



Meet AZN Management: **ASBMR 2026**

Conference call and webcast
for investors and analysts

12 October 2026



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Meet AZN Management @ ASBMR – agenda

Furthering our ambition in Rare Disease

Marc Dunoyer, CEO, Alexion, AstraZeneca
Rare Disease

efzimfotase alfa: developed to address broad HPP population

Gianluca Pirozzi, SVP, Head of Development, Regulatory & Safety

efzimfotase alfa: Phase III HICKORY

Dr. Raja Padidela, Consultant Pediatric Endocrinologist & Metabolic Bone Diseases, Royal Manchester Children's Hospital

efzimfotase alfa: opportunity beyond Strensiq

Marc Dunoyer, CEO, Alexion, AstraZeneca
Rare Disease

Establishing the pipeline for today and tomorrow

Marc Dunoyer, CEO, Alexion, AstraZeneca
Rare Disease

Q&A session



Furthering our ambition in Rare Disease

Marc Dunoyer

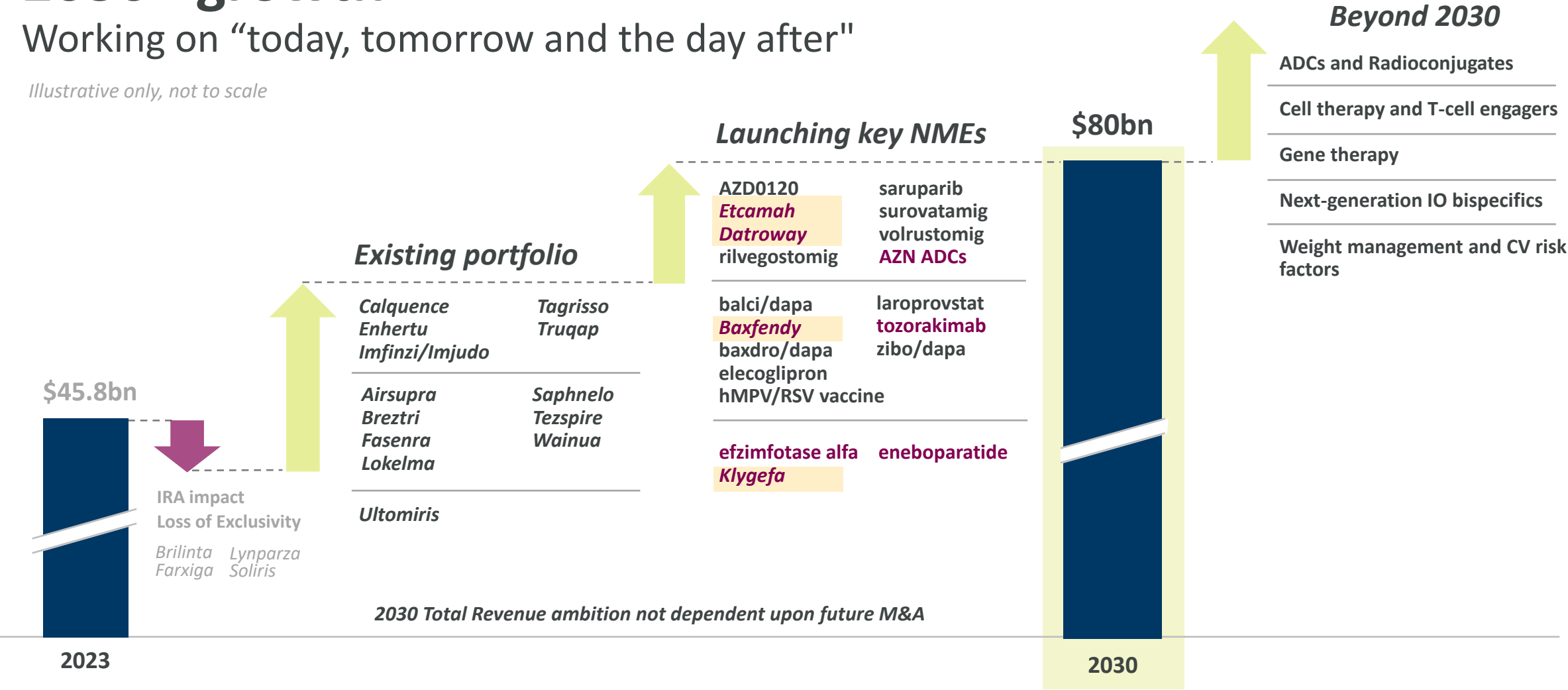
CEO, ALEXION, ASTRAZENECA RARE
DISEASE



Ambition – \$80bn Total Revenue by 2030 & sustained 2030+ growth

Working on “today, tomorrow and the day after”

Illustrative only, not to scale



Launched NME Positive Phase III data for NME

5 Note: Ambition to achieve \$80bn in Total Revenue by 2030 is risk-adjusted, based on long-range plan as of AstraZeneca Investor Day May 2024. Medicines and assets listed reflect key contributors to 2030 Total Revenue ambition; however, this list is not exhaustive. Medicines and assets listed in alphabetical order and sorted by therapy area. Laroprovstat previously AZD0780 and elecoglipron previously AZD5004. Collaboration partners: Daiichi Sankyo (*Enhertu, Datroway*), Amgen (*Tezspire*), Ionis (*Wainua*), Merck & Co., Inc. (*Lynparza*). Appendix: [Glossary](#).



Rare Disease – significant unmet need globally

10,000+ known rare diseases¹
(**<10%** have approved treatment²)

7 in 10
rare diseases begin in childhood¹

80%
of rare diseases are genetic¹

6+ years
average time to diagnosis¹

Our vision is to advance the **next wave of rare disease innovation to revolutionise care** and explore potential cures for patients



