

# Sobi Capital Markets Day 2019

rare **strength**



14 May 2019



# Forward looking statements

*In order to utilise the 'Safe Harbor' provisions of the United States Private Securities Litigation Reform Act of 1995, Swedish Orphan Biovitrum AB (publ) is providing the following cautionary statement. This presentation contains forward-looking statements with respect to the financial condition, results of operations and businesses of Swedish Orphan Biovitrum AB (publ). By their nature, forward-looking statements and forecasts involve risk and uncertainty because they relate to events and depend on circumstances that will occur in the future. There are a number of factors that could cause actual results and developments to differ materially from that expressed or implied by these forward-looking statements. These factors include, among other things, the loss or expiration of patents, marketing exclusivity or trade marks; exchange rate fluctuations; the risk that R&D will not yield new products that achieve commercial success; the impact of competition, price controls and price reductions; taxation risks; the risk of substantial product liability claims; the impact of any failure by third parties to supply materials or services; the risk of delay to new product launches; the difficulties of obtaining and maintaining governmental approvals for products; the risk of failure to observe ongoing regulatory oversight; the risk that new products do not perform as we expect; and the risk of environmental liabilities.*



**Guido Oelkers**  
CEO



**Philip Wood**  
Head of Haemophilia



**Henrik Stenqvist**  
CFO



**Norbert Oppitz**  
Head of Specialty Care



**Milan Zdravkovic**  
Head of R&D and CMO



**Armin Reininger**  
Head of Medical and  
Scientific Affairs



# Introduction



**Guido Oelkers**  
CEO

# We remain committed to our strategic direction



**Drive Haemophilia  
penetration**

**Develop  
Immunology**

**Grow US business  
and strengthen  
position in EMENAR**

**Strengthen  
late-stage pipeline**

I'm very pleased to **welcome** you  
to the first Capital Markets Day  
during my tenure

# We are stronger than ever and have over the past two years made significant achievements



- New management team leading the change
- Two-and-a-half times the size we were in 2016 and on a whole new trajectory
- Earnings guidance for 2019 at same level as 2016's sales
- More than tripled the number of haemophilia patients treated since end of 2016
- Two transformational acquisitions completed
- Built a substantial North American presence
- Strengthened our pipeline

# New management team leading the change



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Head of  
Haemophilia



**Norbert Oppitz**  
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**Armin Reininger**  
Head of Medical  
and Scientific Affairs



**Milan Zdravkovic**  
Head of R&D, Chief  
Medical Officer



**Torbjörn Hallberg**  
General Counsel,  
Head of Legal Affairs



**Christian Dreger**  
Head of Region  
NEMER



**Sofiane Fahmy**  
Head of Region  
SWENA



**Amy Pott**  
Head of Region  
NA



**Anne Marie de  
Jonge Schuermans**  
Head of Technical  
Operations



**Paula Treutiger**  
Head of  
Communication and  
Investor Relations

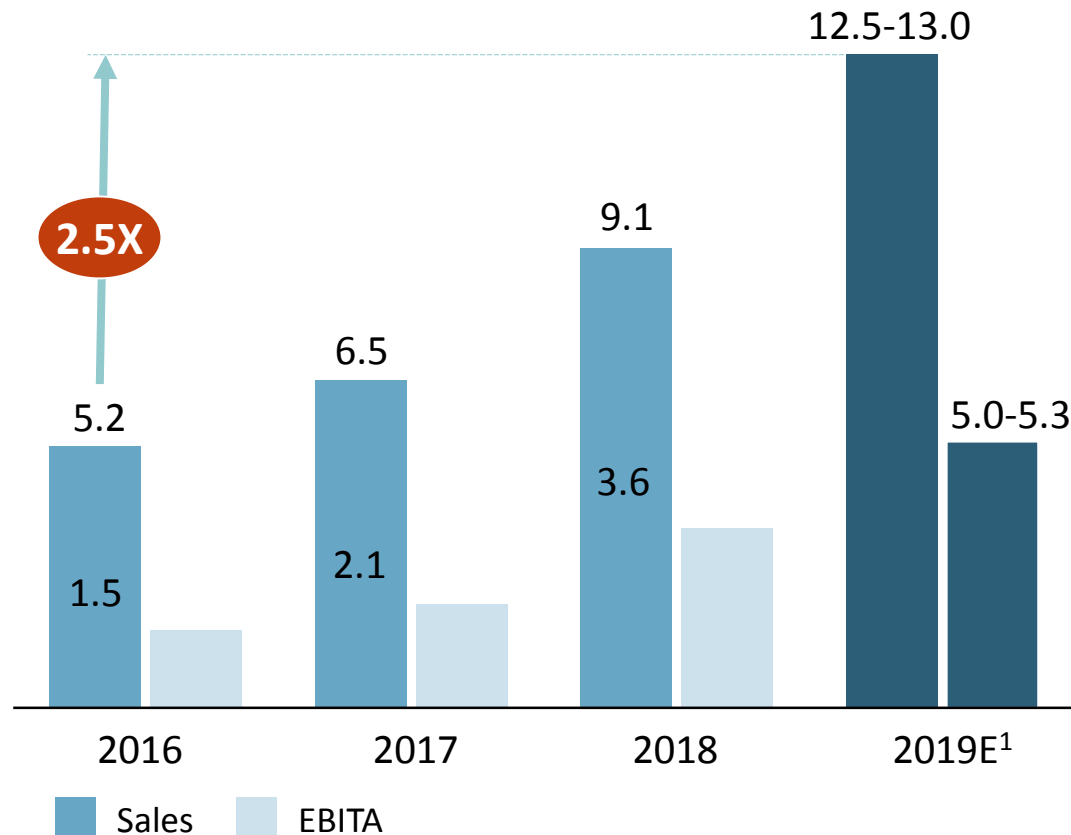


**Fredrik Wetterlundh**  
Head of HR



# 2.5X the size we were in 2016 and on a whole new trajectory

## Overall evolution (SEK bn)



## Portfolio and sales development

- Haemophilia has been the prevailing growth engine
- M&A (on market and late stage)
- Step-change in geographic footprint towards North America
- Other Specialty Care reduced in importance, secondary focus

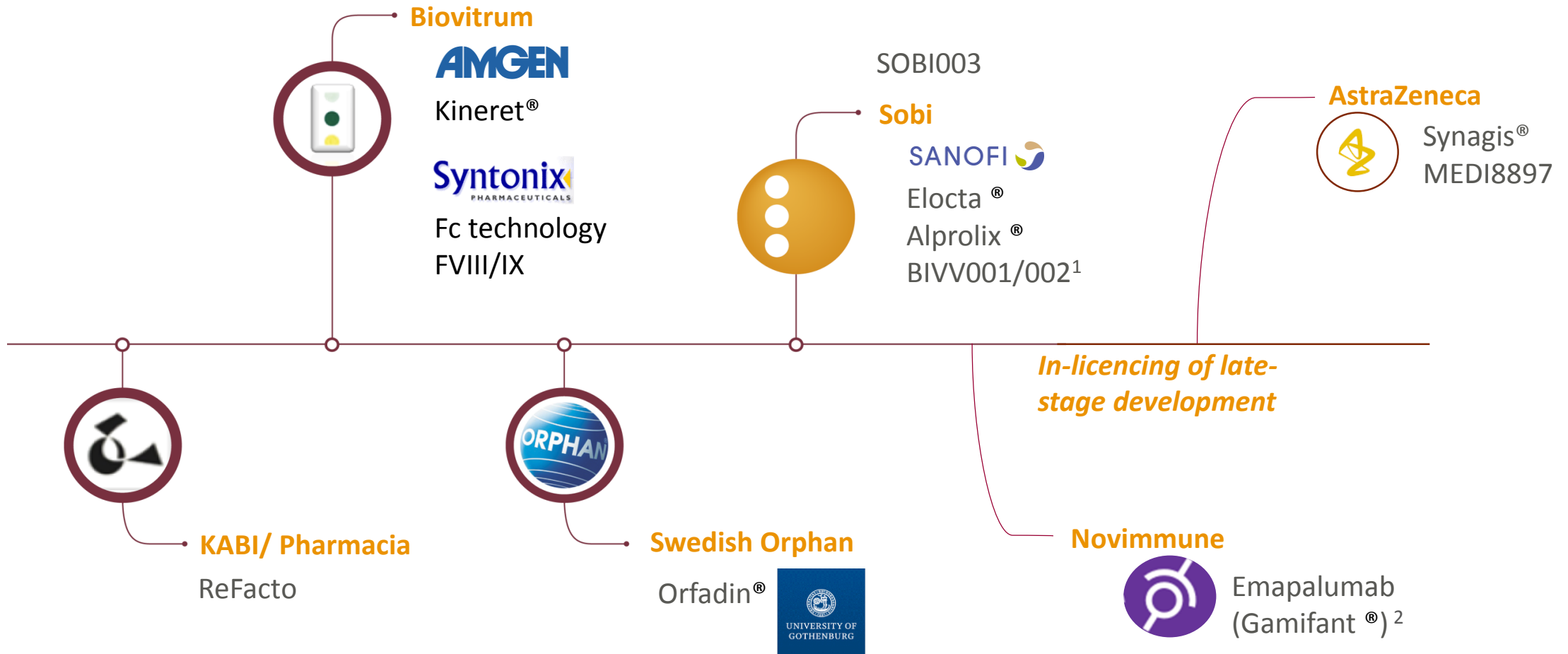
## Strategy and culture developments

- Increased commercial awareness and savviness
- Clear strategic focus on core opportunities
- Evolution towards high performance culture

<sup>1</sup> At current exchange rates as of 20 February 2019; the outlook was first published on 20 February 2019.

# Two deals completed

– sourcing innovation is central to who we are



1 BIVV001/002 are Sanofi development programmes, Sobi has elected to add programmes to the collaboration agreement but not yet opted-in  
 2 Global licensing agreement with Novimmune

A low-angle, close-up photograph of a person's legs and feet as they walk down a set of stairs. The person is wearing light-colored, cuffed trousers and blue denim-style sneakers with tan soles. The background is a bright, slightly blurred outdoor setting with a white railing.

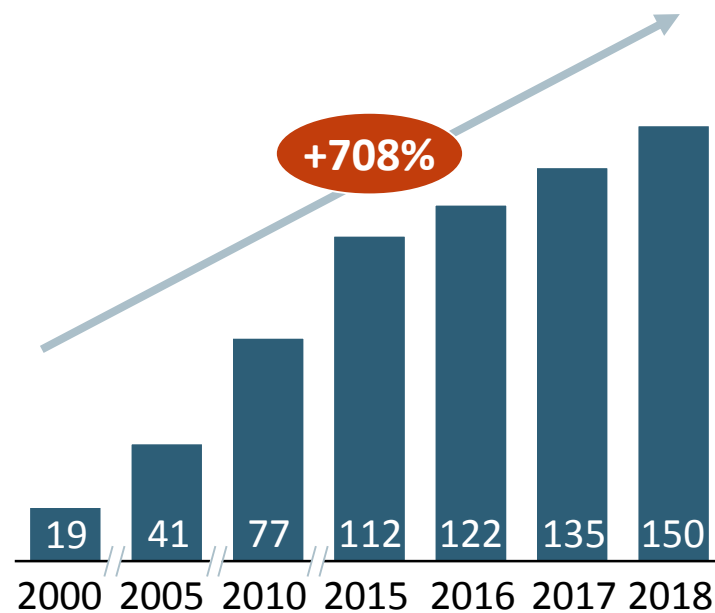
I see ample opportunity to take Sobi to the next level

- Fundamentally attractive market
- Our portfolio is strong and well-positioned for growth
- We will continue to pursue M&A

# The rare disease space is very attractive in the long-term

Worldwide orphan drug market<sup>1</sup> has grown around 7x since 2000...

