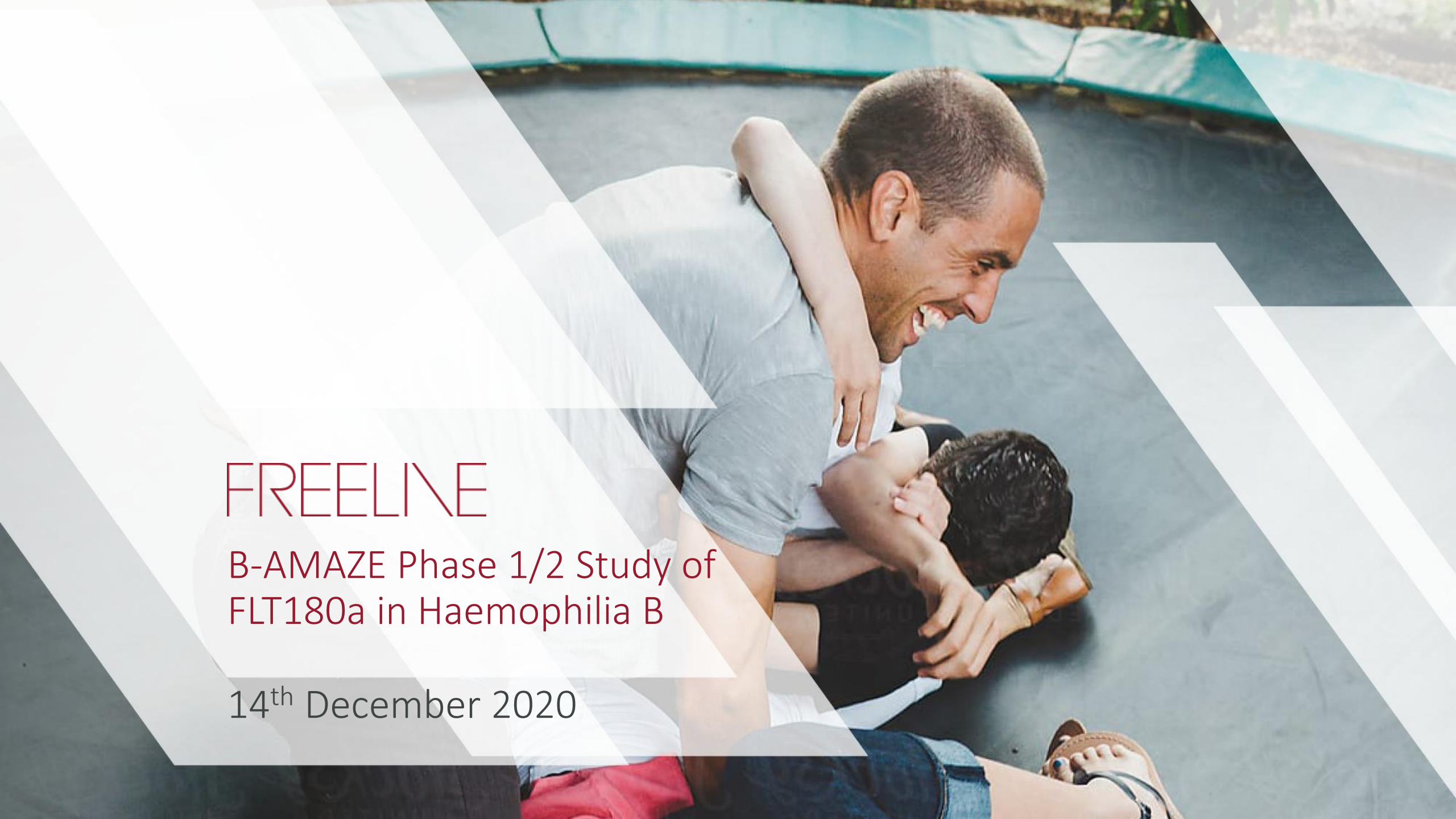

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B-AMAZE Phase 1/2 Study of FLT180a in Haemophilia B

14th December 2020

Legal Disclaimer

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Today's agenda

1	Opening remarks	*Theresa Heggie, CEO*
2	Data update from the B-AMAZE Phase 1/2 Study – Verbrinacogene setparvovec (FLT180a)	*Professor Amit Nathwani, Founder*
3	The importance of being in the normal range	*Professor Guy Young, FLT180a US PI*
4	Haemophilia B programme – next steps	*Dr. Julie Krop, CMO*
5	Summary	*Theresa Heggie, CEO*
6	Q&A	

FREELINE Mission: To be life changers

Our vision

Freeline's vision is to be a fully integrated, next generation, systemic, liver-directed AAV gene therapy company dedicated to transforming the lives of patients suffering from systemic debilitating diseases.

Our mission

To deliver functional cures for monogenic diseases, followed by expansion to address diseases requiring higher protein expression.

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B-AMAZE Phase 1/2 Study data update – Verbrinacogene setparvovec (FLT180a)