Rare Disease – our disease areas of focus



Haematology,
Nephrology &
Transplant

Neurology

Bone &
Endocrine
Disorders

Cardiology &
Amyloidosis

Rare Tumours

Targeting areas of high unmet need with best- or first-in-class potential



efzimfotase alfa: developed to address broad HPP population

Gianluca Pirozzi

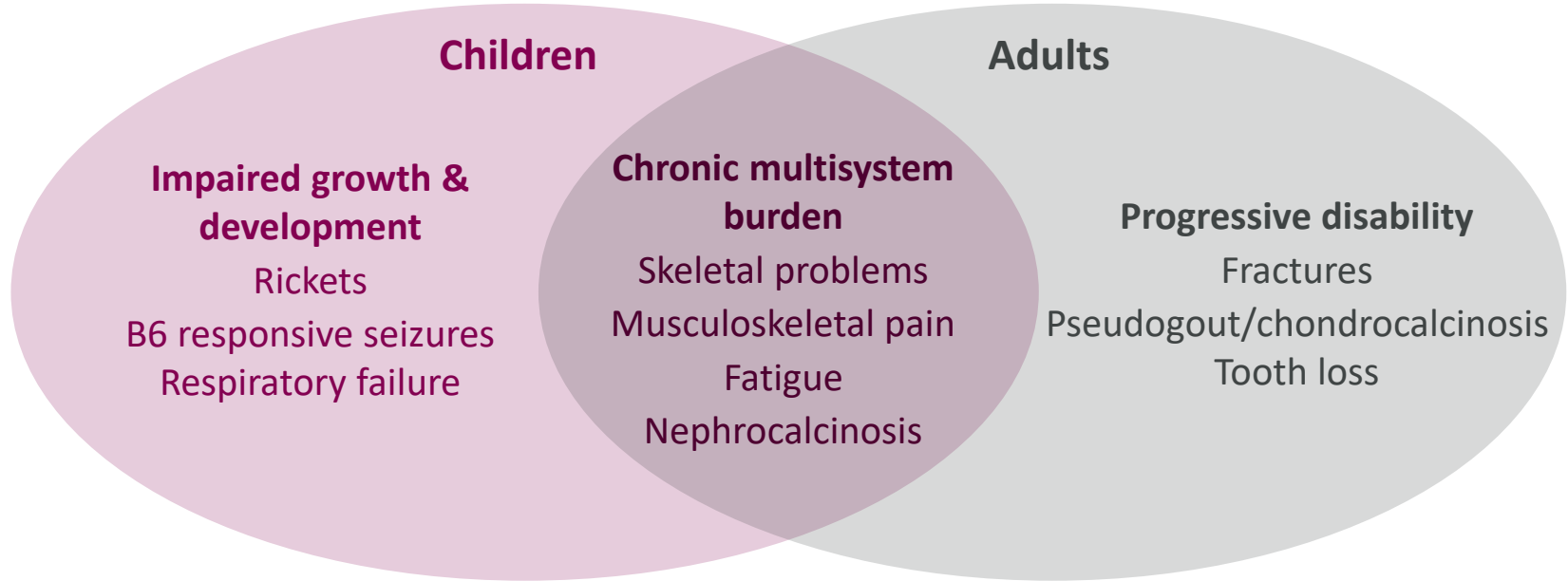
SVP, HEAD OF DEVELOPMENT,
REGULATORY & SAFETY



HPP is an inherited, heterogeneous disease affecting patients of all ages

Hypophosphatasia (HPP) is caused by deficient ALP activity affecting patients of all ages.
HPP is heterogeneous and multisystemic, with a range of skeletal and functional manifestations significantly impacting quality of life

People living with HPP have low ALP levels which can lead to¹:



efzimfotase alfa is a second-generation ERT designed to address broad spectrum of patients with HPP

Improved molecule with key differences vs *Strensiq*

Enhanced enzyme activity	Lower therapeutic dose
Optimised Fc design	Reduced off-target interactions
Enhanced glycosylation	Longer exposure
Manufacturing optimisation	Less wastage

	Strensiq®	efzimfotase alfa
Target patients	Paed onset + bone symptoms	All HPP patients >2yrs
Bone	✓	✓
Physical, & pain and fatigue	Limited to RWE	✓
Robust clinical data, broad spectrum of HPP patients		✓
Administration frequency	3 to 6x per week	Q2W
Fewer injection site reactions		✓
Strong safety profile	✓	✓



HPP – efzimfotase alfa Phase III programme

	 MULBERRY STUDY <i>2–<12 yr</i> <i>Treatment-naïve</i>	 CHESTNUT STUDY <i>2–<12 yr</i> <i>Switch from Strensiq (asfotase alfa)</i>	 HICKORY STUDY <i>≥12 yr</i> <i>Treatment-naïve</i>
Control ^a	Placebo	Active (asfotase alfa)	Placebo
Blinding	Double-blind	Open-label	Double-blind
Treatment allocation	2:1 (N=29)	1:1 (N=43)	2:1 (N=124)
Primary endpoint ^b	RGI-C score	Incidence of TEAEs	6MWT
Key secondary endpoints ^b	RSS	RGI-C, RSS	STS, LEFS, BPI-SF ^c , FACIT-Fatigue

Three complementary studies to evaluate efficacy and safety in a **broad HPP population** with diverse disease manifestations using **skeletal, functional, and safety endpoints**

11 a. In the CHESTNUT trial, treated patients must have been treated with 6 mg/kg per week asfotase alfa for at least the 6 months before study initiation. In the HICKORY and MULBERRY trials, treatment-naïve patients must have had no prior exposure to asfotase alfa. b. Endpoints were assessed as change from baseline to week 25, except for RGI-C (which was assessed at week 25) and incidence of TEAEs (which was cumulative throughout the randomized period). c. Pain severity score. Appendix: [Glossary](#).



HPP: efzimfotase alfa – key takeaways from MULBERRY and CHESTNUT trials

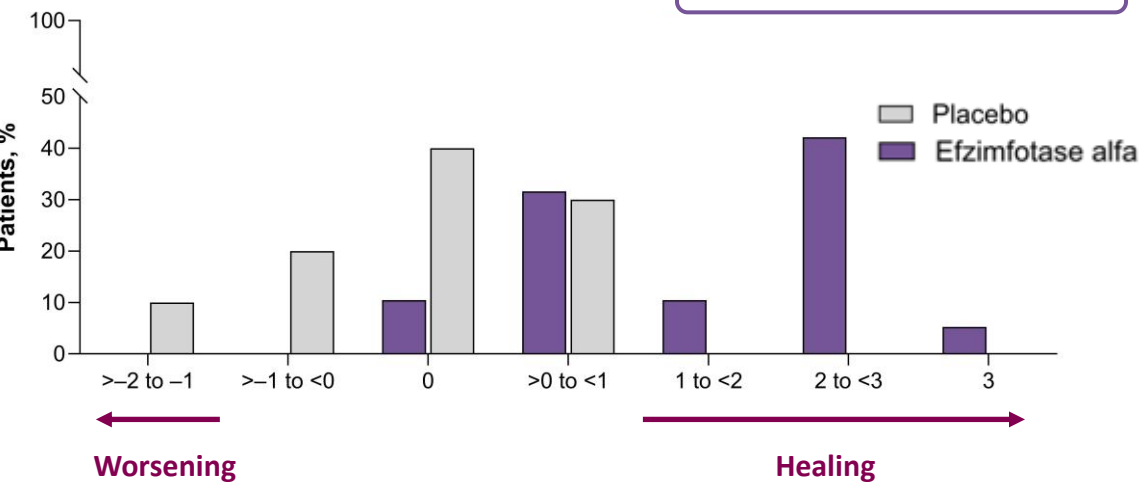
Primary endpoint | Bone Health by RGI-C^{a,1}



