - Further develop plans for Freeline manufacturing facility
Clinical-stage, fully integrated, next generation, systemic AAV gene therapy company dedicated to transforming the lives of patients suffering from systemic debilitating diseases

- Potent capsid & high protein levels
- Durable efficacy in the normal range
- Broad proprietary pipeline
- Committed to functional cures
- Quality driven by CMC & Analytics
- Leadership with deep expertise
Thank you