Prof. Amit Nathwani, UCL

The Freeline mission:
To be life changers

Haemophilia gene therapy: Current state of the art

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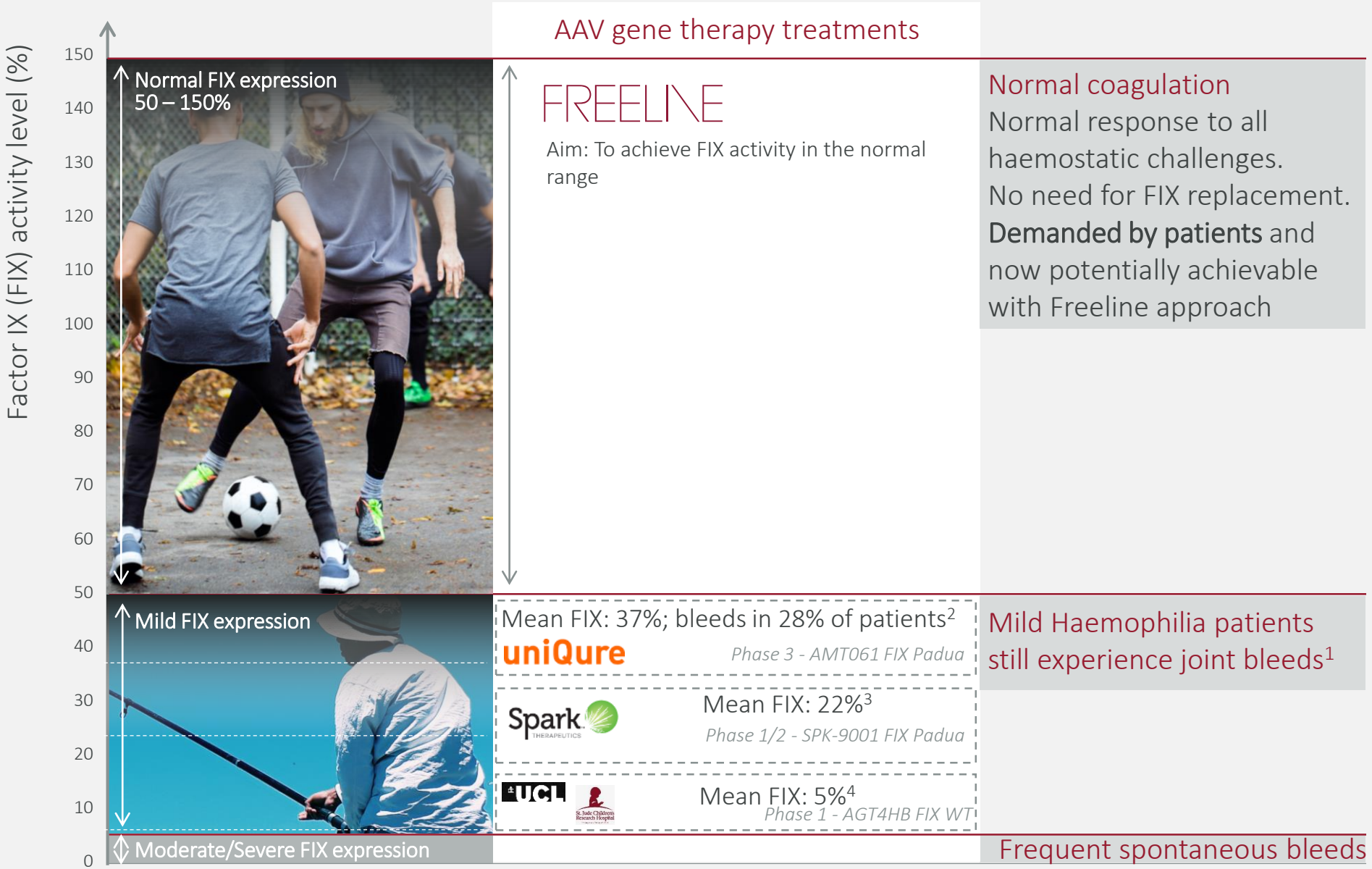

1. The frequency of joint hemorrhages and procedures in nonsevere hemophilia A vs B. Soucie et al. 2018 blood advances
2. uniQure's late-breaking ASH abstract; first data from the Phase 3 HOPE-B Gene Therapy Trial. 54 patients week 26 data
3. Pfizer R&D Day Sep 2020 – 4 year follow-up data in 15 patients from Phase 1/2 trial. Note, now in Phase 3 development
4. Nathwani et al; N Engl J Med 2014; 371:1994-2004

Freeline is committed to developing a functional cure for people with haemophilia B using its potent, proprietary, AAV gene therapy that has the potential to normalise FIX activity levels

Protection during vigorous activities

"…I don't have a very sporty life…spontaneous bleeds occur when I travel or play sports…and therefore I am still at home most of the time for fear of bleeding…"

Freedom from fear of trauma

"Now that my toddler is walking, I find myself more worried for each fall and bruise I see"

Enabling patients to lead active unconstrained lives

"I've got new hopes for the future. Before the gene therapy treatment, travel wasn't an option, but now I can chuck on a backpack and go, as long as the gene therapy continues to work."

Source of quotes: market research conducted including 15 patient interviews and one of the first patients in Freeline's FLT180a clinical trial

FLT180a builds on our experience in Haemophilia B product candidates using scAAV2/8-LP1-FIXco