MULBERRY
 STUDY
 2–<12 yr, treatment-naïve



CHESTNUT
 STUDY
 2–<12 yr, open-label
 switch from asfotase alfa



- Met primary objective: similar **TEAE** incidences with **efzimfotase alfa (90.5%^d)** and **asfotase alfa (86.4%^d)**
- Met secondary objectives: maintained prior therapeutic benefits of asfotase alfa on **bone health**, **physical function**, and **quality of life**

RGI-C, Week 25 ^b	efzimfotase alfa (n=19)	Placebo (n=10)
Observed median	1.670	0.000
Median difference (95% CI)	1.67 (0.66, 2.00)	
P value ^c	0.0003	

Meaningful improvements in **bone health**, **physical function** and **quality of life**, with **favourable safety**

a. RGI-C rates the change in overall rickets severity from baseline using a 7-point scale from -3 (severe worsening) to +3 (complete healing), with 0 indicating no change. b. Observed mean values were 1.333 for efzimfotase alfa and -0.134 for placebo. c. Assessed by Wilcoxon rank-sum test. d. 95% CIs were 69.6%–98.8% for efzimfotase alfa and 65.1%–97.1% for asfotase alfa. 1. Whyte MP, et al. J Bone Miner Res. 2018;33(5):868-874. Appendix: [Glossary](#).



efzimfotase alfa – Phase III HICKORY

Dr. Raja Padidela,

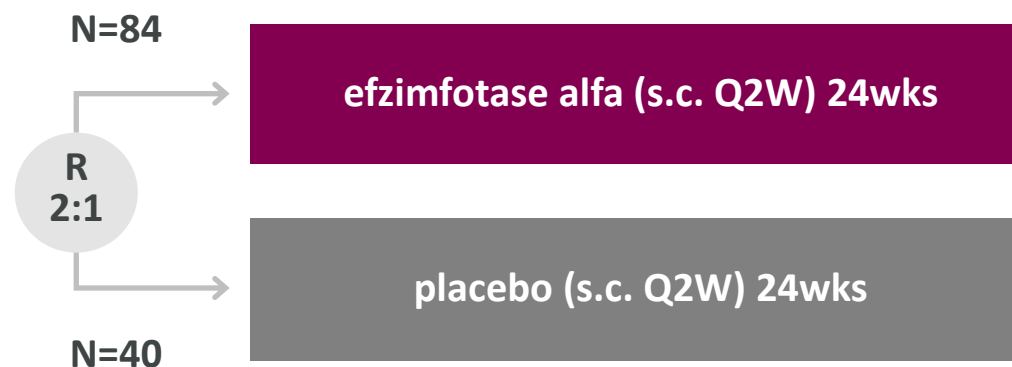
CONSULTANT PAEDIATRIC
ENDOCRINOLOGIST & METABOLIC BONE
DISEASES, ROYAL MANCHESTER
CHILDREN'S HOSPITAL



HICKORY – Trial Design

Study population:

- Treatment-Naïve patients with HPP
- ≥ 12 years of age



Primary endpoint:

- 6-minute walk test

Key secondary endpoints:

- 30-second Sit-to-Stand, Lower Extremity Functional Scale
- Functional and HRQoL: BPI-SF, FACIT-Fatigue
- Safety, PK/PD, immunogenicity

Patient identification:

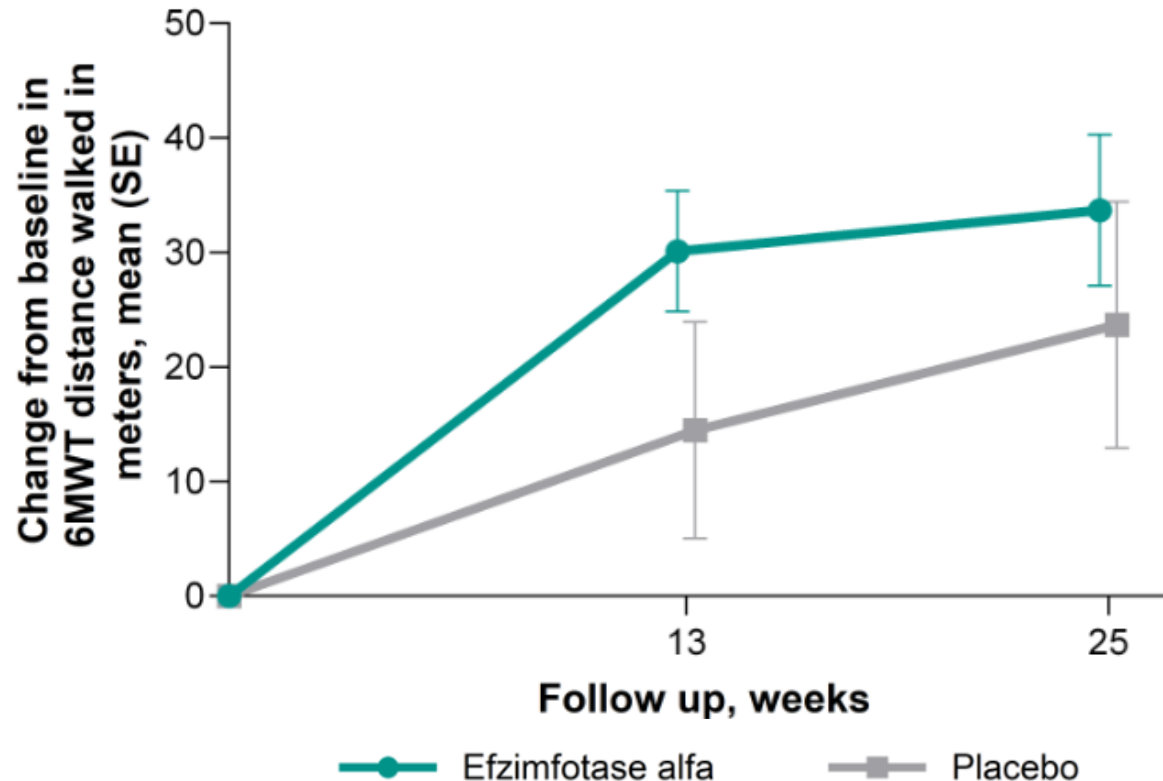
- Documented *ALPL* gene or Plasma PLP above the upper limit of normal
- Serum ALP activity below the age- and sex-adjusted normal range



HICKORY – Baseline characteristics

	efzimfotase alfa (n=84)	Placebo (n=40)
Sex, n (%)		
Female	61 (72.6)	31 (77.5)
Age, median (min, max), years	45.5 (12, 75)	43.5 (12, 78)
Race, n (%)^{a,b}		
White	59 (70.2)	30 (75.0)
Asian	17 (20.2)	8 (20.0)
Hispanic or Latino ethnicity, n (%)	12 (14.3)	7 (17.5)