USD billion



... with limited pressure vs. the rest of the pharmaceuticals industry

- **High unmet need:** Approximately 7,000 rare diseases globally – around 95% have no FDA approved treatment
- **Attractive opportunity:** Rare disease therapeutics can generally command a higher price than non-orphan products (e.g., Alexion’s Soliris c. \$410K per year)
- **Faster time-to-market:** multiple ways to speed up R&D projects (e.g., orphan development designation, priority review by FDA, conditional approvals in case of unmet medical needs)
- **Limited competition:** few companies active in orphan indications – translating to sustainably high share for first entrants
- **Limited generic threat:** orphan drugs less likely to face generic competition, often less attractive targets for biosimilars vs. much larger specialty biologics

<sup>1</sup> Evaluate estimates total orphans drugs sales by adding up the orphans drugs sales of individual companies. Thus this chart shows estimated sales in orphan indications only (as opposed to total sales by drugs with certain orphans indications) . 2000-2012 data are estimates. 2017-18 and forecasts

# Large unmet need and life-saving Sobi treatments

**50%**

of primary HLH patients fail to reach HSCT due to inadequate response to conventional therapies

Median survival

**<2 months**

if HLH untreated after diagnosis

Without treatment, hereditary tyrosinaemia (HT-1), quickly becomes life-threatening owing to liver failure and coagulation deficiencies

**~57k RSV**

hospitalisations each year in the US with

**associated morbidity**

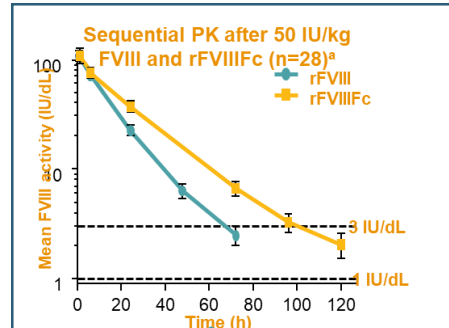


# In summary: Sobi's portfolio is well positioned for growth

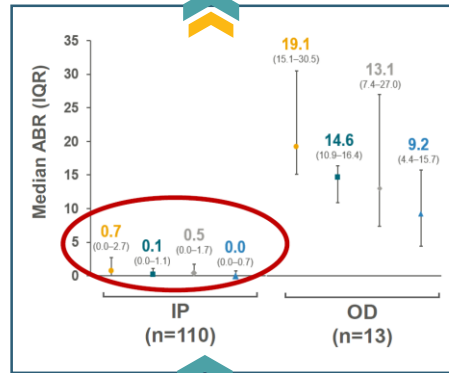
	Short Term	Mid-term
<b>ELOCTA</b> <sup>®</sup> <small>efromonolcoag aif2 (recombinant human coagulation factor VIII, Fc fusion protein)</small>	↑	↗
<b>ALPROLIX</b> <sup>™</sup> <small>[Coagulation Factor IX (Recombinant), Fc Fusion Protein]</small>	↑	↗
BIVV001		↑
<b>SYNAGIS</b> <sup>®</sup> <small>PALIVIZUMAB</small>	↗	↗
MEDI8897		↑
<b>gamifant</b> <sup>®</sup> <small>emapalumab</small>	↑	↑
<b>Kineret</b> <sup>®</sup> <small>(anakinra)</small>	↗	↗

2019 guidance of SEK 12.5-13.0 bn revenues and SEK 5.0-5.3 bn EBITA remains unchanged

# Our competitive portfolio positions us well for the new realities



Competitive PK profile



Individualising therapy



Liberate life campaign

## Five important facts:

1. European markets are more complex than US
2. Our portfolio is differentiated and competitive
3. Sobi is totally focused on continuing our success; current trends are encouraging
4. Opportunities for growth related to penetration and internationalisation
5. BIVV001 is likely to become an important pillar in future treatment

**ELOCTA<sup>®</sup>**  
elmorectap alpha  
 (recombinant human coagulation factor VIII,  
 Fc fusion protein)

Example:

# Preparing the future on a solid footing

## *Strategic Imperatives*



1. Significant unmet medical need in HLH
2. First approved treatment in primary HLH
3. Good start of launch, but more to gain
4. Material opportunity in indication expansion (secondary HLH, HSCT) and internationalization



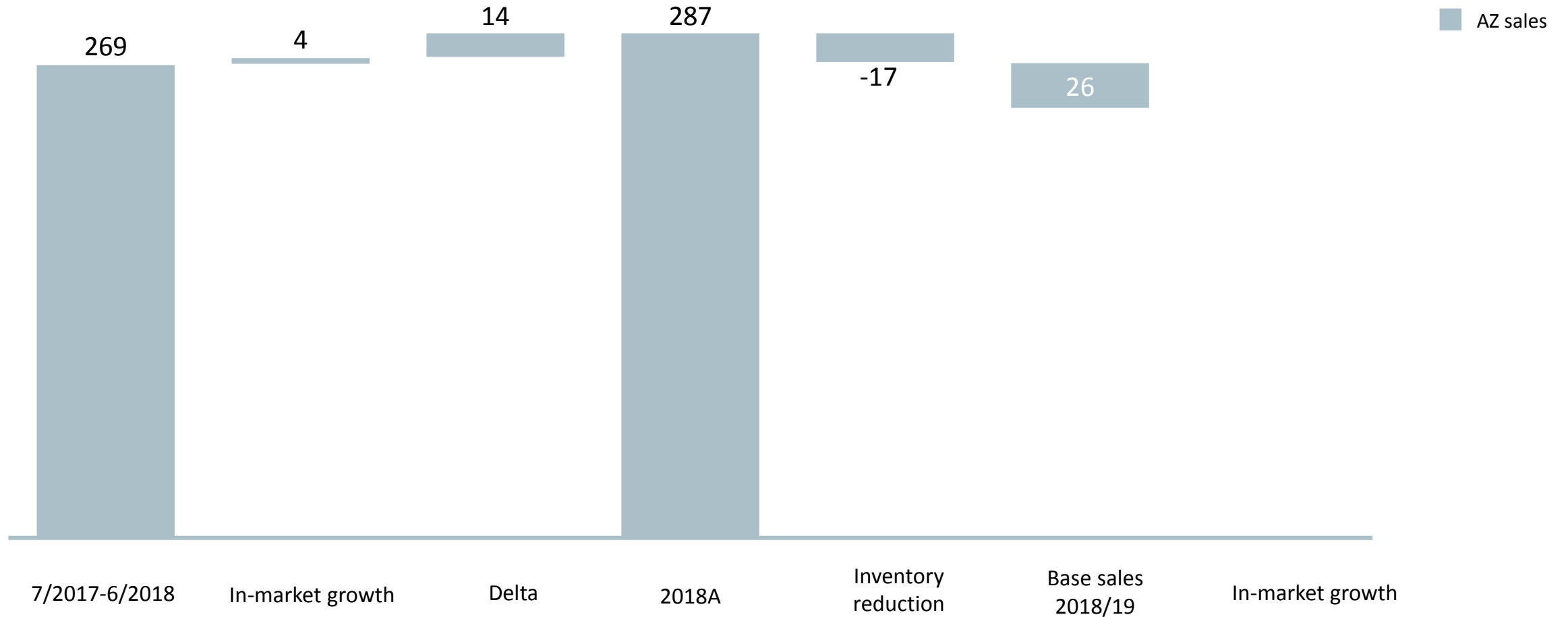
1. Product has been growing in- market (2% in Q1)
2. We believe in opportunities for value creation



1. Growing scientific interest in Kineret
2. Strong underlying trend



# 2019 impacted by one-off adjustments

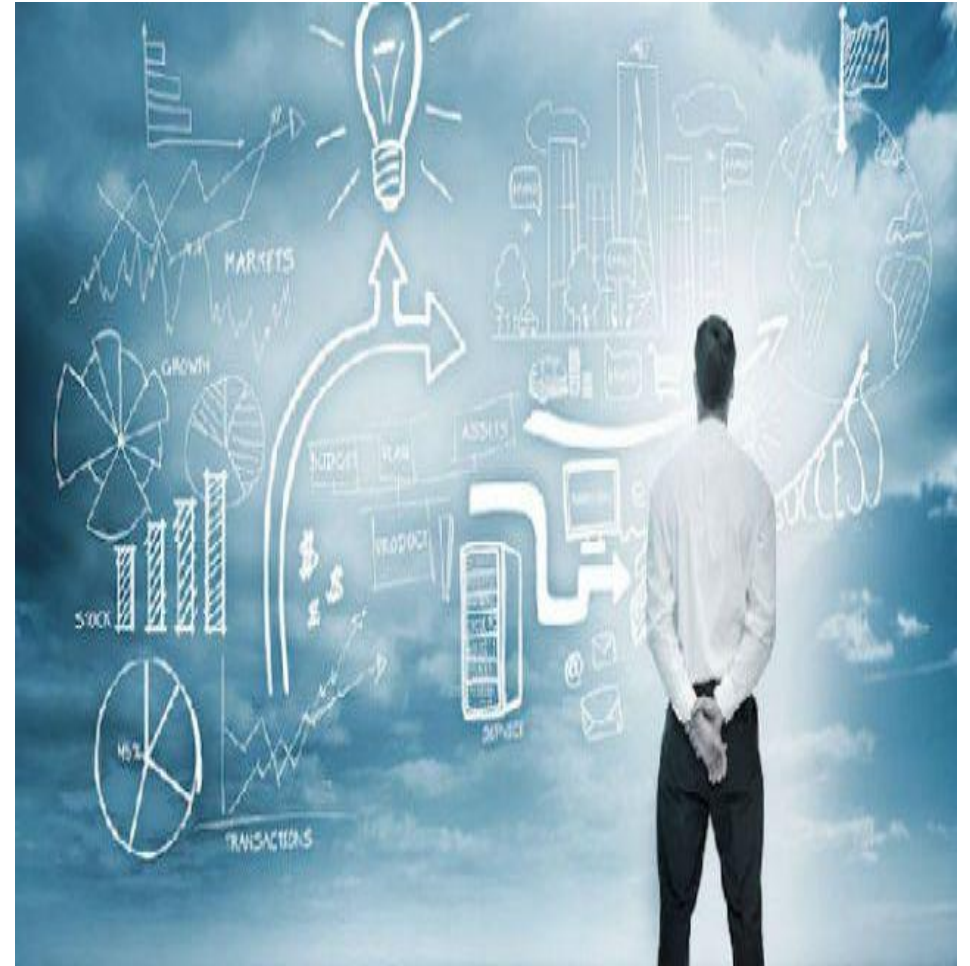


# Continued M&A – we are looking into all three types

	<b>Bolt-ons</b> <span style="background-color: orange; border-radius: 50%; padding: 5px 10px; display: inline-block;">1</span>	<b>Geography</b> <span style="background-color: orange; border-radius: 50%; padding: 5px 10px; display: inline-block;">2</span>	<b>Bold move</b> <span style="background-color: orange; border-radius: 50%; padding: 5px 10px; display: inline-block;">3</span>
<b>Objective</b>	<ul style="list-style-type: none"> <li>Continue to build and partner adjacencies across franchises</li> </ul>	<ul style="list-style-type: none"> <li>Build scale geographically</li> </ul>	<ul style="list-style-type: none"> <li>Build scale across pipeline and commercial capabilities</li> </ul>
<b>Focus</b>	<ul style="list-style-type: none"> <li>Late stage, on-market</li> </ul>	<ul style="list-style-type: none"> <li>Commercial infrastructure in countries with no/limited presence</li> </ul>	<ul style="list-style-type: none"> <li>Transformational M&amp;A – large acquisition/merger</li> </ul>

# Key messages

- Rare diseases is a highly attractive market segment
- Our haemophilia business continues being competitive and has significant growth potential
- Gamifant has the potential to become a material growth driver for Sobi
- Synagis is a growing asset under our leadership
- Kineret continue to deliver strong double digit growth
- Our main pipeline assets BIVV001 and MEDI8897 are progressing well have the potential to change the scale of Sobi
- SOBI003 is on a good way and is delivering against milestones set out





A large white speech bubble with a tail pointing towards the bottom right, containing the text 'Financial update'.

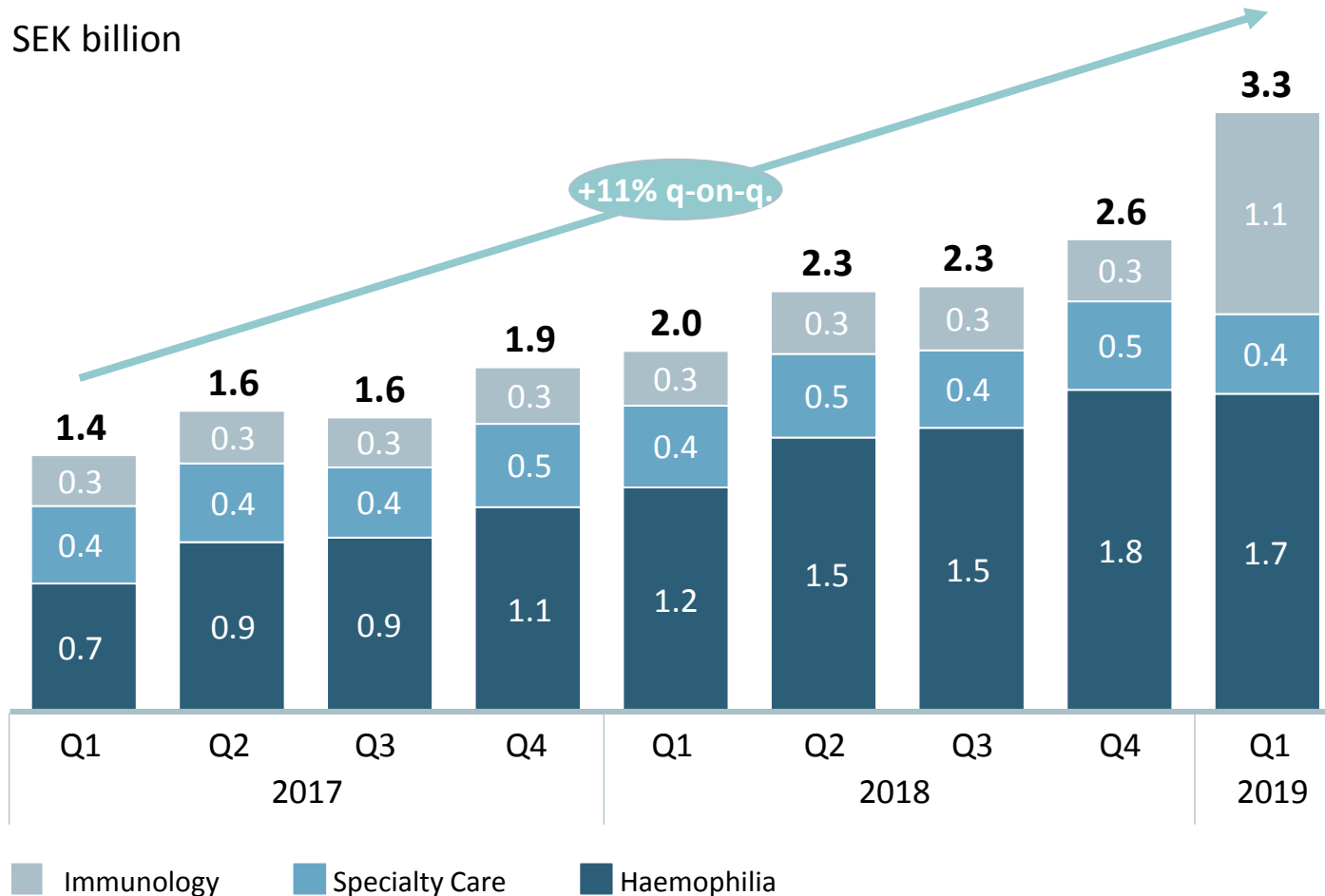
# Financial update

A small white circle positioned above the speaker's name.