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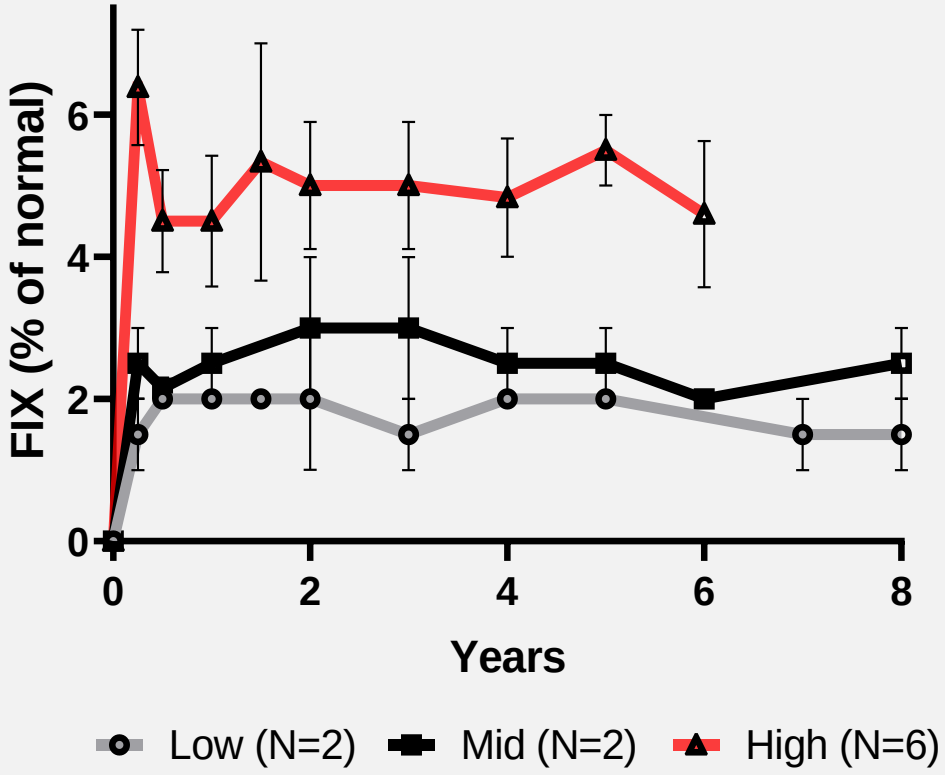
St Jude UCL study established the long term durability of AAV vectors

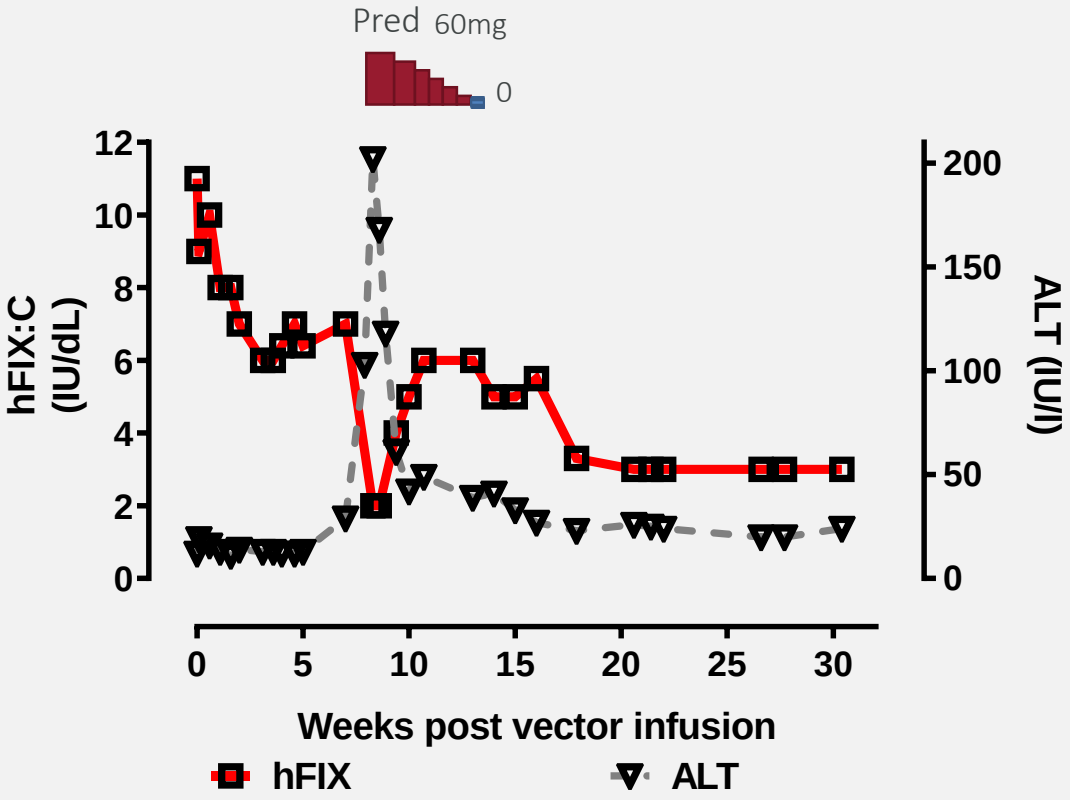
FIX expression



- Stable expression following a single administration of AAV2/8-LP1-hFIXco
- Median follow-up 6.7 +/- 1.0 years (5.1-8.6; median, SD, range)
- >80% reduction in bleed rates
- >60% reduction in FIX concentrate use
- No long-lasting or late toxicities

Reiss et al; ASH 2018; Nathwani et al; N Engl J Med 2011 and 2014

Transaminitis is the only vector related toxicity following systemic administration of AAV vectors



- Subclinical, self limiting transaminitis
- Occurs with all serotypes
- Occurs between 4-14 weeks after gene transfer
- Severity is dose dependent
- Responds to corticosteroids
- Delay in administration of corticosteroids can lead to reduction or loss of transgenic FIX protein expression

Patient 6 from original St. Jude/UCL study

FLT180a, Next generation AAV vector

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Our rationally designed AAVS3 capsid enables:

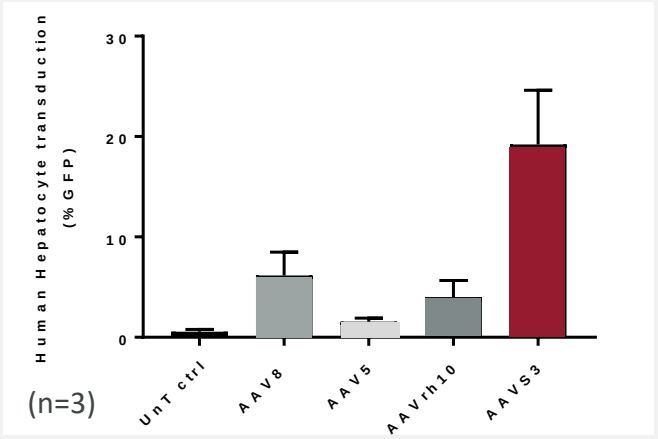
- Potent liver transduction
- High protein expression
- Low dose levels and improved safety margin