HICKORY – efzimfotase alfa showed improvement in 6MWT but not statistical significance



6MWT
change from baseline
at week 25^a

efzimfotase alfa
(n=84)

Placebo (n=40)

LS mean difference
vs PBO (SE),
P value

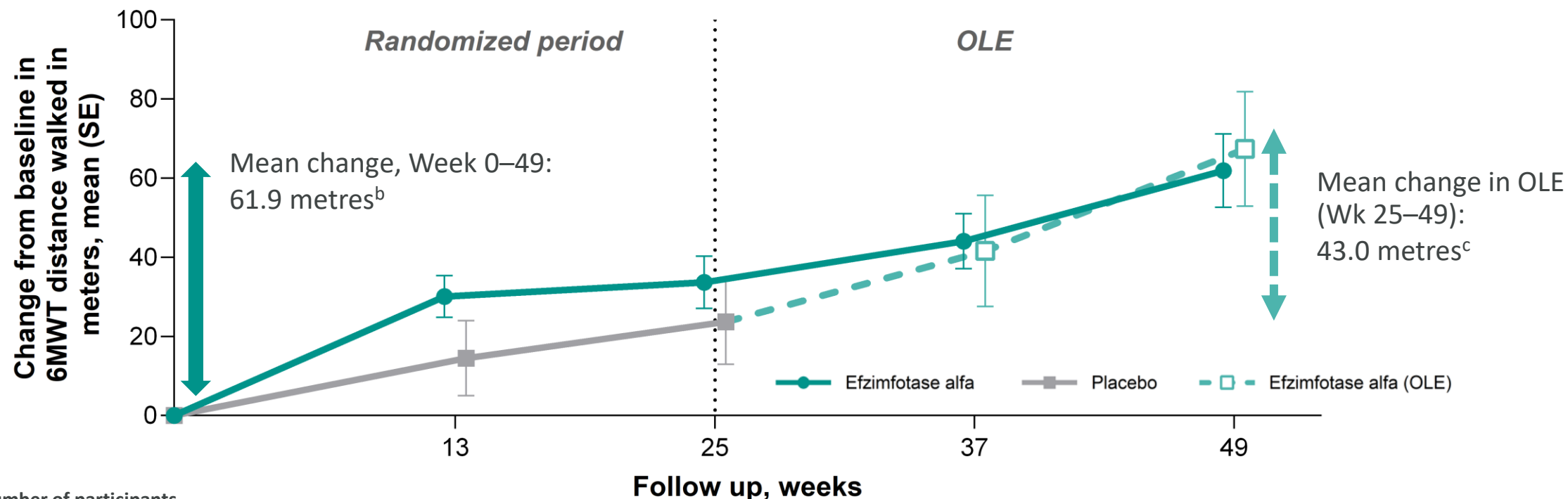
17.05 (12.223)
0.1675

a. Graph shows descriptive statistics of 6MWT performance; mean (SE) change from baseline in distance walked for efzimfotase alfa are 30.1 (5.3) at week 13 and 33.7 (6.6) at week 25; mean (SE) values for placebo are 14.5 (9.5) at week 13 and 23.7 (10.8) at week 25.

6MWT assesses mobility and endurance by the distance walked in 6 minutes. Higher = better functional capacity; Lower = worse capacity.

Appendix: [Glossary](#).

HICKORY – efzimfotase alfa 6MWT results during randomised period and OLE^a



Number of participants

efzimfotase alfa	84	81	77	75	72
Placebo	40	39	39	38	36

- Patients originally randomised to efzimfotase alfa had a mean improvement of 33.7 metres after 25 weeks of treatment, and 61.9 metres after 49 weeks
- Patients **switching** in OLE from placebo to efzimfotase alfa had mean **improvement of 43.0 metres after 25 weeks of treatment**

a. Mean values for 6MWT distance walked (meters) were 344.2 (efzimfotase alfa) and 294.4 (placebo) at baseline and were 377.7 (efzimfotase alfa) and 322.4 (placebo) at week 25. b. Patients continuing efzimfotase alfa in the OLE had clinically meaningful improvements in 6MWT distance walked (≥43 meters in adolescents, ≥31 meters in adults¹) at week 37 (mean [SD] change from week 1: 44.1 [60.3] meters) and at week 49 (mean [SD] change from week 1: 61.9 [78.4] meters). c. Patients switching to efzimfotase alfa in the OLE had clinically meaningful improvements in 6MWT distance walked at week 49 (mean [SD] change from week 25: 43.0 [71.0] meters). 1. Phillips D, et al. JBMR Plus. 2019;3(6):e10131.

Appendix: [Glossary](#).

HICKORY – key secondary endpoints numerically favoured efzimfotase alfa

Key secondary endpoint hierarchy ^a	30-second Sit-to-Stand	Lower Extremity Functional Scale	BPI-SF Pain Severity	FACIT-Fatigue
	MWPC: 1 to 4 reps ^b	MWPC: 2 to 13 ^b	MWPC: –2.25 to –0.50 ^b	MWPC: 6 to 14 ^{b,c}
Week 25				
LS mean difference vs placebo (SE)	0.42 (0.455)	3.56 (2.173)	–0.60 (0.300)	5.74 (1.733)
Nominal P value	0.3581	 0.1055	 0.0508	 0.0016