**Henrik Stenqvist**  
CFO

# Strong revenue growth in focus business areas

SEK billion

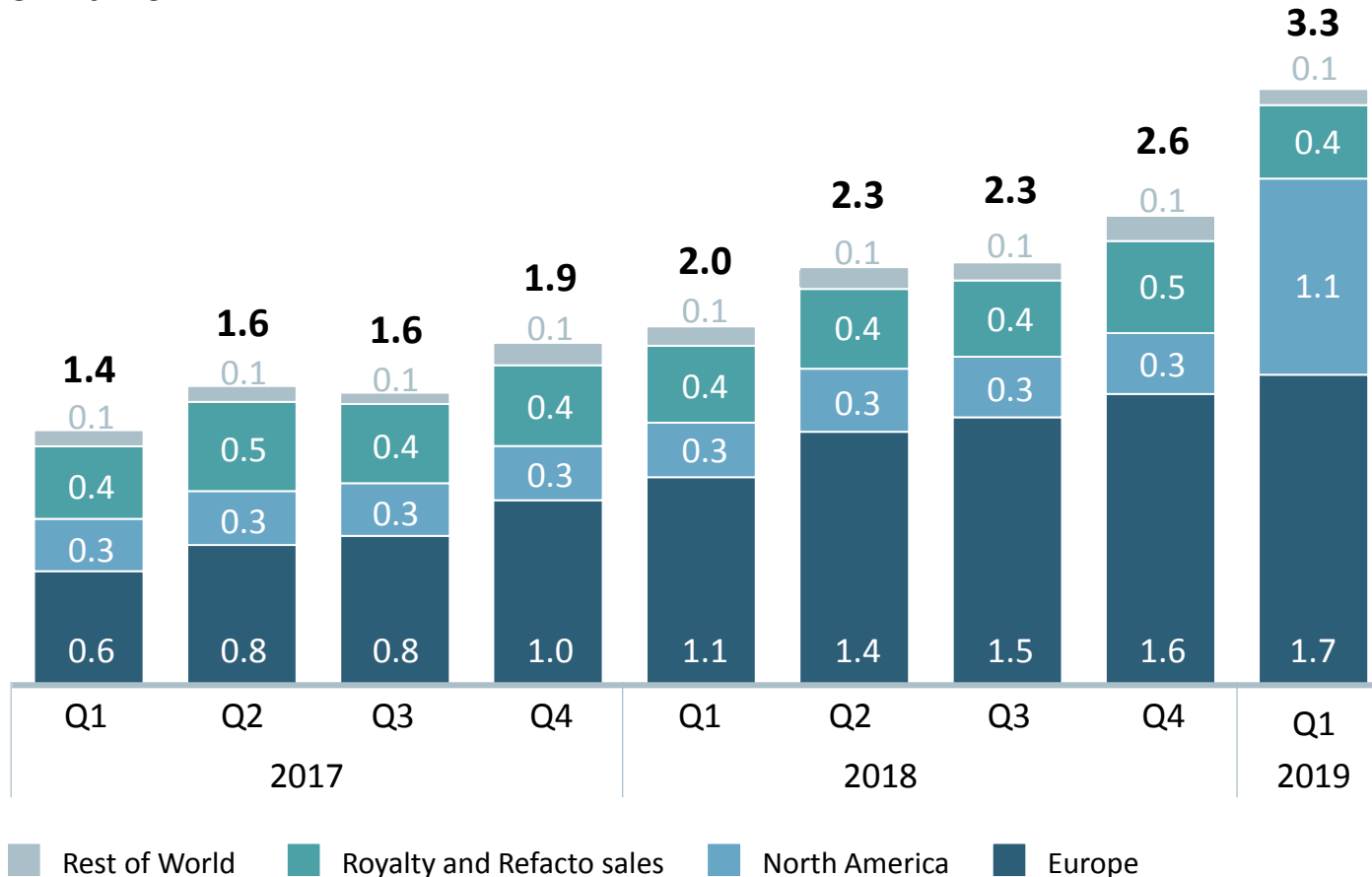


## Comments

- Continued strong growth in Haemophilia
- Impact from Immunology acquisitions transforming the company
  - Synagis
  - Gamifant
- Stable performance in Specialty Care
  - Generic impact Orfadin

# Regional revenue development

SEK billion

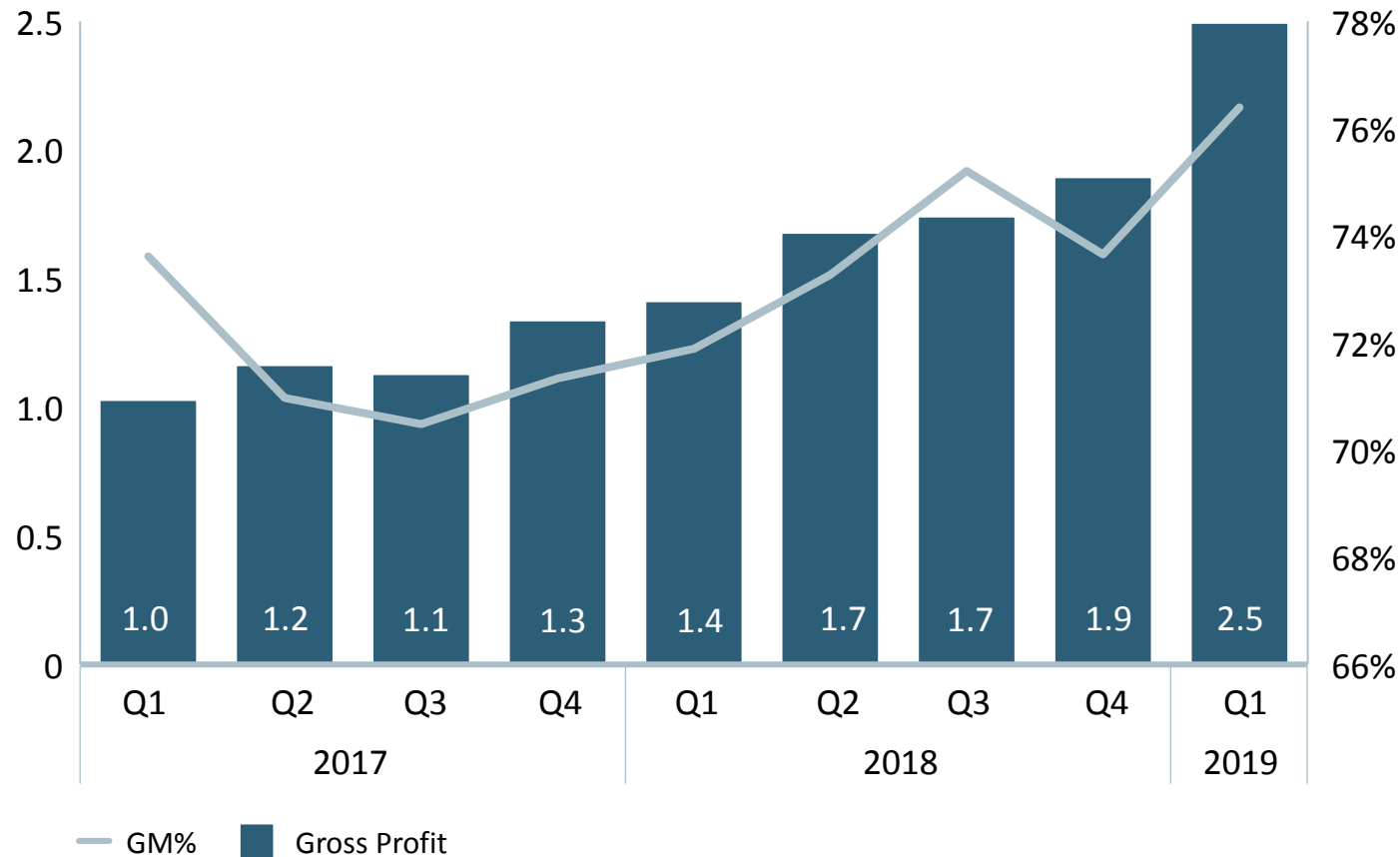


## Comments

- Strong growth in Europe from Haemophilia
  - Further fuelled by Gamifant launch
- Larger footprint in the US from Synagis introduction and Gamifant launch
- Balanced geographical presence

# Gross profit

SEK billion



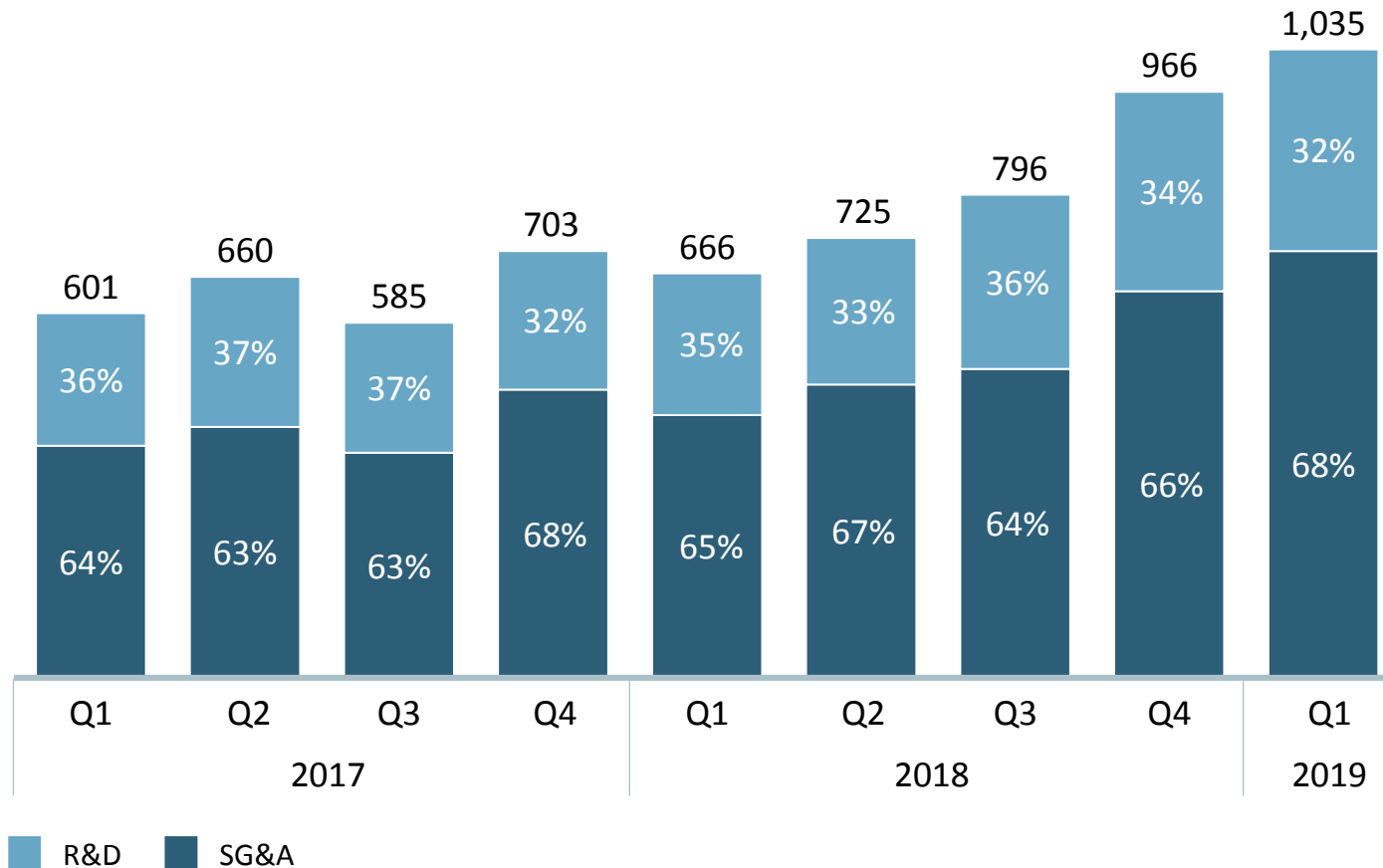
## Comments

- Strong margin trend
- Mainly driven by increased sales from products like Haemophilia , Synagis and Gamifant
- Positive impact from improved Cogs