Expression = Cassette x Gene x Capsid

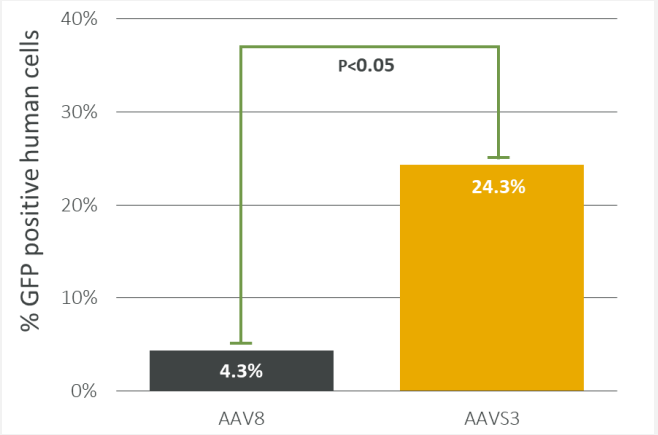
Cassette	Gene	Capsid (AAVS3)
Potent liver specific promoter Optimised intron	FIX-Padua gain-of-function mutation	Synthetic **human** adapted capsid with high tropism for liver *(Wild type capsids are poor transducers of human hepatocytes)*

Higher transduction of human hepatocytes with AAVS3

Primary Hepatocytes



FRG-Xenograft mouse model



B-AMAZE Phase 1/2 Study designed to establish a dose that delivers FIX activity in the middle of the normal range

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Objective

To assess the safety and efficacy following FLT180a administration

Key inclusion criteria

- Severe or moderate Haemophilia B ≤ 2%
- Adults ≥18 years

Key exclusion criteria

- Neutralising antibodies to AAVS3
- Liver disease

Endpoints

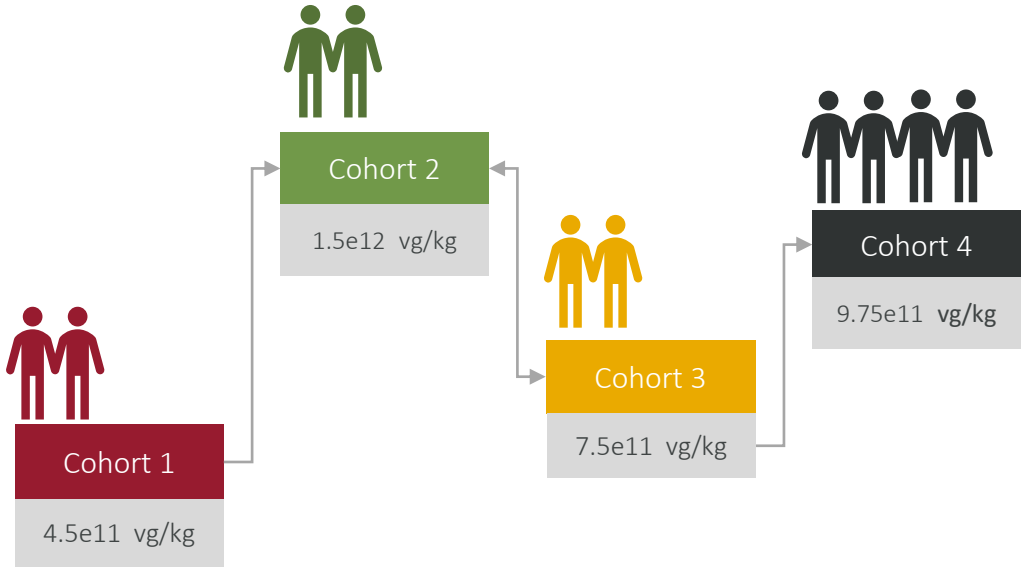
- Safety
- FIX activity level

Target range for dose finding

- 70 to 150%

Adaptive dose escalation design:

Aim is to establish effective dose (50 – 150% FIX)



Immune management strategy	• Prophylactic/reactive immunosuppression with Corticosteroids +/- Tacrolimus • Intensive monitoring

Sponsor: University College London
Funding: Freeline

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

Phase 1/2 Study: key baseline parameters

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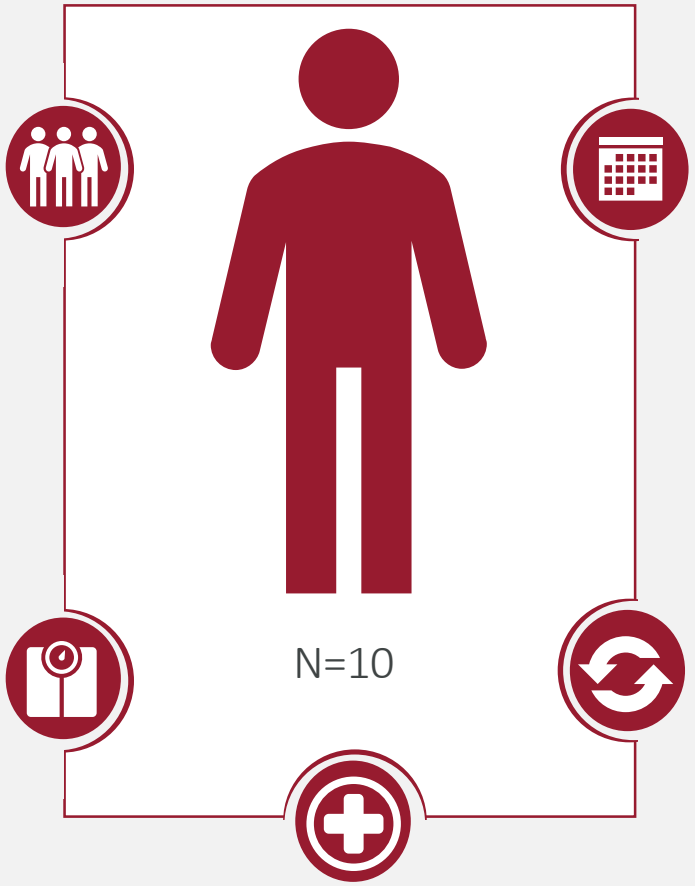
Severe haemophilia B