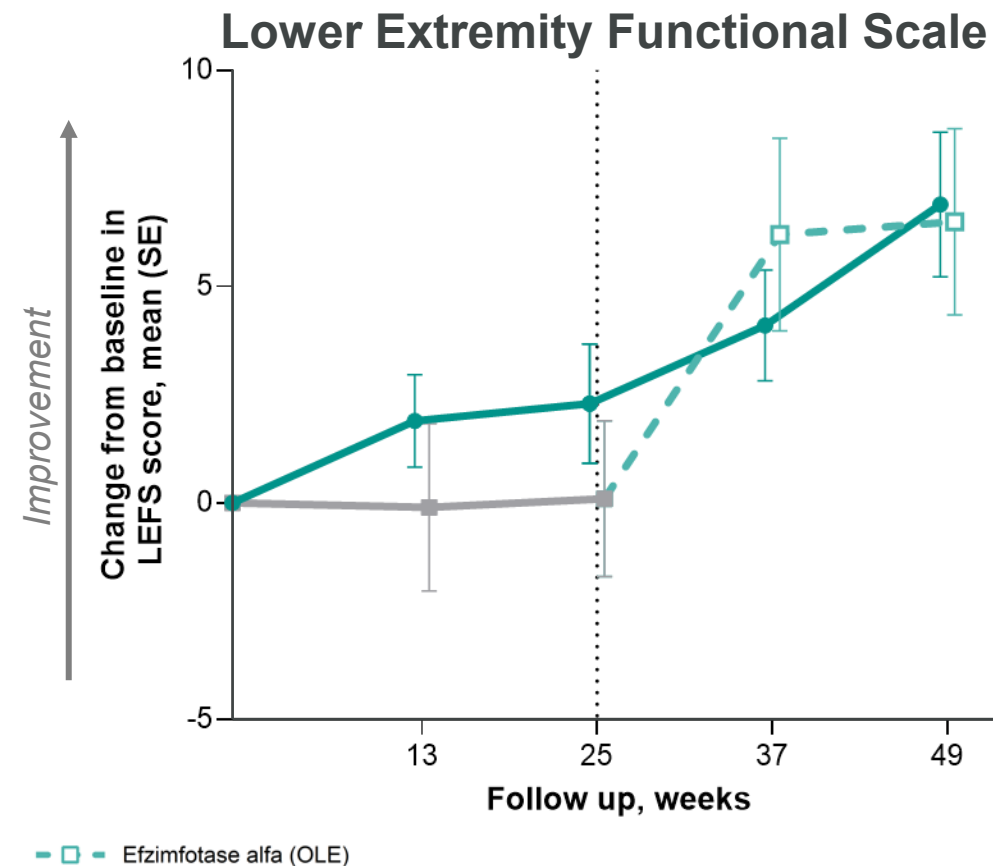
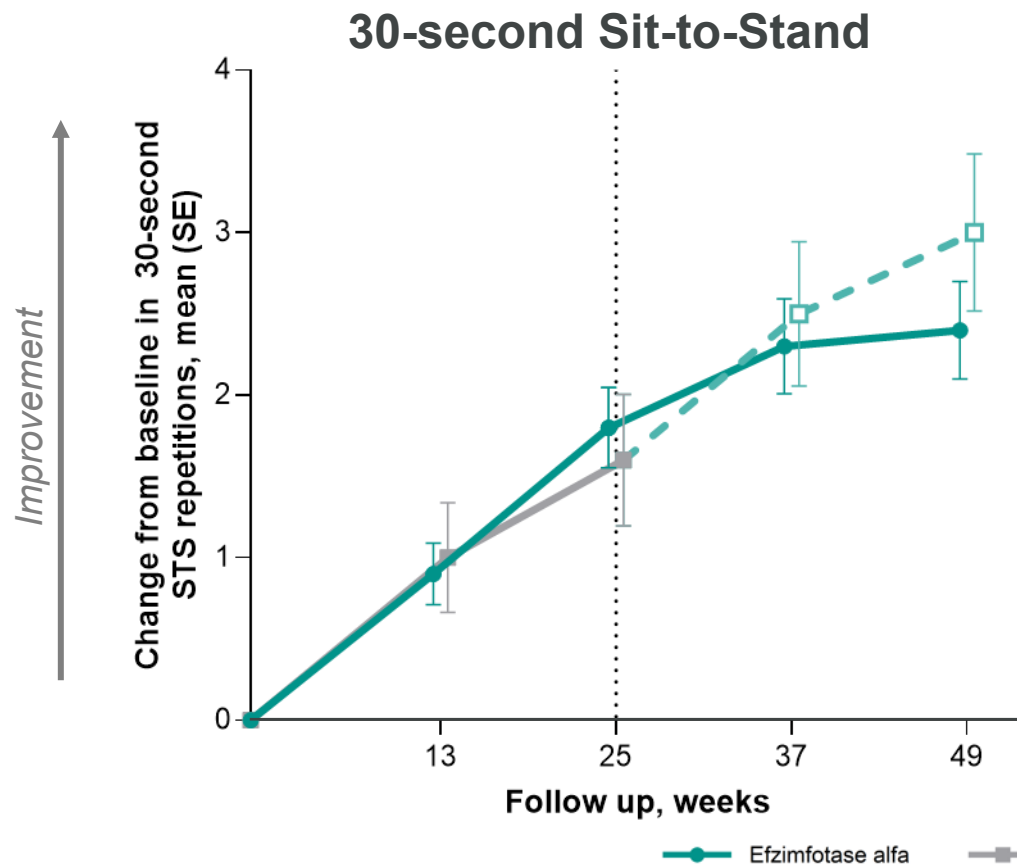
Improvement in other secondary endpoints further support clinical benefit:

- **BPI-SF pain interference score** ($P=0.0137$)^d and **TSQM-9 effectiveness score** ($P=0.0456$)^e

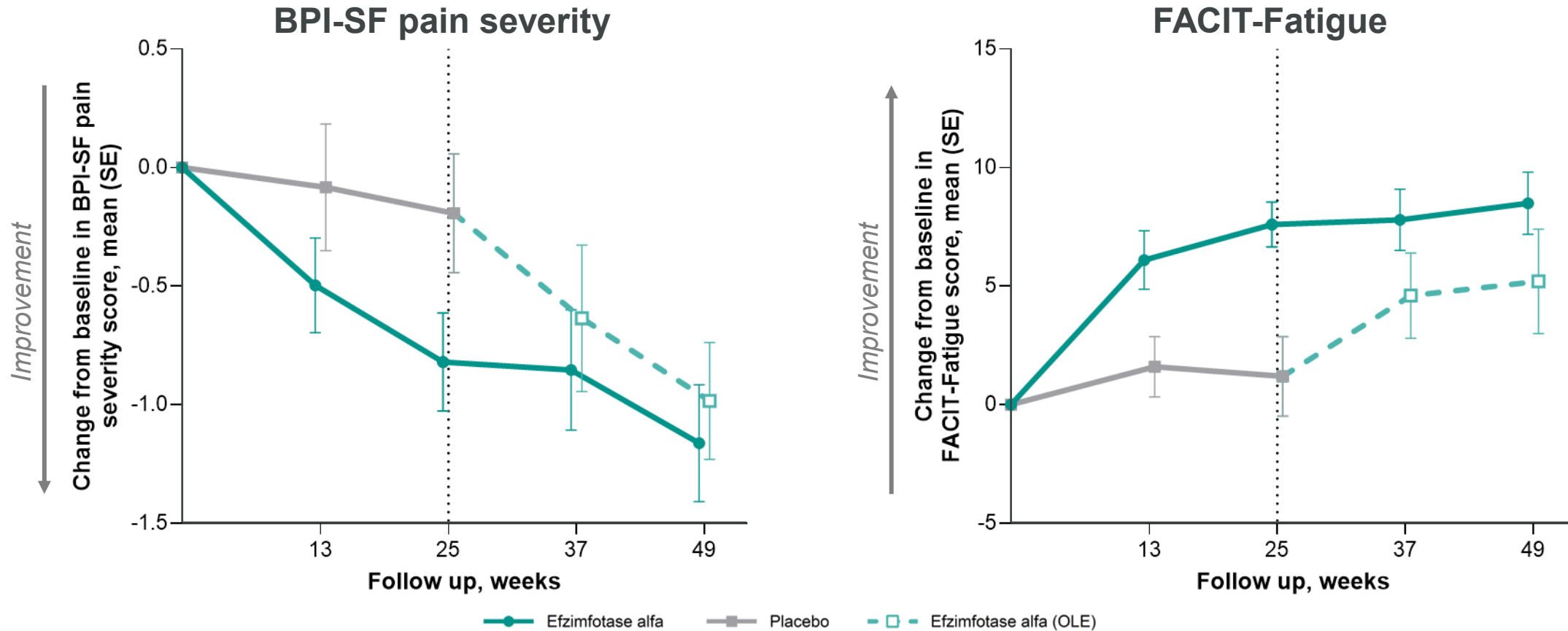
 Nominally significant  Clinically meaningful