# OPEX development

SEK million

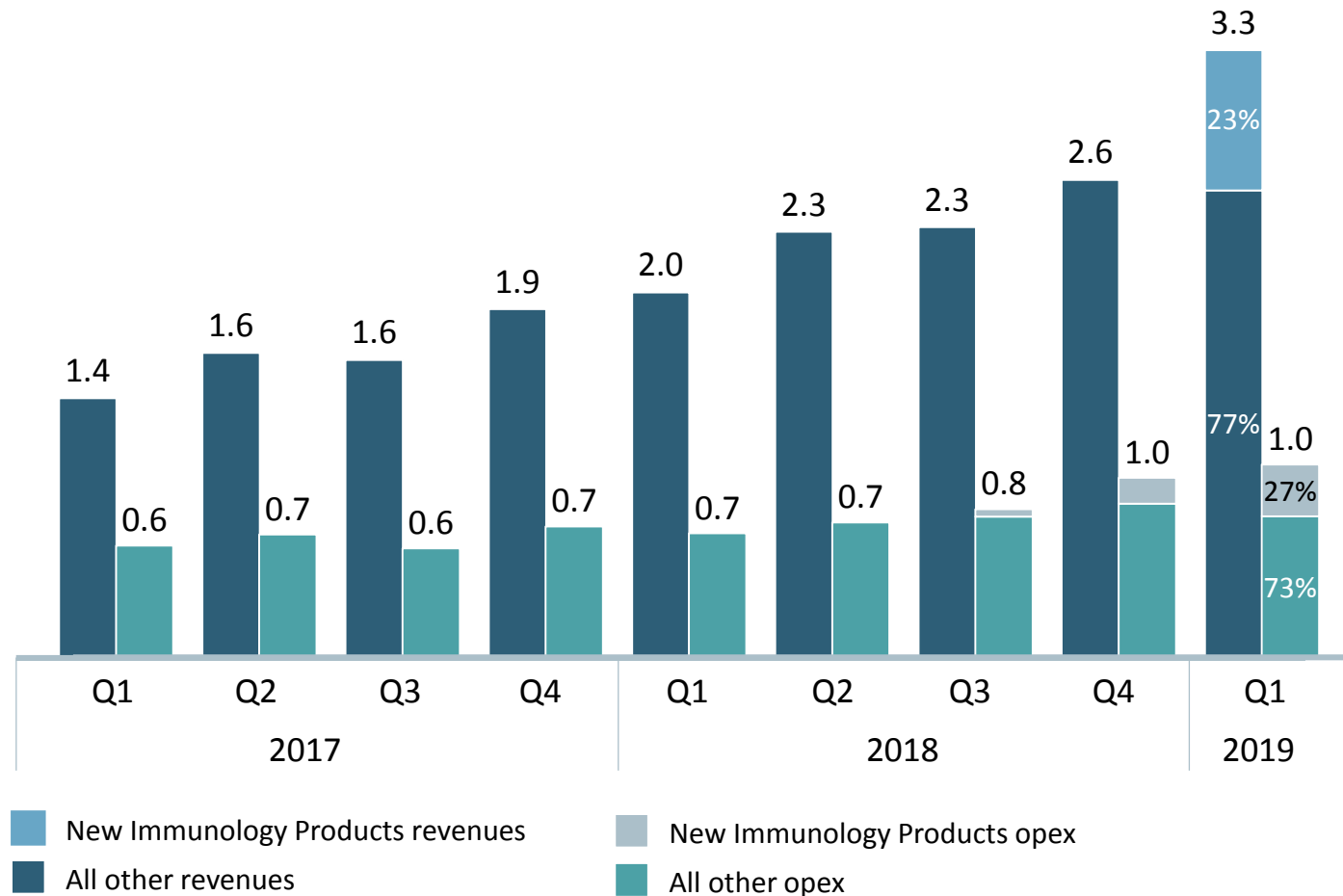


## Comments

- Increasing investments to fuel short term and long term growth
  - Immunology franchise; Synagis takeover and Gamifant launch
  - Expanding R&D activities to capture Emapalumab opportunity
  - Haemophilia commercial investments

# OPEX development – impact from new immunology products

SEK billion

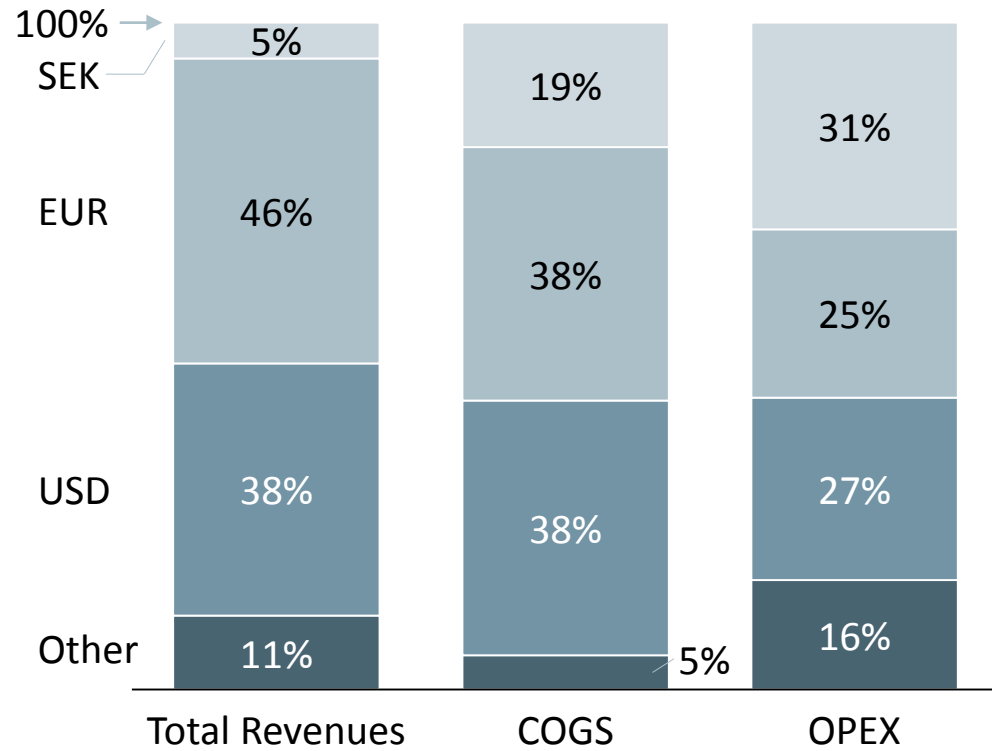


## Comments

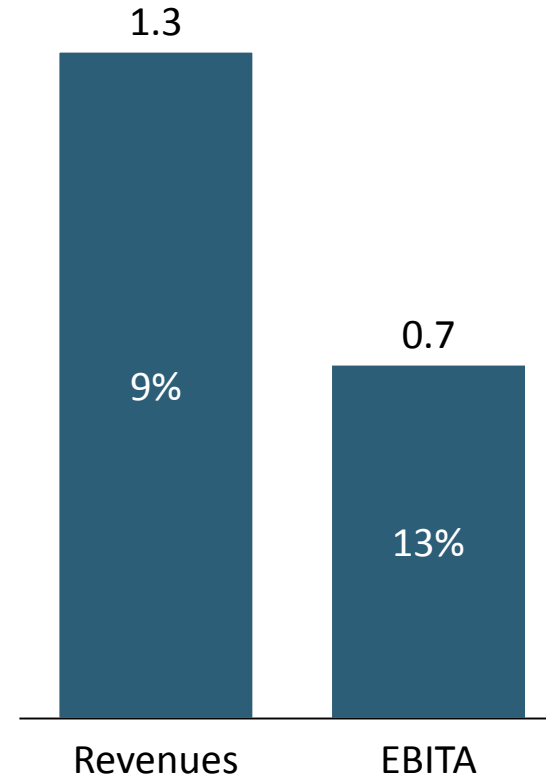
- Opex increase from investments in new assets
  - Synagis
  - US sales force
  - Commercial activities
  - Emapalumab
  - Research project portfolio
  - Gamifant launch in the US
  - Launch preparations in Europe
- Other opex increase from investments in Haemophilia

# P&L currency exposure

**Currency Mix by P&L Line**  
(Percent)

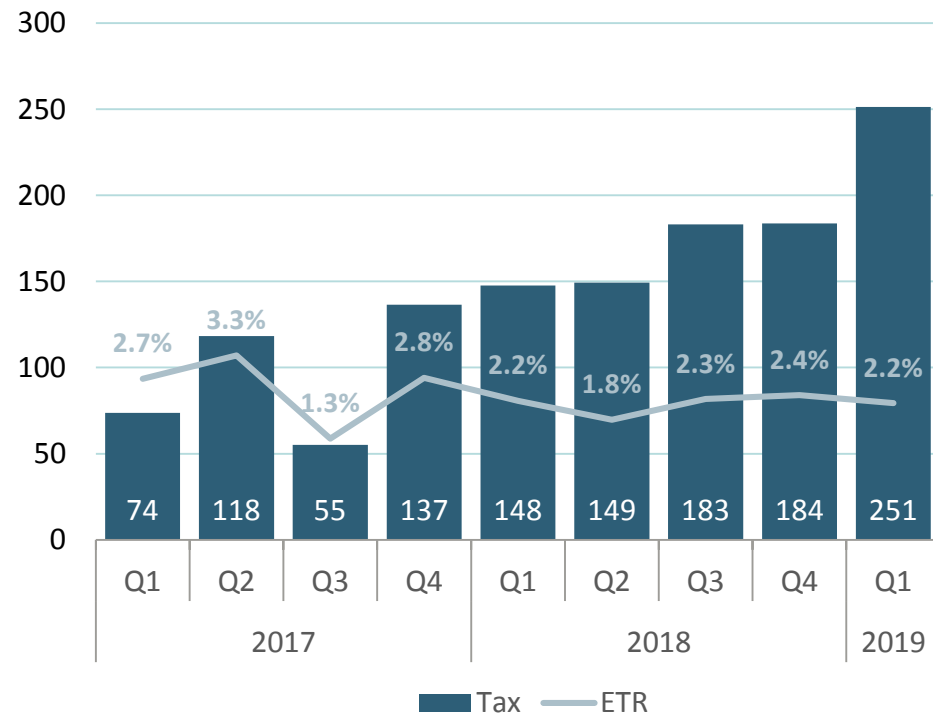


**Sensitivity analysis (SEK 10% change vs all other currencies)** (SEK billion)



# Tax

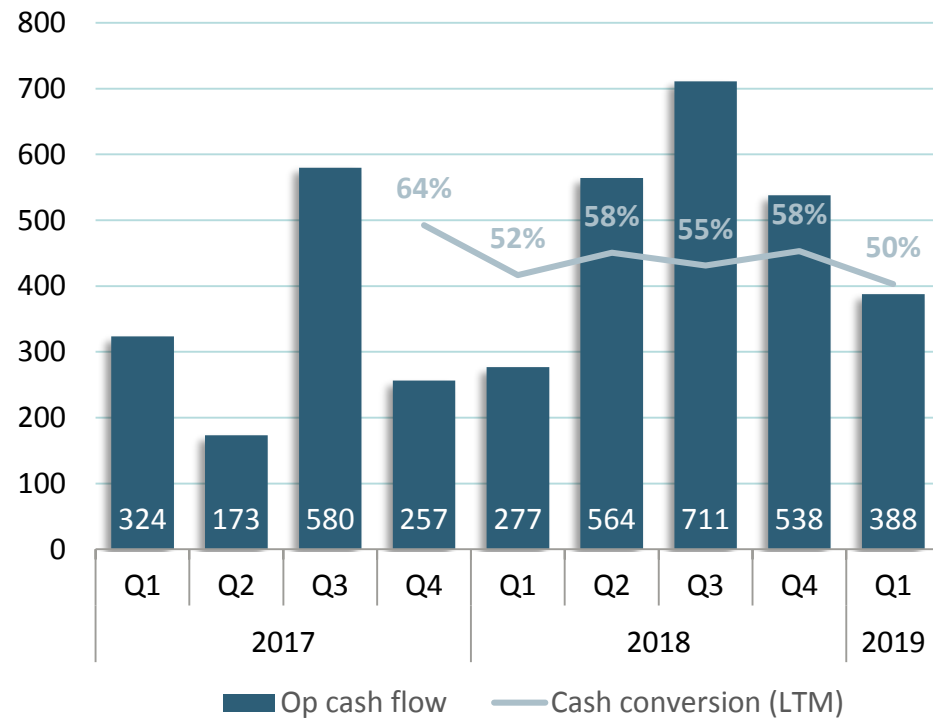
## Tax development (SEK million)



- Lower ETR driven by reduced tax rate in Sweden (the dominating country from a tax perspective)
  - Marginal impact from Synagis and US tax
  - Impact from increased costs in Switzerland (emapalumab) has a marginal negative impact on ETR