≤ 2% FIX activity



Age

25 to 67 years

Bodyweight

68 to 100 kg

Annual FIX replacement

~40K to ~420K

IU per year

ABRs

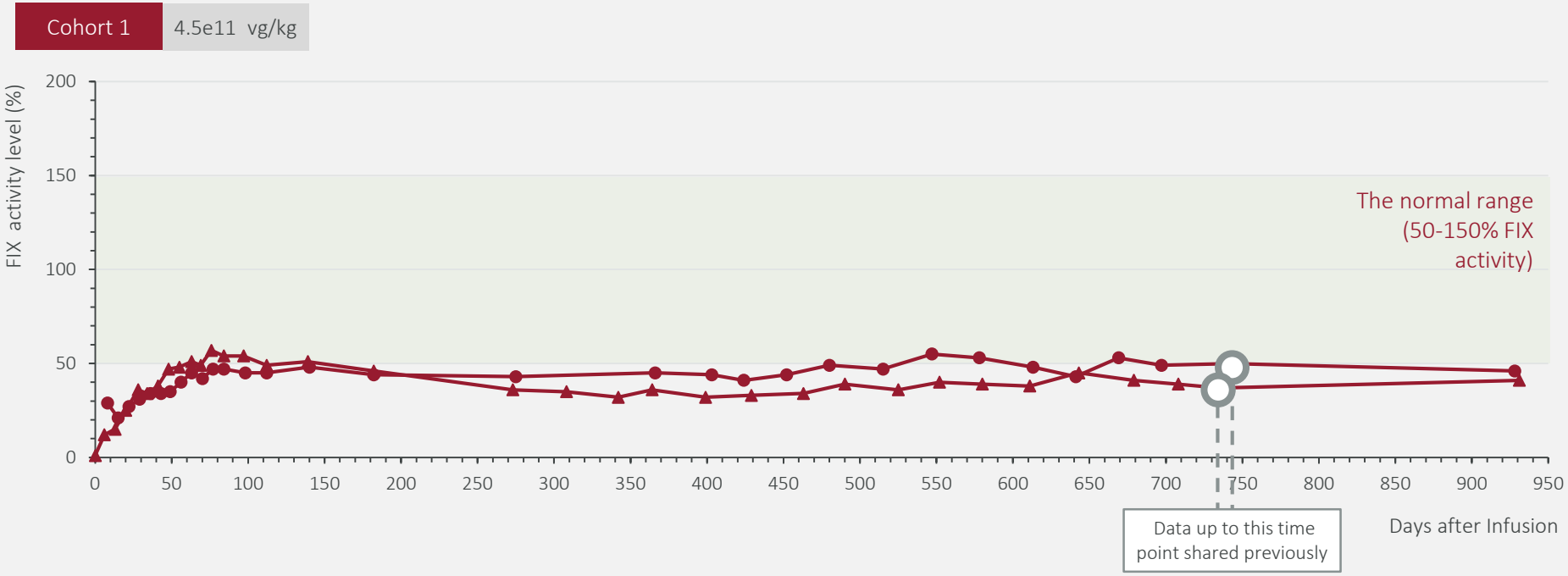
0.33 to 6.33

Verbrinacogene setparvovec (FLT180a): favourable safety profile and well tolerated

FREELINE Key safety results

- No infusion reactions and no discontinuations of infusion
- No other allergic reactions to date
- Most common drug related SAE was transient transaminitis. Manifests as an elevation in ALT +/- a decrease in expression and is not a safety signal
- A single patient in the highest dose cohort developed thrombosis of AV fistula in the context of supraphysiological FIX levels

No patients in the trial required supplemental FIX post treatment.* Patients receiving the low dose show durable FIX activity (~44%) for almost 3 years just below the normal range