a. Key secondary endpoints were statistically tested in a hierarchical order: 30-second Sit-to-Stand, Lower Extremity Functional Scale, BPI-SF pain severity, FACIT-Fatigue. b. MWPC values were calculated for adolescents and adults with HPP, using data from the HICKORY study (unpublished). c. MWPC was rounded from 5.5 to 6.0 since patient FACIT-Fatigue scores are whole numbers. d. BPI-SF pain interference LS means difference (SE): –1.03 (0.407). e. TSQM-9 effectiveness score LS means difference (SE): 9.89 (4.888). **30-second Sit-to-Stand** assesses lower-body strength and functional mobility by the number of full stands completed in 30 seconds; Range: count of stands (no fixed max; age/sex norms apply); Higher = better strength/mobility; Lower = worse performance. **Lower Extremity Functional Scale** assesses difficulty with everyday lower-extremity activities; Range: 0–80; Higher = better function/less difficulty; Lower = worse function/greater difficulty. **BPI-SF** assesses average intensity of pain via four items (worst, least, average, current); Range: 0–10 (mean of items); Higher = more severe pain; Lower = less pain. **FACIT-Fatigue** assesses severity and impact of fatigue on daily functioning; Range: 0–52 total (after proper item scoring); Higher = less fatigue/better functioning; Lower = more fatigue/poorer functioning. Appendix: [Glossary](#).

HICKORY – efzimfotase alfa continued improvement in physical function in the OLE



HICKORY – efzimfotase alfa continued improvement in pain and fatigue in the OLE



HICKORY – combined analysis of prespecified paediatric-onset subgroups

LS mean difference vs placebo (SE), Nominal P value	6MWT MCID: 31 meters (adults); 43 meters (adolescent) ^b	30-second Sit-to-Stand MWPC: 1 to 4 reps	Lower Extremity Functional Scale MWPC: 2 to 13	BPI-SF Pain Severity MWPC: –2.25 to –0.50	FACIT-Fatigue MWPC: 6 to 14 ^c
Paediatric-onset HPP (n=60) ^a	35.6 (16.87) ✓ 0.0386	1.3 (0.61) ✓ 0.0384	3.7 (3.31) ✓ 0.2645	–1.0 (0.45) ✓ 0.0260	3.5 (2.64) 0.1876
Adult-onset HPP (n=64)	–2.70 (17.32) 0.8764	–0.43 (0.62) 0.4927	3.5 (2.91) ✓ 0.2376	–0.26 (0.40) 0.5222	7.41 (2.29) ✓ 0.0021

Results in the adult-onset group may be due to various factors, including extreme values in the placebo group

✓ Nominally significant, clinically meaningful

✓ Clinically meaningful

a. Includes adolescents and adults with pediatric-onset HPP. b. MCID = 31 meters for adults, 43 meters for adolescents.¹ c. MWPC was rounded from 5.5 to 6.0 since patient FACIT-Fatigue scores are whole numbers. 6MWT assesses mobility and submaximal functional exercise capacity by the distance walked in 6 minutes. Higher = better functional capacity; Lower = worse capacity. STS assesses lower-body strength and functional mobility by the number of full stands completed in 30 seconds; Range: count of stands (no fixed max; age/sex norms apply); Higher = better strength/mobility; Lower = worse performance. LEFS assesses difficulty with everyday lower-extremity activities; Range: 0–80; Higher = better function/less difficulty; Lower = worse function/greater difficulty. BPI-SF assesses average intensity of pain via four items (worst, least, average, current); Range: 0–10 (mean of items); Higher = more severe pain; Lower = less pain. FACIT-Fatigue assesses severity and impact of fatigue on daily functioning; Range: 0–52 total (after proper item scoring); Higher = less fatigue/better functioning; Lower = more fatigue/poorer functioning.

1. Phillips D, et al. JBMR Plus. 2019;3(6):e10131. Appendix: [Glossary](#).

Favourable safety across Phase III programme



- Efzimfotase alfa had a **favourable safety** and **tolerability profile** across all 3 trials, including patients switching from asfotase alfa
- Efzimfotase alfa is administered Q2W and patients achieved a median of **98.8% injection site reaction–free days** while on treatment^a
- The **annualised rate of injection site reactions** was **5 times lower** with efzimfotase alfa than with asfotase alfa^b



Conclusions from HICKORY and broader programme

- In the **HICKORY overall population**, clinical benefit was observed in **physical function, pain and fatigue**, despite not meeting the primary endpoint of 6MWT
- **Paediatric-onset** subgroup: **6MWT** showed nominally significant, clinically meaningful **improvement**, together with measures of pain and physical function
- **Adult-onset** subgroup: **fatigue** showed nominally significant, clinically meaningful **improvement**
- In the **OLE**, **physical function, pain and fatigue continued to improve** with efzimfotase alfa
- HICKORY results were **consistent** with clinical benefits observed in MULBERRY and CHESTNUT



Positive results in a **broad HPP population ≥2 years old** with a favourable safety profile