# Cash flow

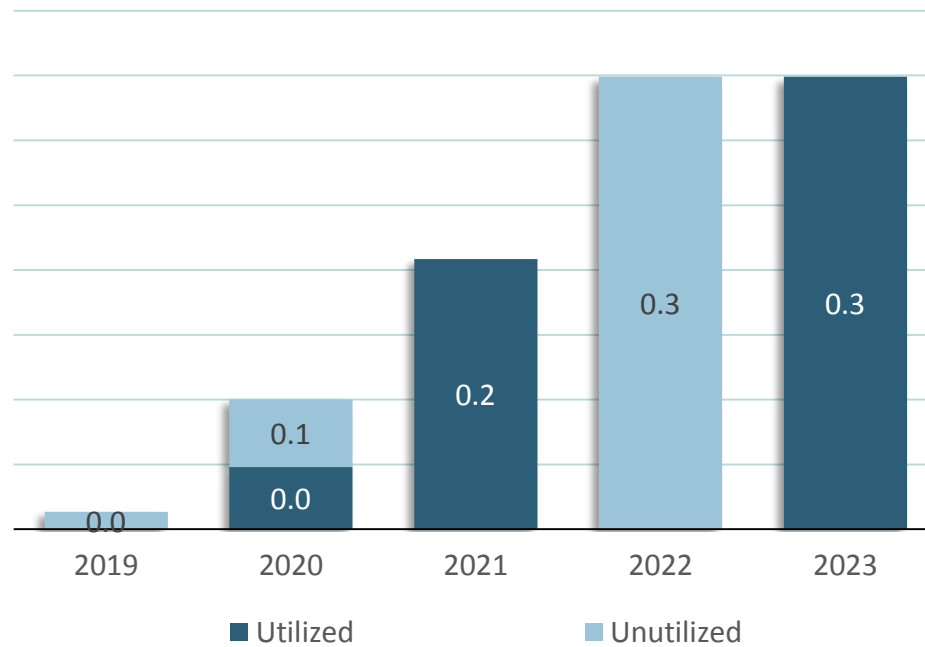
Operating cash flow development (SEK million)



- Continued strong cash conversion
- Cash conversion and operating cash flow will have a seasonal impact due to Synagis

# Financing and leverage

**Maturity profile of credit facilities** (SEK billion)



	Utilized	Unutilized	Total
Average time to maturity, years	3.7	3.3	3.5

- Net Debt SEK 5.6 bn
- Pro forma leverage of 1
- Underlying strong cash flow decreases leverage
- Considerable debt capacity for further M&A
- Funding is M&A driven, leverage of 3-4

# Summary

- Building new pillars of growth: Immunology
- Continuous strong and balanced growth
- Strong ongoing trend in gross margin
- Maintained strong profitability – despite focused investments in growth areas
- Low leverage and continued strong cash generation – creating headroom for M&A





# Haemophilia

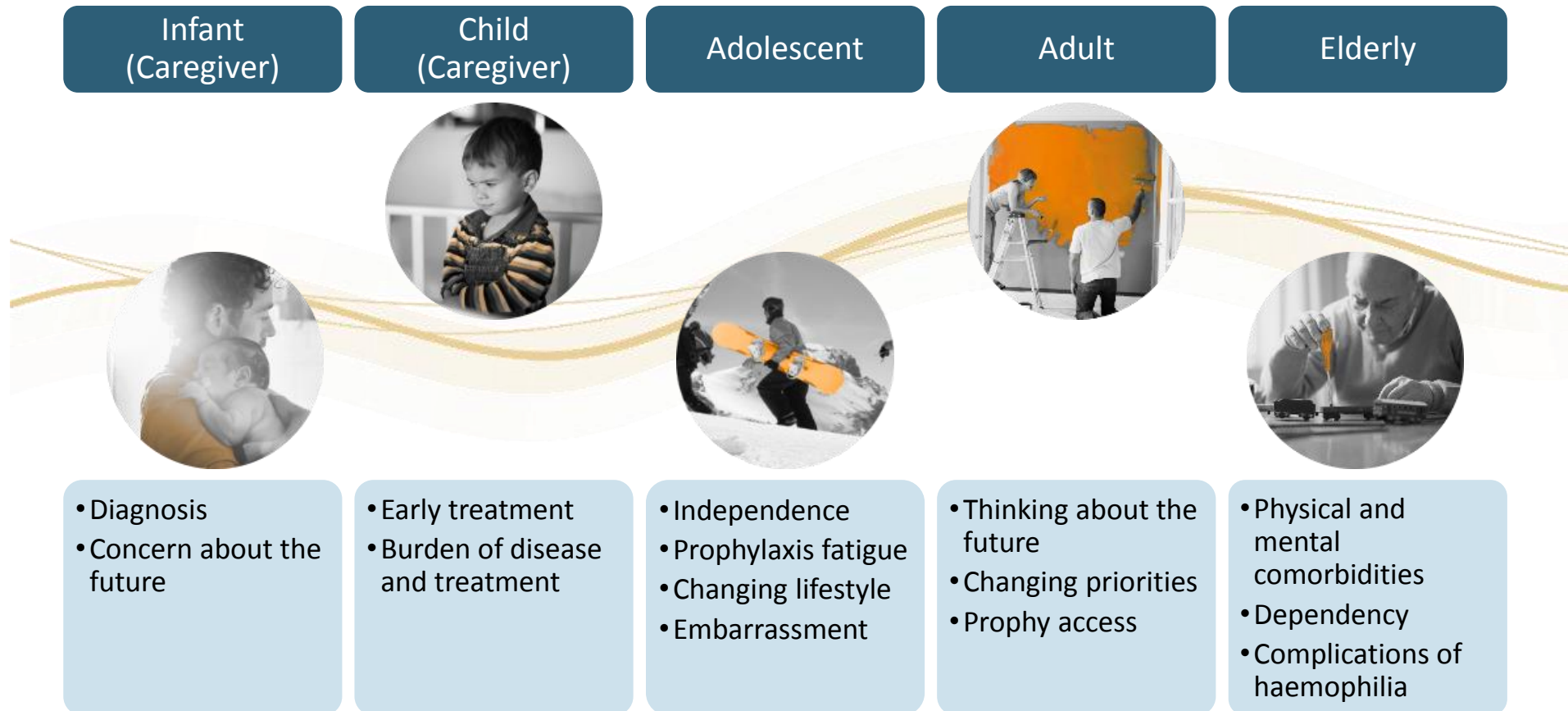


**Philip Wood**  
Head of Haemophilia

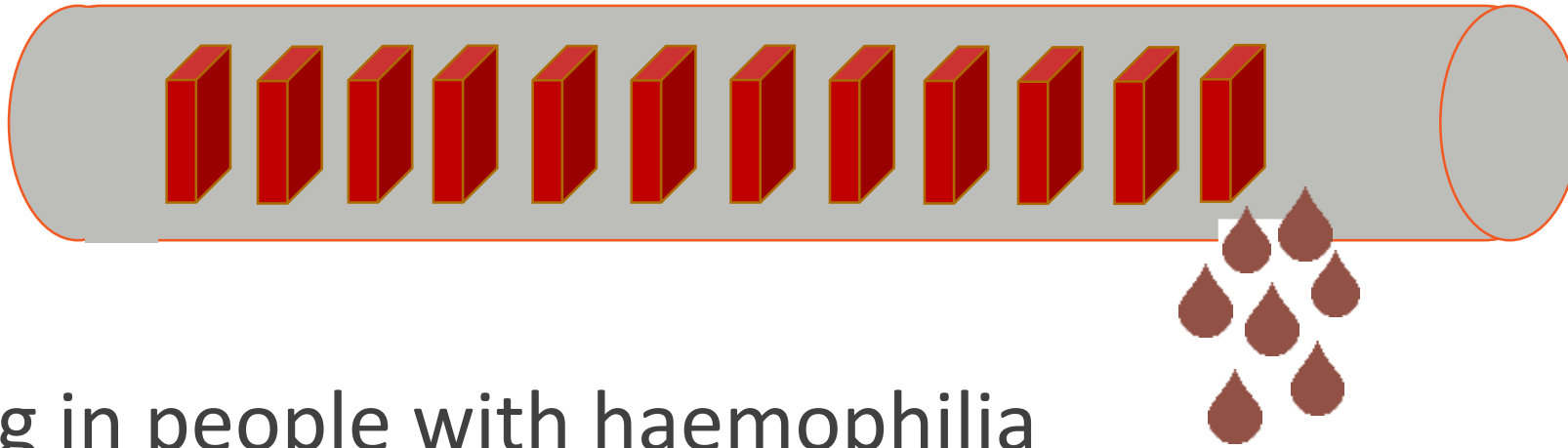
**Armin Reininger**  
Head of Medical and Scientific Affairs

# Haemophilia is chronic disease that affects peoples' lives

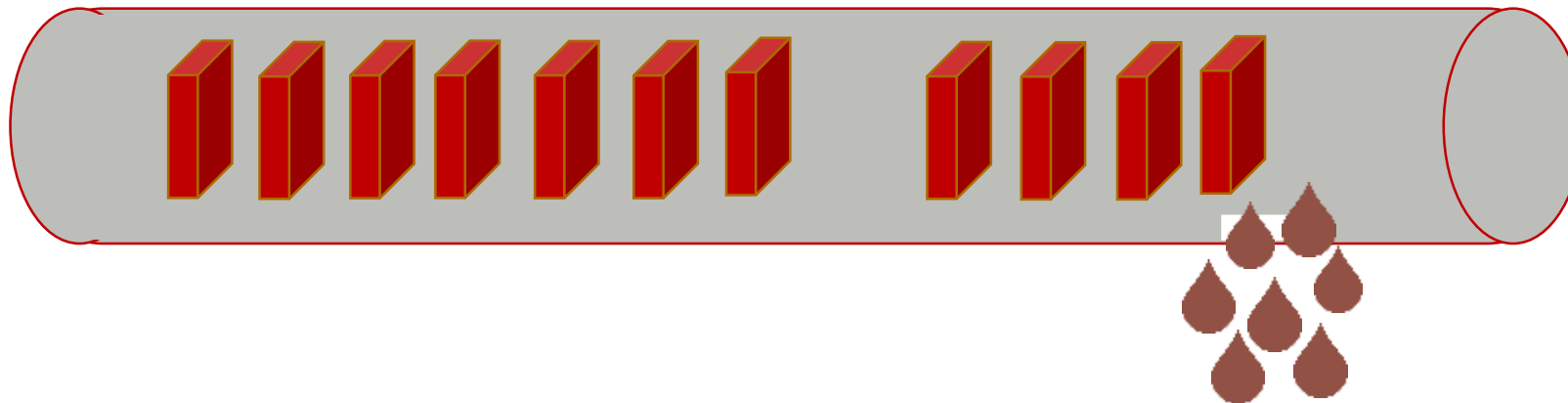
Haemophilia touches all stages of a life-span with clinical, psychological and social implications that require customized care



## Clotting in healthy individuals



## Clotting in people with haemophilia



# Haemophilia clinical manifestation and consequences

## HAEMOPHILIA BLEEDINGS



- Joint bleeding - haemarthrosis
- Muscle hemorrhage
- Soft tissue
- Life threatening-bleeding

## HAEMOPHILIA COMPLICATIONS



- Joint arthritis/arthropathy
- Flexion contractures
- Chronic pain
- Muscle atrophy
- Compartment syndrome
- Neurologic impairment

# Haemophilia also has significant psycho-social impact

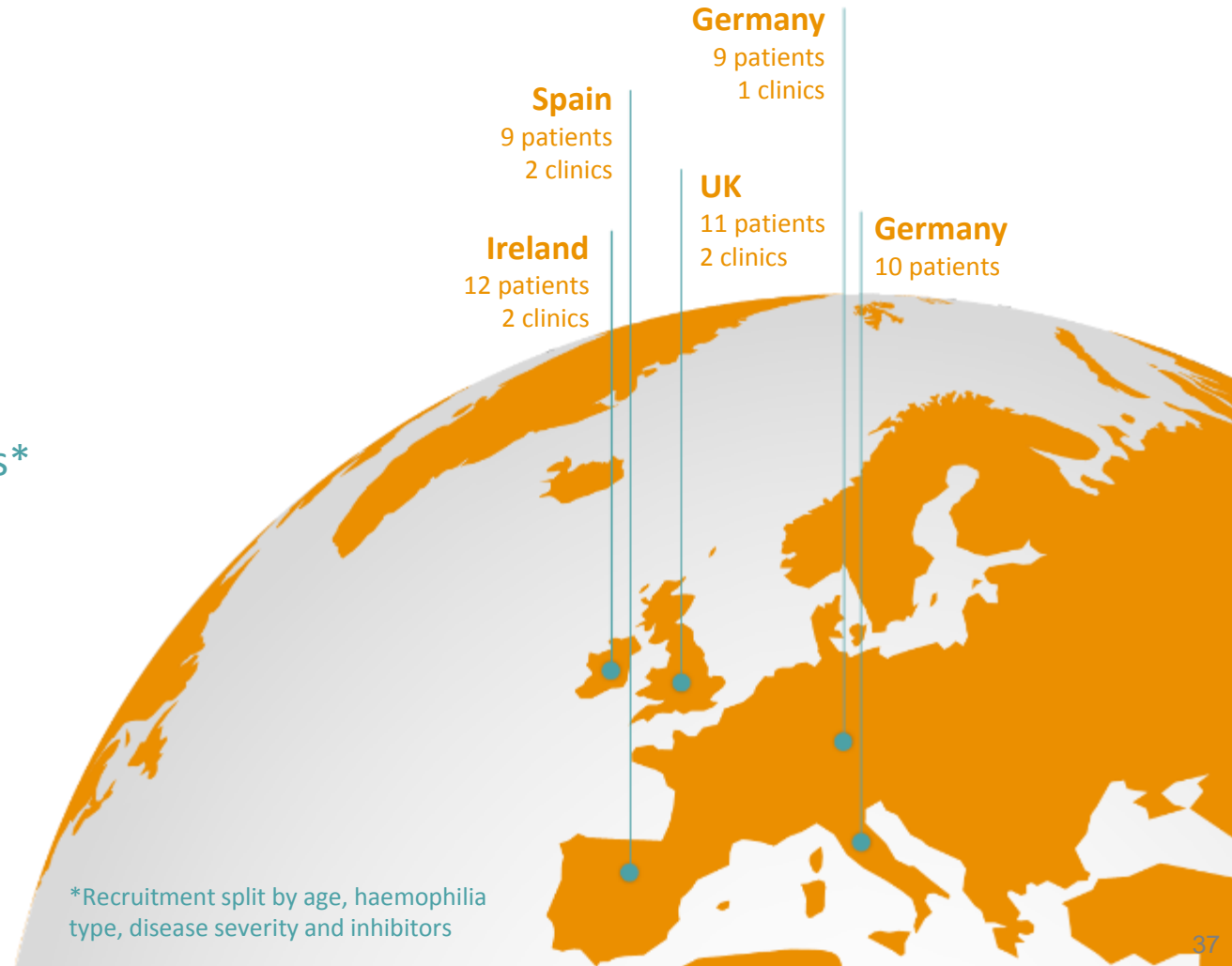
In 2018, Sobi undertook a large-scale, pan-European ethnographic study of the lives of people living with haemophilia

**18**  
HCPs

**51**  
PwH and their families\*

**5** experts

**500+**  
Hours of ethnographic research



\*Recruitment split by age, haemophilia type, disease severity and inhibitors

In general, people with haemophilia and their carers perceive their lives as entirely “normal”



“He lives a normal life.