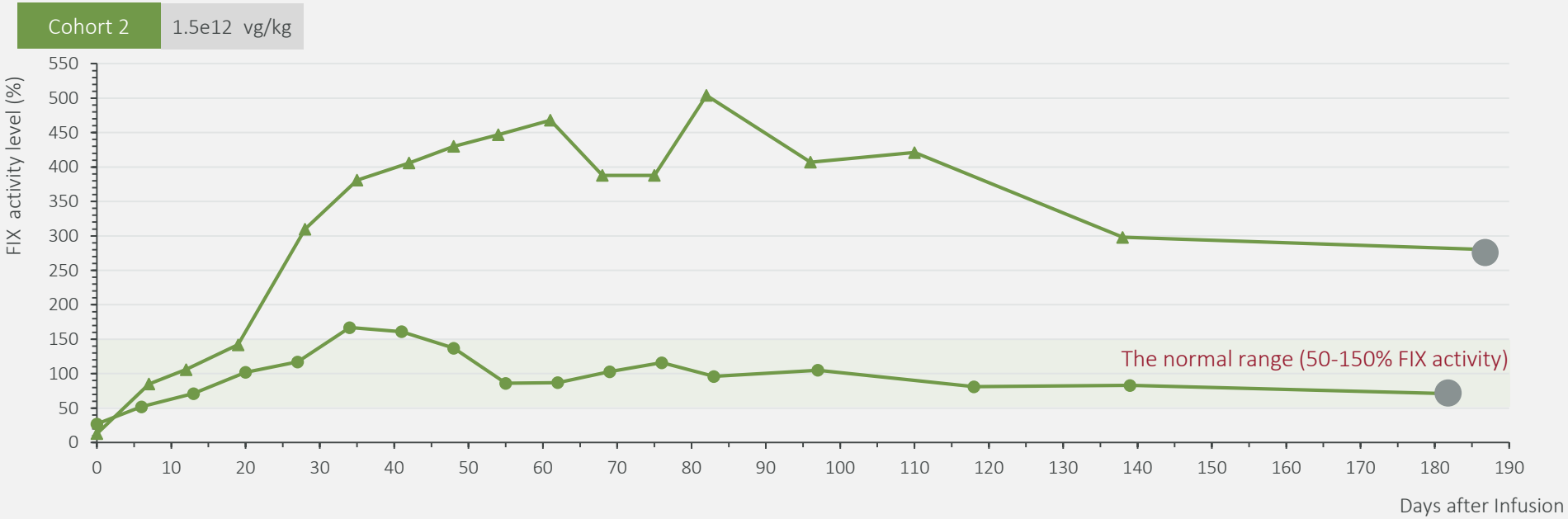
One-stage assay, central laboratory measurement

Data as of 21st August 2020

Data up to this time point shared previously

*In cohort 3 (7.5e11 vg/kg) one patient lost expression and resumed FIX prophylaxis

1.5e12 vg/kg dose demonstrates potency of the AAVS3 capsid but is not the go forward dose for the haemophilia B program



One-stage assay, central laboratory measurement

Data as of 21st August 2020

Had completed 6 month follow-up at previous data update (July 2020, ISTH)

A dose between 7.5e11 & 9.75e11 vg/kg has the potential to achieve FIX activity in the normal range

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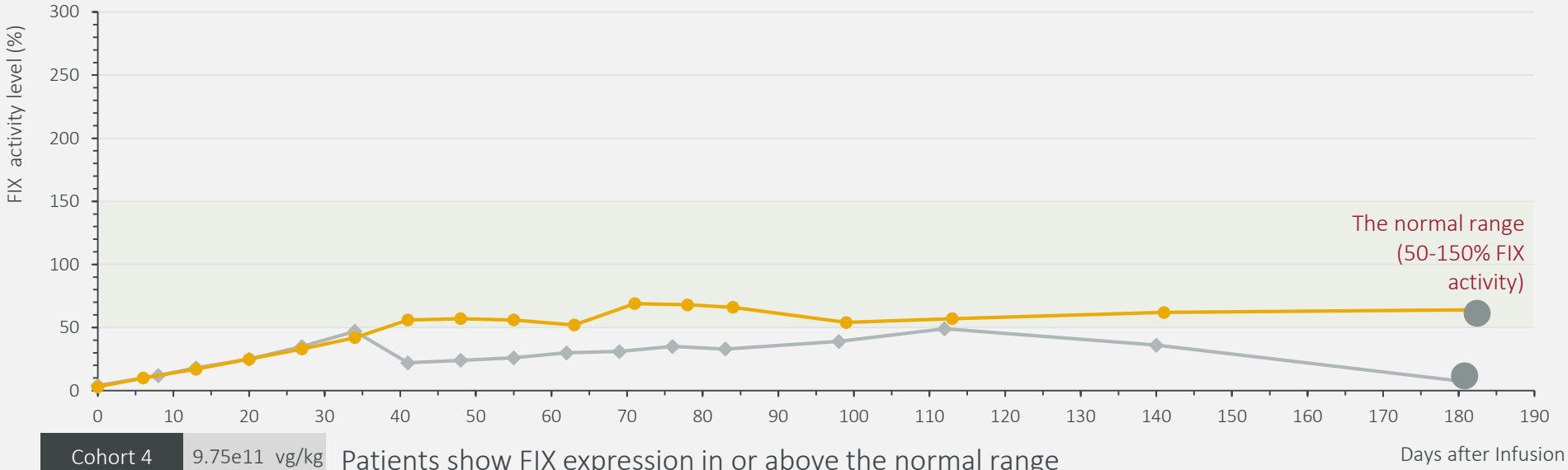
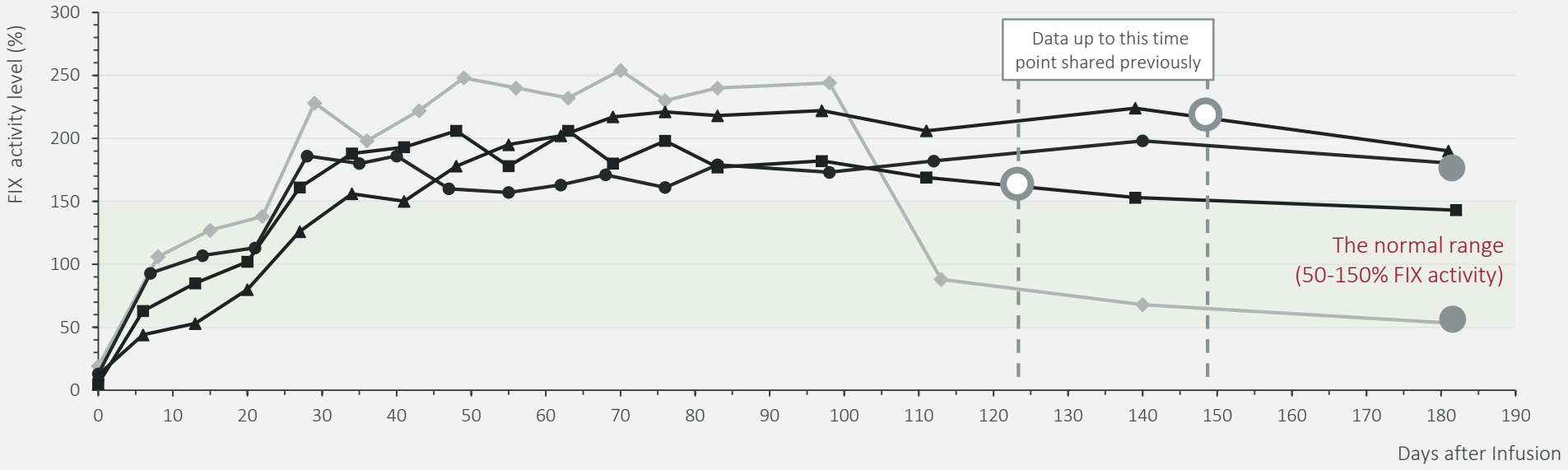
Cohort 3 | 7.5e11 vg/kg