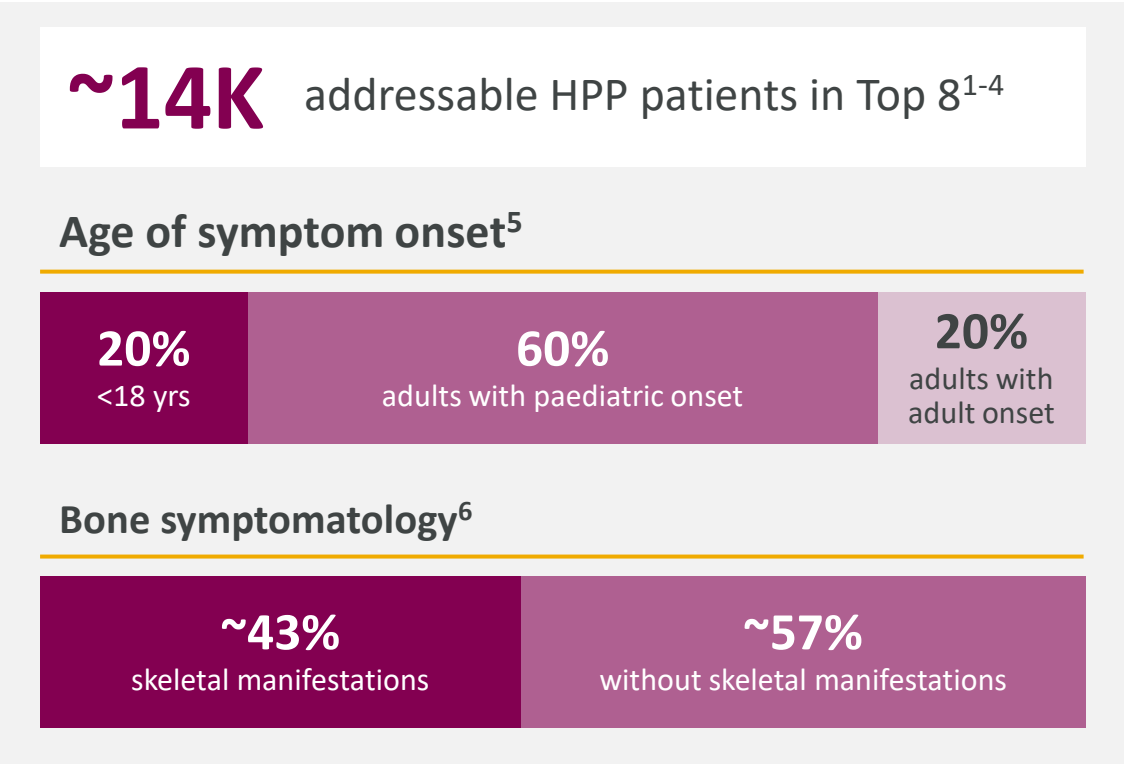
efzimfotase alfa – opportunity beyond *Strensiq*

Marc Dunoyer

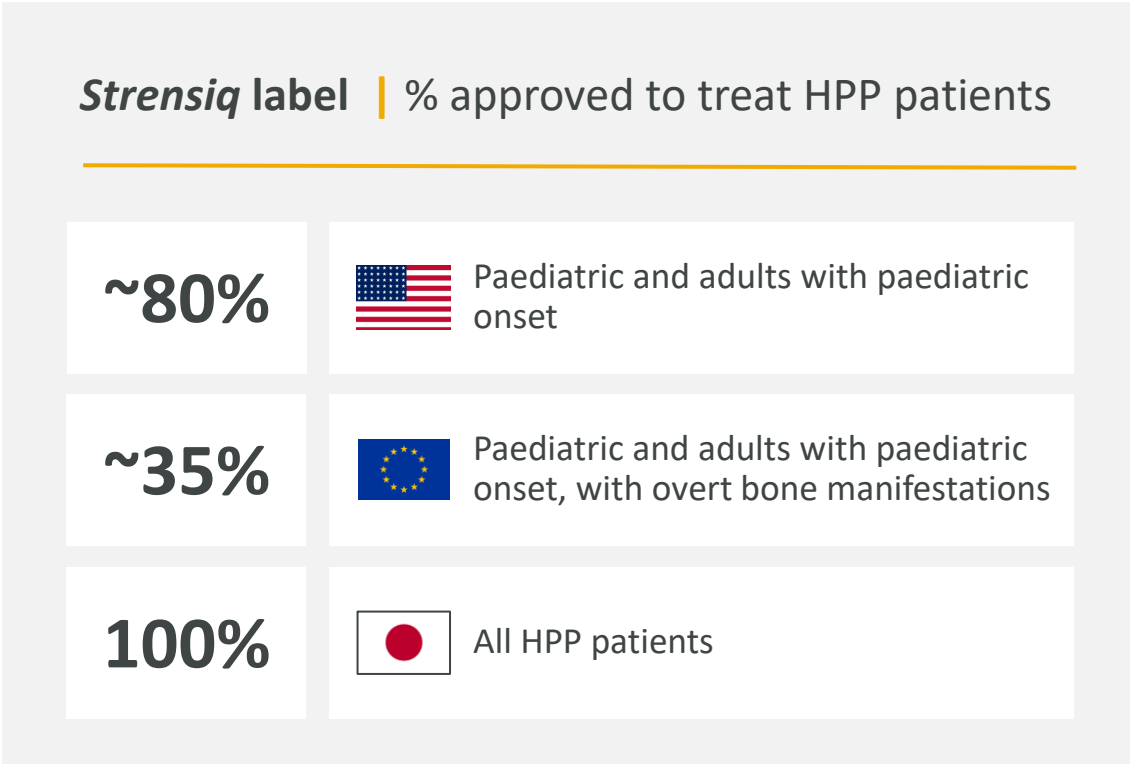
CEO, ALEXION, ASTRAZENECA RARE
DISEASE



HPP – efzimfotase alfa broader clinical evidence supporting patient reach across the spectrum of HPP



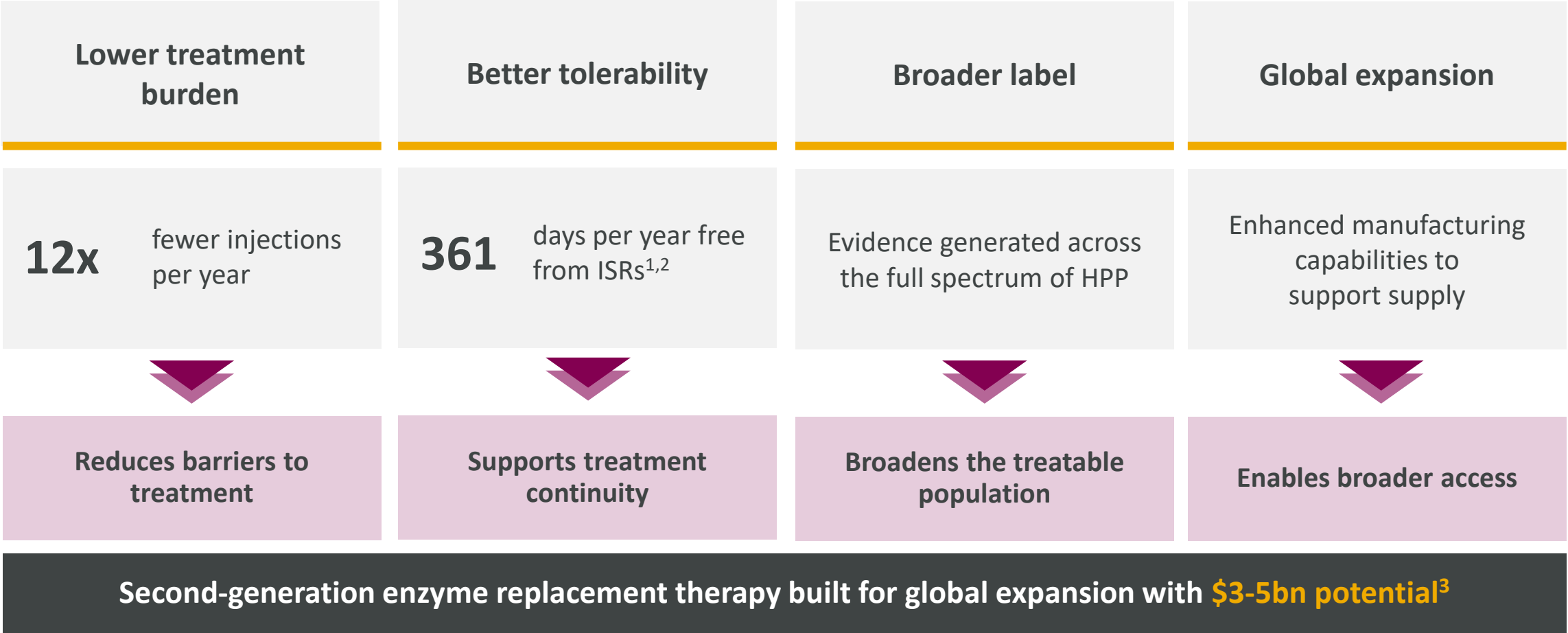
efzimfotase alfa first programme to include **all HPP patients >2yrs**