He’s a normal kid.”

– Miquel’s (child) father

A photograph of a woman with blonde hair kissing a young child with blonde hair on the cheek. The scene is set outdoors, possibly on a boat, with a blue sky and a white structure visible in the background. The lighting is bright and warm, suggesting a sunny day. A large orange circle is overlaid on the left side of the image, containing a quote.

**“The days without treatment are my ‘worrying days’.”**

● **But day by day, people with haemophilia often act cautiously – finding it difficult to know what their treatment allows them to do**

Nick’s (child) mother considers him to be completely safe on treatment days and allows him to do most of the things that the nurses tell her he can do

On non-treatment days she believes his factor levels are practically zero. Therefore, she is afraid to let him out of her sight and significantly limits his activities.



## and many feel they have to make trade-offs on activity levels

based on assumptions about future  
quality of life

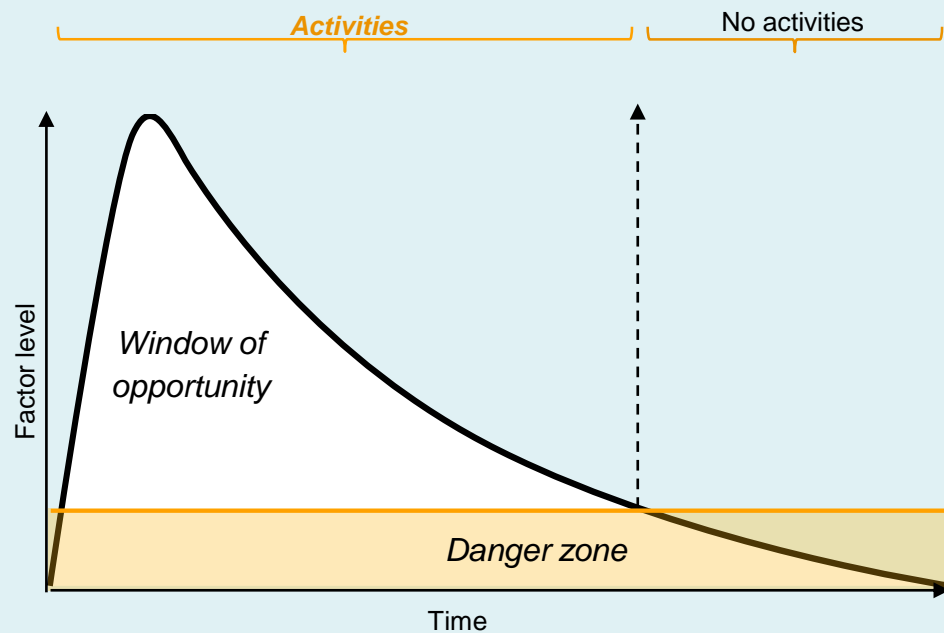
**“Will I be in a wheelchair when I  
grow older? Will I be able to be  
there for my grandchildren?  
These things I fear.”**

Mia (20s) is aware that the  
bleeds she has now will affect  
her mobility in the future.  
Therefore she tries to arrange  
her life so that she will have to  
walk the 500 meters into town  
only once a day



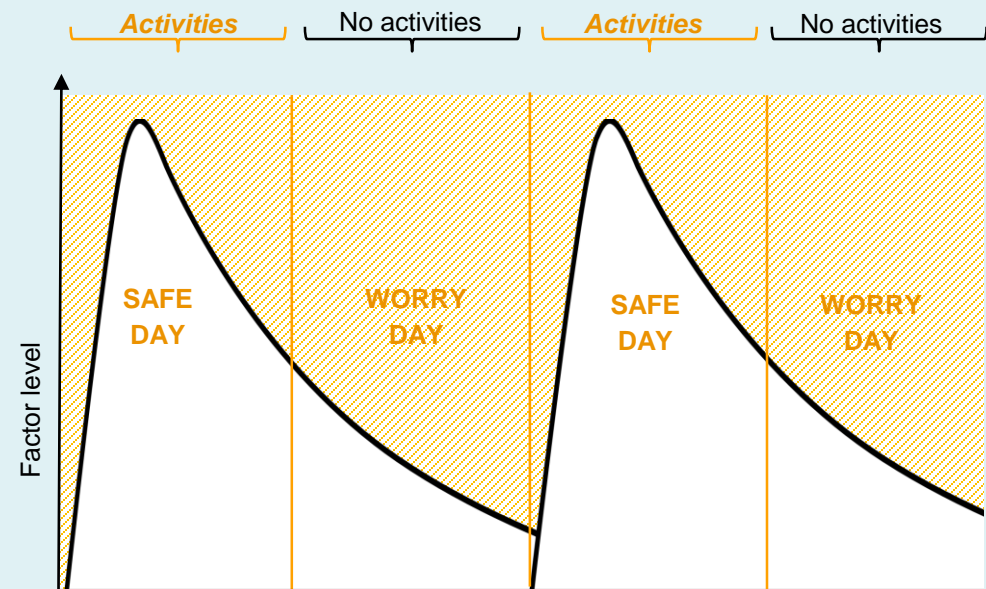
# The patient's understanding and perception of factor levels seldom match the medical community's view

While HCPs have a clear, clinical understanding of protection and activities based on factor levels...



\*Graphs are illustrative

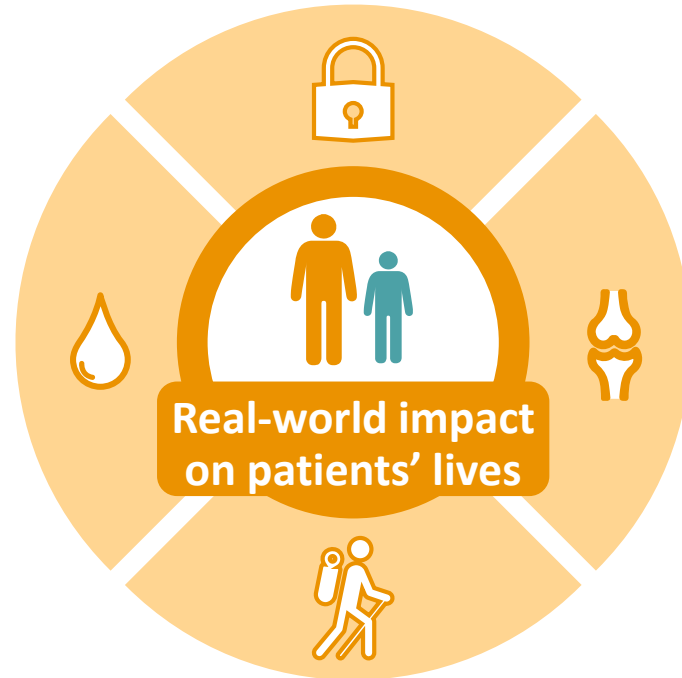
...people living with haemophilia develop mental models of their own to make sense of protection



# Higher expectations for protection beyond bleeds

No safety compromises  
across age groups

Long-term  
protection from  
bleeds

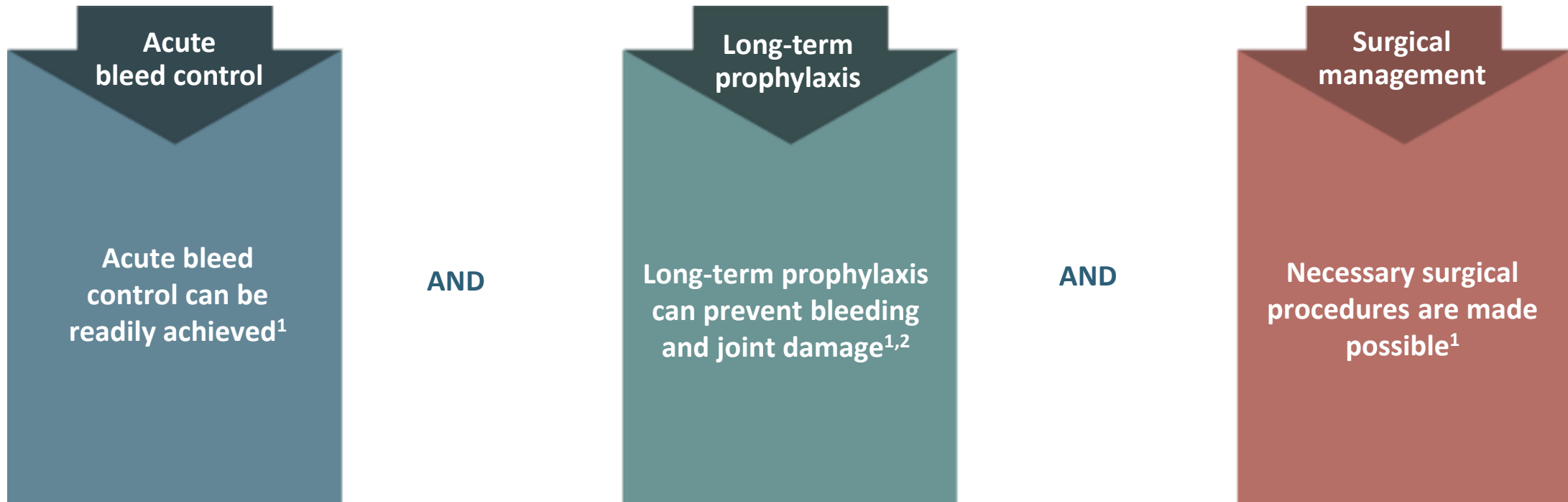


Long-term protection  
of joint health

Removal of burdens of haemophilia

# Clotting factor replacement can manage all clinical situations a patient can experience throughout the entire life<sup>1,2</sup>

Clotting factor replacement therapy provides:



1 Srivastava A, Brewer AK, Mauser-Bunschoten EP, Key NS, Kitchen S, Llinas A, et al. Guidelines for the management of haemophilia. Haemophilia. 2013;19(1):e1-e47.  
 2 Rocino A, Frachini M, Coppola A. Treatment and prevention of bleeds in haemophilia patients with inhibitors to factor VIII/IX. J Clin Med. 2017;6(4):46.

# Benefits of extended half-life technologies in haemophilia treatment

## Standard Half Life factors<sup>1-5</sup>



- frequent injections
- delayed start of prophylaxis
- suboptimal adherence to therapy
- breakthrough and subclinical bleeds
- joint disease

## Extended Half Life factors<sup>6-15</sup>



- higher protection for longer
- improve bleed prevention
- optimize number of weekly injections
- optimize weekly consumption