Patient with controlled ALT levels showed stable expression in the normal range



Cohort 4 | 9.75e11 vg/kg

Patients show FIX expression in or above the normal range



One-stage assay, central laboratory measurement

Data as of 21st August 2020

ALT = alanine aminotransferase

Had completed 6 month follow-up at previous data update (July 2020, ISTH)

Data up to this time point shared previously

Patient experienced loss of expression due to transaminitis

*In cohort 3 (7.5e11 vg/kg) one patient lost expression and resumed FIX prophylaxis

Verbrinacogene setparvovec (FLT180a): potential to provide a functional cure by normalising FIX activity

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Key learnings from the B-AMAZE Phase 1/2 Study

- ✓ Demonstrated that the dose with potential to achieve FIX activity in the normal range is expected to be between 7.5e11 and 9.75e11 vg/kg
- ✓ Stable and durable response up to almost 3 years post treatment to date
- ✓ No bleeds requiring supplemental FIX
- ✓ Favourable safety profile
- ✓ Short course of prophylactic tacrolimus combined with prophylactic prednisone and close monitoring expected to preserve expression and eliminate the need for FIX supplementation

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The importance of being in the normal range

Prof. Guy Young,
Children's Hospital Los Angeles

The Freeline mission:
To be life changers

Haemophilia B programme – next steps

Dr. Julie Krop

The Freeline mission:
To be life changers

Successful EOP2 meeting with FDA supports initiation of pivotal phase 2b/3 trial

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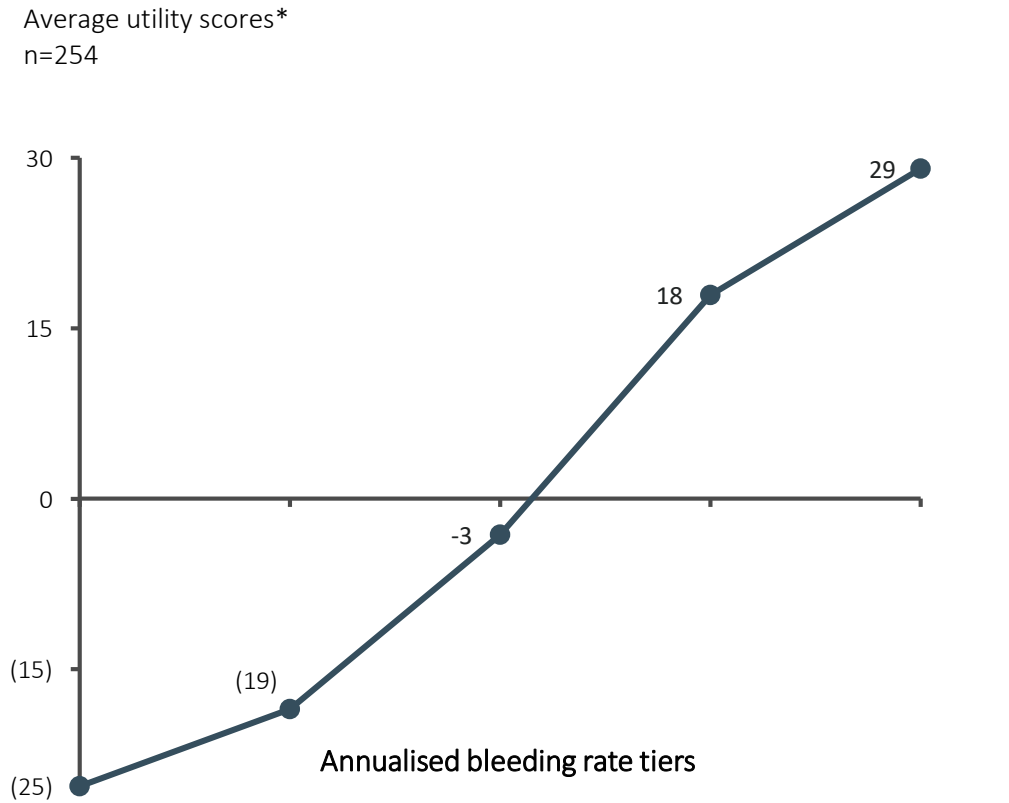
The Freeline mission:
To be life changers

Summary

Theresa Heggie

Physician market research indicates a strong preference for a gene therapy that consistently achieves FIX expression in the normal range



Eliminating bleeds is a important consideration for physicians in selecting gene therapy