Additional national reimbursement and access restrictions apply



HPP – efzimfotase alfa has the potential to expand the treatment opportunity beyond *Strensiq*



26 1. Simmons JH, et al Efficacy and Safety of Alkaline Phosphatase (ALP) Enzyme Replacement Therapy (ERT) Efzimfotase Alfa in Children with Hypophosphatasia (HPP): Results of MULBERRY and CHESTNUT as Part of a Three-trial Phase 3 Clinical Program. Presented at ICCBH congress; 2026 Jun 28, Montreal, Canada. 2. The median number of ISR-free days is based on estimates of annualised patient-level ISR days. ISR = injection site reaction. 3. Peak Year sales non-risk adjusted. Appendix: [Glossary](#).



Establishing the pipeline for today and tomorrow

Marc Dunoyer

CEO, ALEXION, ASTRAZENECA RARE
DISEASE



Multiple launch opportunities across high-value and underserved rare disease indications

									
I CAN IgAN		TMA-313/4 HSCT-TMA		PREVAIL gMG		HICKORY/ MULBERRY/CHESTNUT HPP		CAEL-301/2 AL-A	
C5 inhibitor, mAb		C5 inhibitor, dual binding nanobody		Enzyme replacement Fc fusion protein		Novel anti-fibril, mAb			
Terminal complement inhibition may lead to nephron preservation and delay progression of nephropathy		Ability to address life- threatening complications of stem cell transplant in paediatric patients		Convenient QW self- administered s.c. to treat earlier and broader population		Next generation therapy with the potential to address broad HPP patient population		Remove accumulation of kappa-fibrils in organs, particularly in the heart and kidneys	
Filed in the US and JP		Filed paediatrics in the US		Approved in JP, filed in major markets		Filed in major markets		Approved in JP, in discussions with other regulators	
US Priority Review				US Priority Review					



Expanding Rare Disease growth opportunity through novel targets and modalities

Haematology,
Nephrology &
Transplant

Ultomiris
(C5 mAb) **DGF**

tarperprumig
(Factor P bispecific nanobody)
ANCA

ALXN2030
(C3 siRNA) **AMR**

ALXN1920
(Factor H fusion protein) **PMN**

ALXN2230
(multifunctional fusion
protein)

Neurology

ALXN2230
(multifunctional fusion
protein)

Bone &
Endocrine
Disorders

eneboparatide
(PTH1R agonist peptide)
HypoPT



Cardiology &
Amyloidosis

cliramitug
(depleter mAb) **ATTR-CM**

AZD0120
(CD-19/BCMA CAR-T) **AL-A**

ALXN2350
(BAG3-AAV) **DCM**

Rare Tumours

elrelesertib
(AZD1390) (ATMi s.molecule)
GBM



Closing Remarks and Q&A Session

Key External Expert



Dr. Raja Padidela

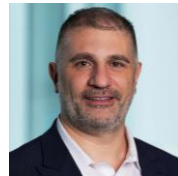
CONSULTANT PAEDIATRIC
ENDOCRINOLOGIST & METABOLIC
BONE DISEASES, ROYAL
MANCHESTER CHILDREN'S
HOSPITAL

AstraZeneca Leadership



Marc Dunoyer

CEO, ALEXION, ASTRAZENECA RARE
DISEASE



Gianluca Pirozzi

SVP, HEAD OF DEVELOPMENT,
REGULATORY & SAFETY



Appendix



Glossary

6MWT	6-Minute Walk Test
AAV	Adeno-associated virus
ADC	Antibody-drug conjugate
AL-A	Light-chain amyloidosis
ALP	Alkaline phosphatase
ANCA	Antineutrophil cytoplasmic antibodies
ATMi	Ataxia telangiectasia mutated kinase inhibitor
ATTR-CM	Transthyretin amyloid cardiomyopathy
BPI-SF	Brief Pain Inventory-Short Form
CI	Confidence Interval
CV	Cardiovascular
DCM	Dilated cardiomyopathy
DGF	Delayed graft function
ERT	Enzyme replacement therapy
FACIT-Fatigue	Functional Assessment of Chronic Illness Therapy-Fatigue
Fc	Fragment crystallizable region
GBM	Glioblastoma
gMG	Generalised myasthenia gravis
HPP	Hypophosphatasia
HRQoL	Health-related quality of life
HSCT-TMA	Hematopoietic stem cell transplantation-associated thrombotic microangiopathy
HypoPT	Hypoparathyroidism
IgAN	Immunoglobulin A nephropathy
IO	Immuno-oncology

IRA	Inflation Reduction Act
ISR	Injection site reaction
LEFS	Lower Extremity Functional Scale
LS	Least squares
mAb	Monoclonal antibody
MCID	Minimum clinically important difference
MWPC	Meaningful within-patient change
NME	New molecular entity
OLE	Open-label extension
PBO	Placebo
PD	Pharmacodynamics
PK	Pharmacokinetics
PLP	Pyridoxal 5'-phosphate
PMN	Primary membranous nephropathy
Q2W	Every two-week
QW	Every week
RGI-C	Radiographic Global Impression of Change
RSS	Rickets Severity Score
s.c.	Subcutaneous
SD	Standard deviation
SE	Standard error of the mean
siRNA	Small interfering ribonucleic acid
STS	Sit-to-Stand
TEAE	Treatment-emergent adverse event
TSQM-9	Treatment Satisfaction Questionnaire for Medication-9 items



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