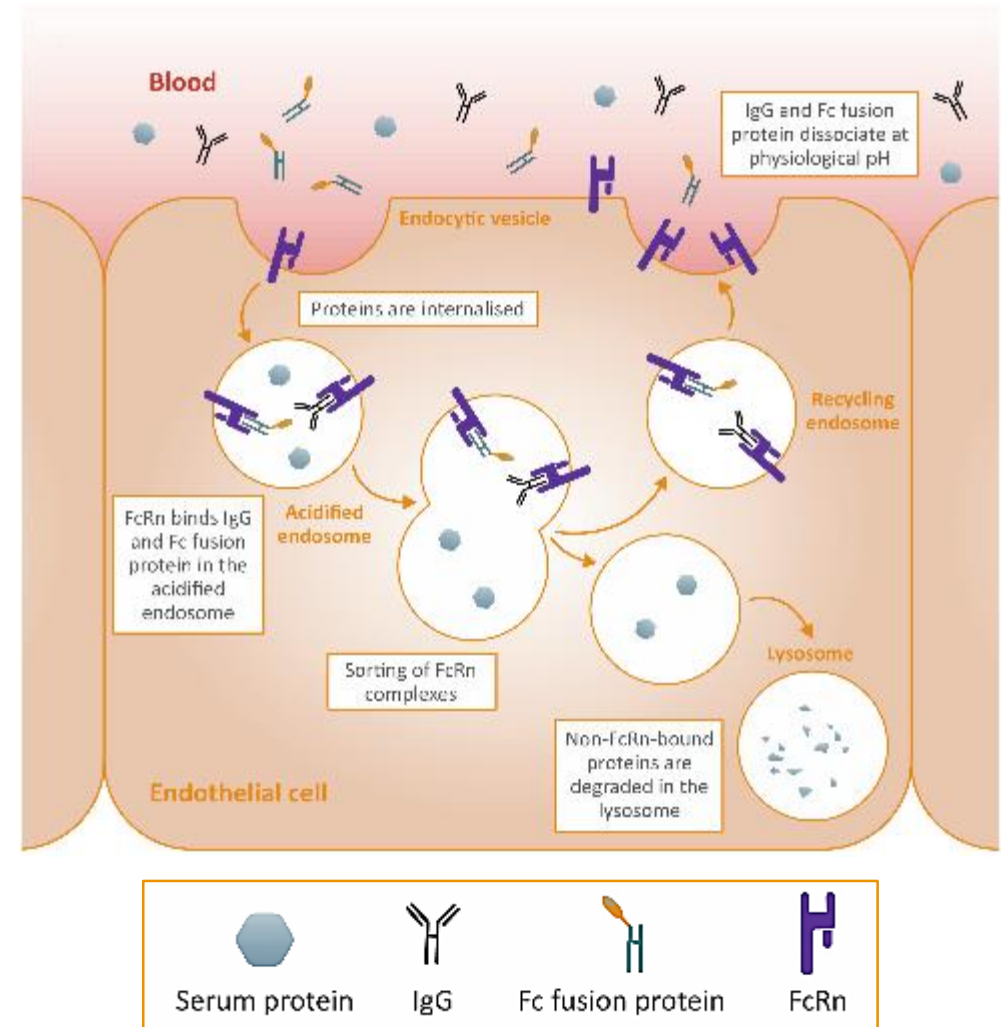
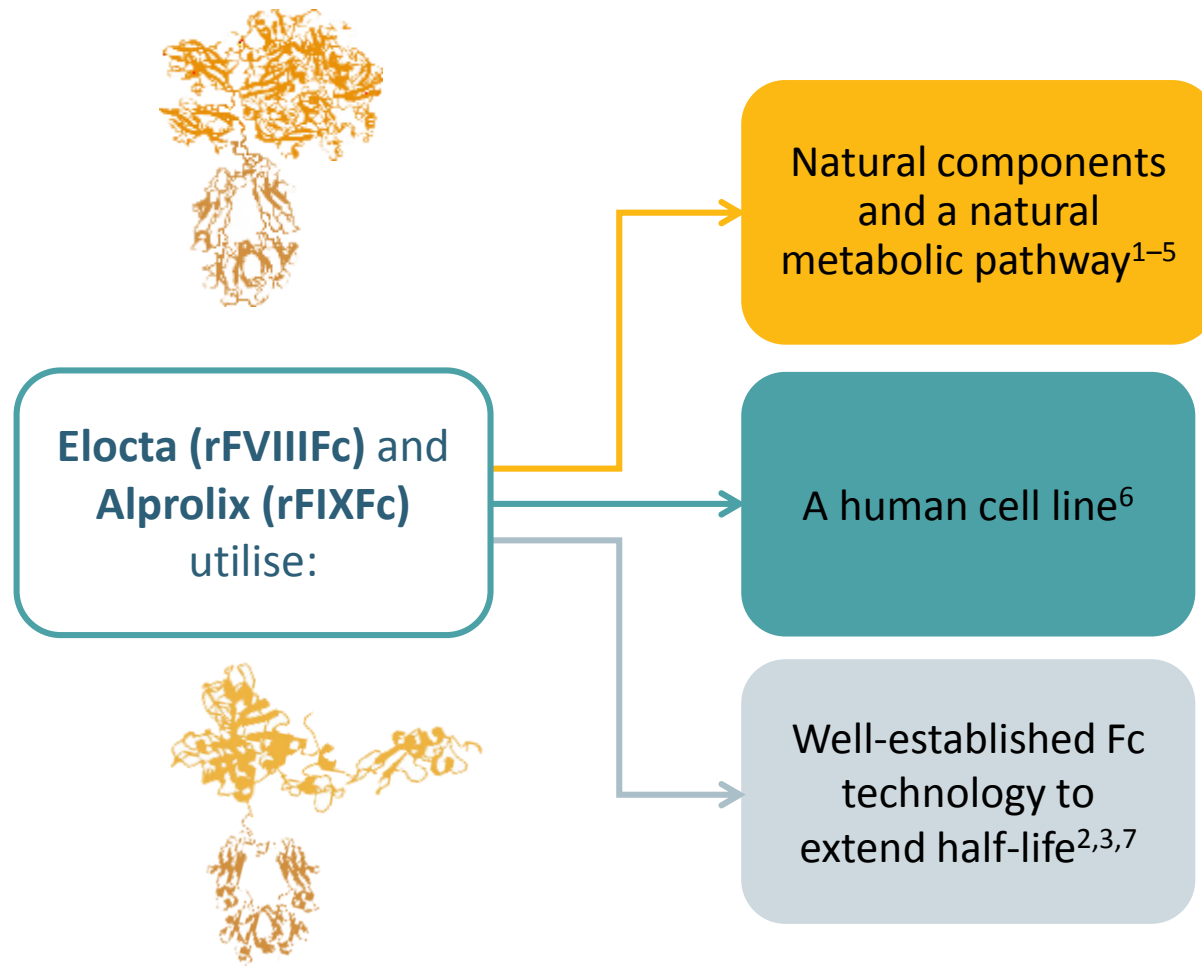
- supports health-related quality of life through increased protection against bleeds, reduced treatment burden and improved adherence

1 Carcao. Haemophilia 2014; 2 Ahnström et al. Haemophilia 2004; 3 Berntorp et al. Haemophilia 2017; 4 Oldenburg et al. Blood 2015; 5 Gringeri et al. Haemophilia 2014

6 Pipe. Thromb Res 2009; 7 Dumont et al. Blood 2012; 8 Shapiro et al. Blood 2012; 9 Berntorp et al. Haemophilia 2017; 10 Berntorp et al. Haemophilia 2016; 11 Shapiro et al. J Thromb Haemost 2014; 12 Powell et al. NEJM 2013; 13 Powell et al. Br J Haematol 2015; 14 Dunn et al. Haemophilia 2018; 15 Wang&Young Haemophilia 2018

NOTE: Approximate values taken from Summaries of Product Characteristics for Refacto AF, Kogenare/Helixate FS, Advate, NovoEight, Nuwiq, Kovaltry and Afstyla; BeneFIX and Rixubis

# Fc technology used in Elocta<sup>®</sup> and Alprolix<sup>®</sup>



1 Peters et al. J Thromb Haemost 2013; 2 Dumont et al. Blood 2012; 3 Powell et al. Blood 2012; 4 Roopenian & Akilesh. Nat Rev Immunol 2007; 5 Shapiro. Expert Opin Biol Ther 2013; 6 McCue et al. Biologicals 2015; 7 Rath et al. Crit Rev Biotechnol 2015

# Elocta and Alprolix best-in-class EHL products



Well-established safety and efficacy profiles – real-world experience from thousands of patients



Replacing the missing factor – fundamental in haemophilia treatment



Standard of care in many countries



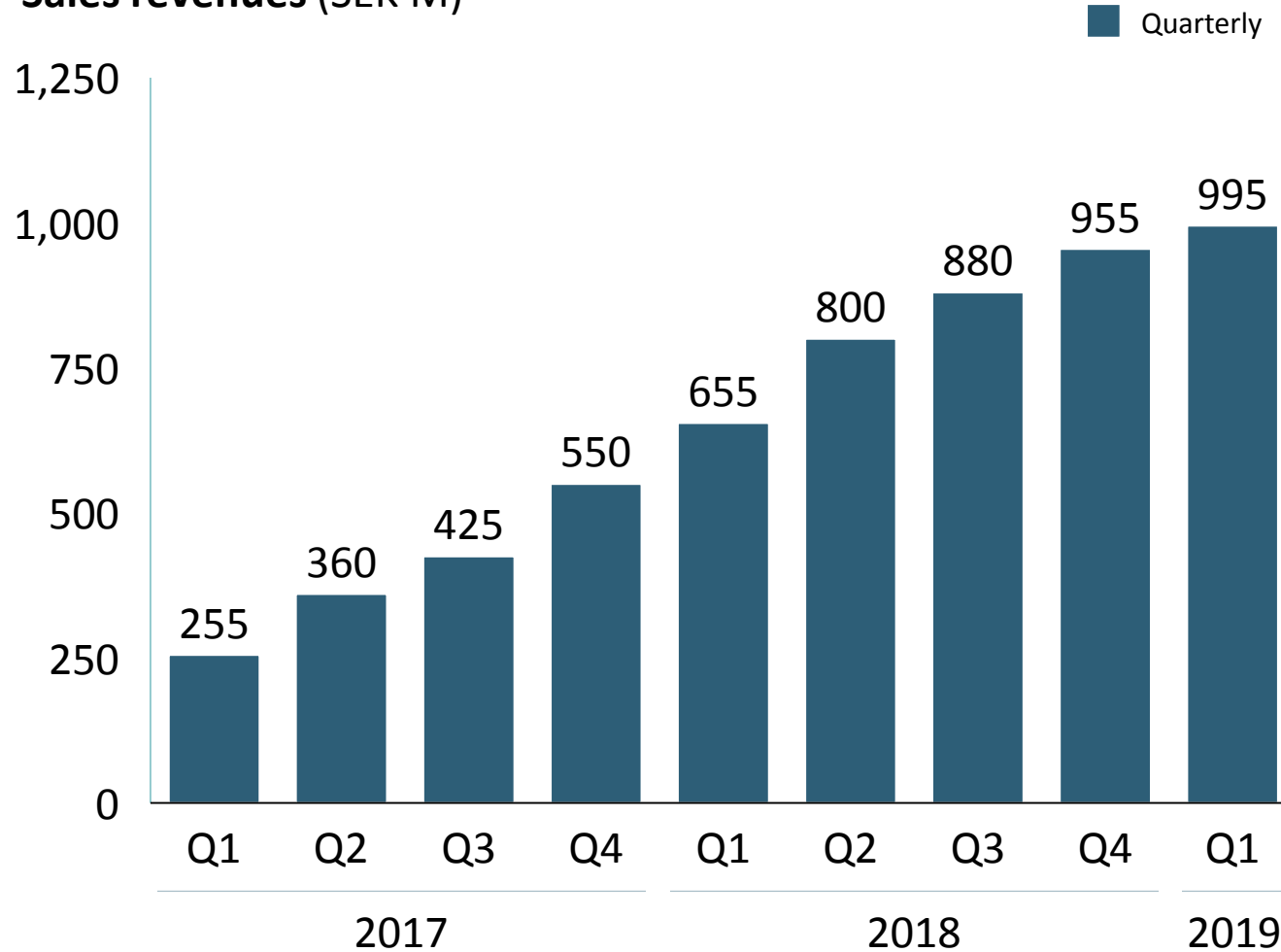
Suitable for people with haemophilia across all age groups and clinical settings, including surgery, with strong potential for individualised treatment



Creates possibilities to live an active life with less worry about the suboptimal protection and effectiveness of their therapy

# Elocta – individualising therapy is gaining further momentum

Sales revenues (SEK M)



FY 2018 product revenues of SEK 3,261 M (1,557)

- 109 per cent revenue growth (98 per cent at CER)

Q1 product revenues of SEK 991 M (649)

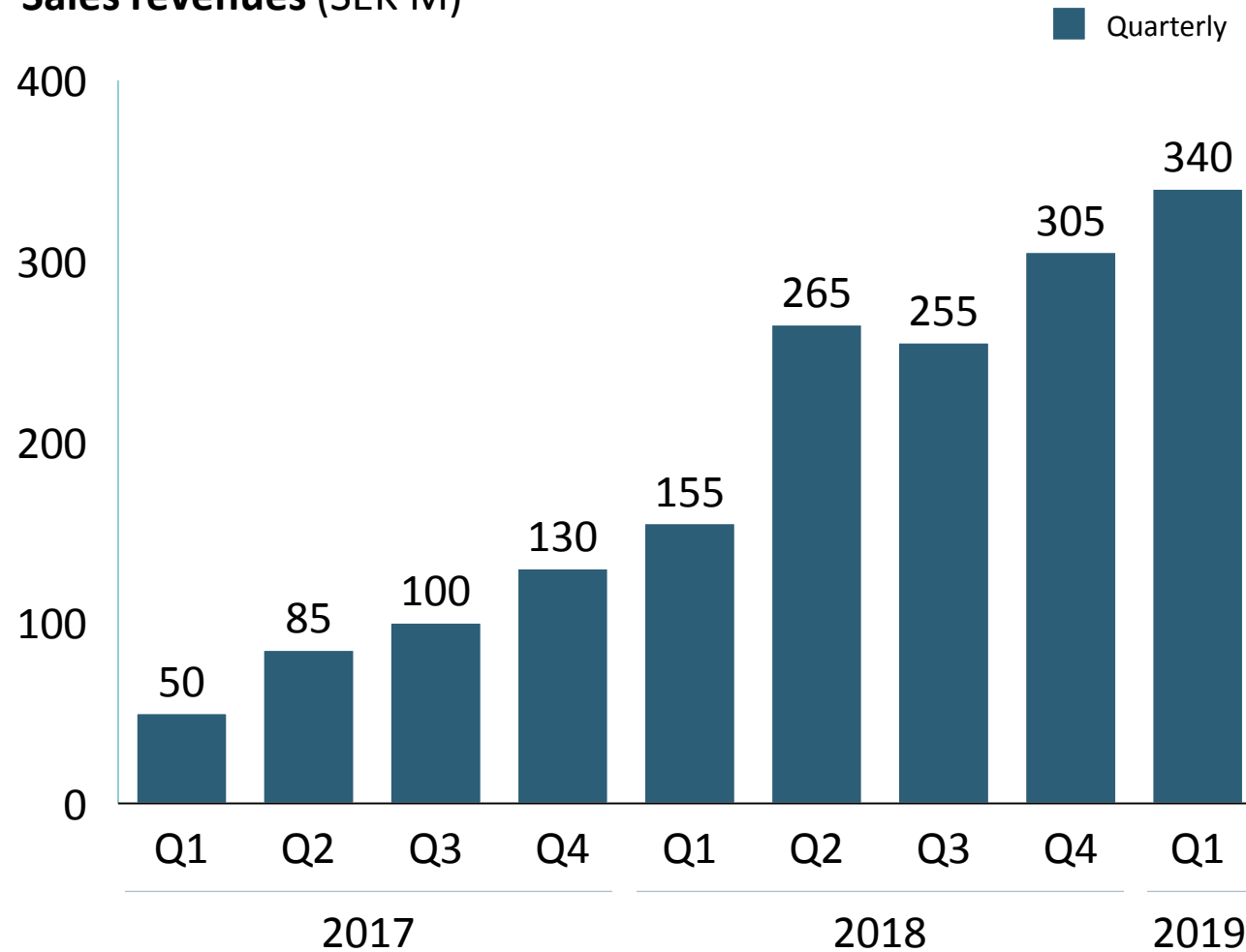
- 53 per cent revenue growth (46 per cent at CER)