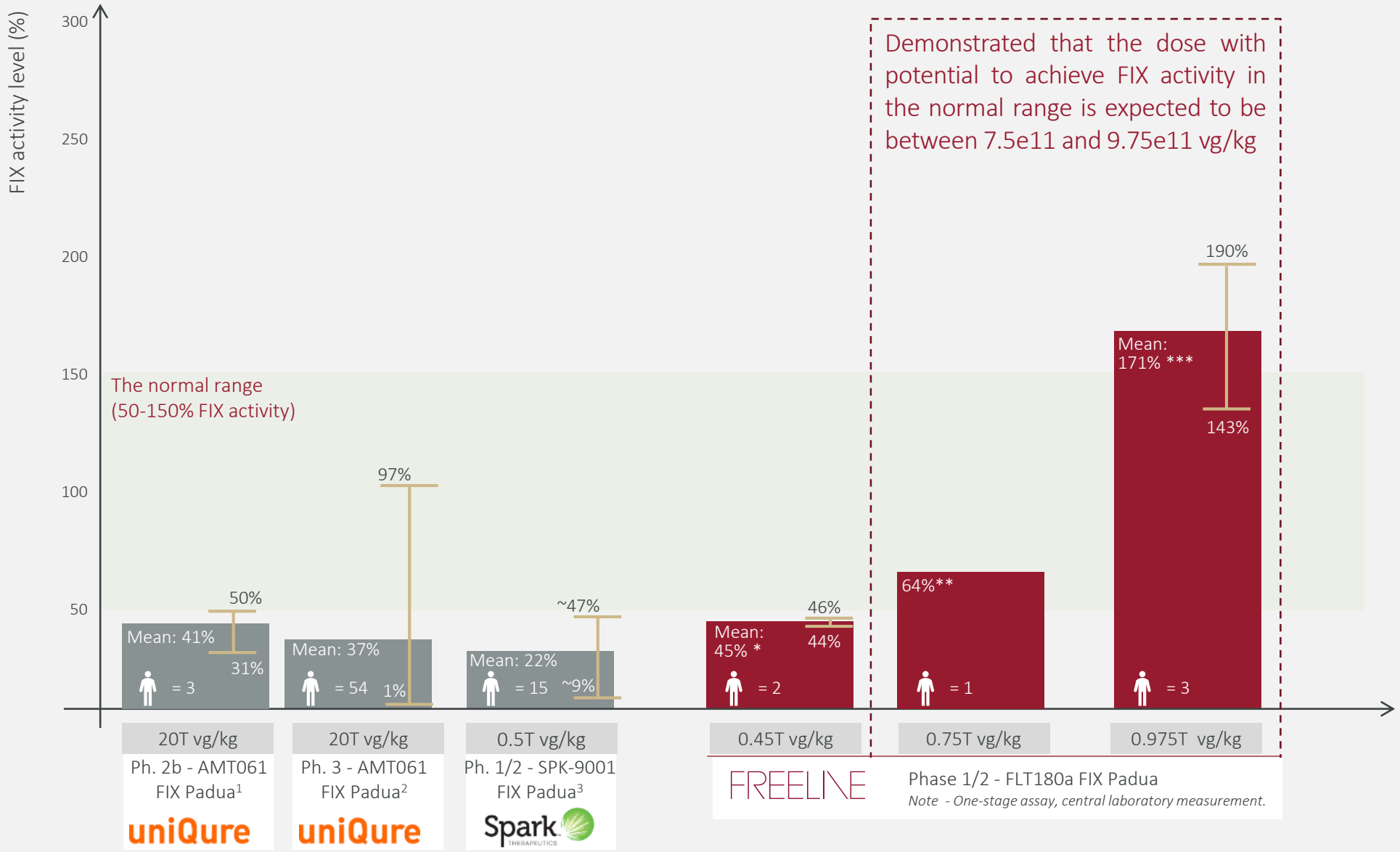
The inflection point between tiers 3 and 4 shows that physicians have high preference for a gene therapy which eliminates bleeding

"…Stopping bleeds is the most important clinical outcome…If I were to recommend I would choose a gene therapy that eliminates spontaneous bleeds…"

*Shows the relative physician preference for each level within the ABR attribute– more positive values equate to higher physician preference; ^percent of patients who experience at least 1 bleed

Source: Market research - interviews, survey and analysis

Verbrinacogene setparvovec (FLT180a) has the potential to deliver FIX activity in the normal range at low doses



T= e12

Freeline = One-stage assay, central laboratory measurement

* 4.5e11 dose: mean value calculated based on following FIX levels: patient 1, 44%% (week 26), patient 2 46% (week 26)

** 7.5e11 dose: value of patient 5 64% (week 26). Patient 4 experienced loss of expression due to transaminitis

*** 9.75e11 dose: mean value calculated based on following FIX levels: patient 8 180% (week 26), patient 9 190% (week 26), patient 10 143% (week 26). Patient 7 experienced loss of expression due to transaminitis

1. Miesback et al; Blood 2018 131:1022-1031

2. uniQure's late-breaking ASH abstract; first data from the Phase 3 HOPE-B Gene Therapy Trial. 54 patients week 26 data

3. Pfizer R&D Day Sep 2020 – 4 year follow-up data in 15 patients from Phase 1/2 trial. Note, now in Phase 3 development

Verbrinacogene setparvovec (FLT180a): potential to provide a functional cure by normalising FIX expression

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1. Dose for the pivotal trial: 6 month data from Phase 1/2 trial indicates that a dose between 7.5e11 and 9.75e11 vg/kg has the potential to deliver FIX activity in the normal range and eliminate need for supplemental FIX
2. Demonstrated durability: Stable and durable response up to almost 3 years post treatment to date in first patient cohort
3. Favourable safety profile: FLT180a has had no infusion reactions or discontinuations of infusion and no antibodies to FIX
4. Immune management regimen evolves: Shorter period of prophylactic immune management with close monitoring to preserve expression and protect patients
5. Next steps: Aim to initiate FLT180a pivotal trial in 2021

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Q&A

FREELINE Our mission: To be life changers