Reimbursed in 26 countries

Focus on further penetration in current markets

# Alprolix – continued impressive performance

Sales revenues (SEK M)



FY 2018 product revenues of SEK 974 M (363)

- 168 per cent revenue growth (153 per cent at CER)

Q1 2019 product revenues of SEK 337 M (153)

- 120 per cent revenue growth (110 per cent at CER)

Reimbursed in 22 countries

A few more markets to enter

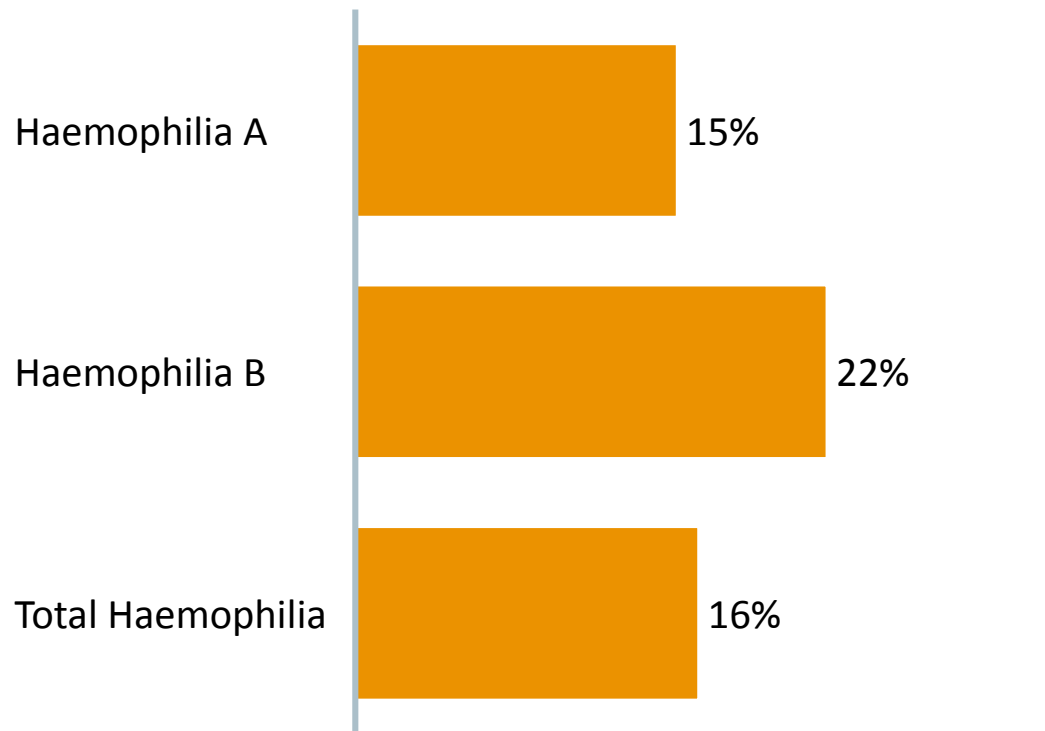
Focus on further penetration in existing markets



# Our market shares will approach our patient share over time

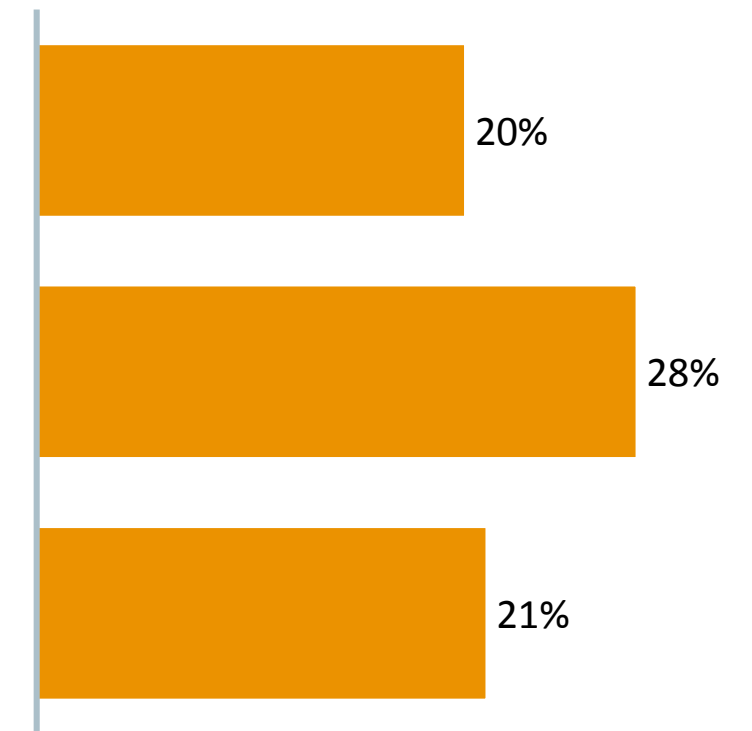
## Sobi value market share

Per cent, end-of-2018



## Sobi prophylaxis patient share

Per cent, end-of-2018



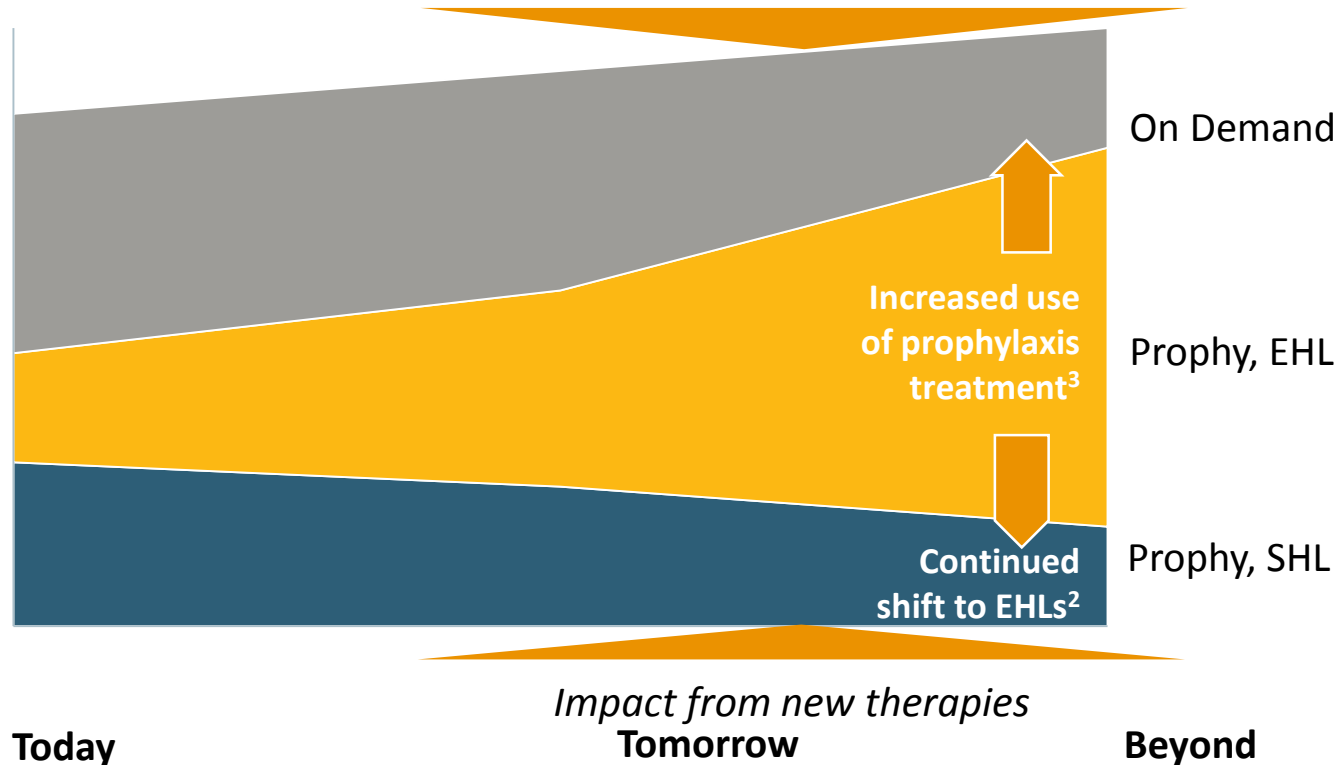
Based on company estimates in the Sobi territory

# Growth further fuelled by SHL-to-EHL conversion and on demand-to-prophylaxis conversion

Good opportunity for Elocta to expand its position in the FVIII market

## Patients, treated for haemophilia A, in Sobi territories<sup>1</sup>

*Impact from new therapies*



## Our thoughts:

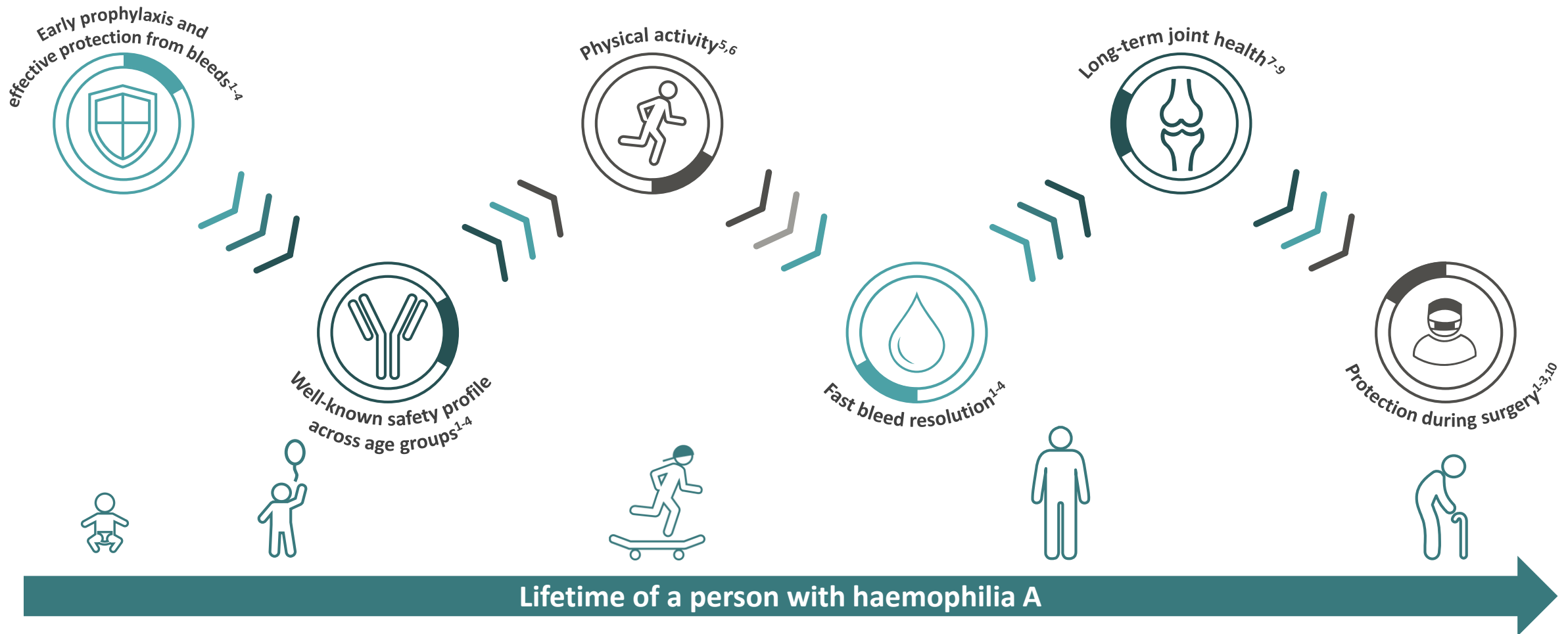
- Switches will accelerate with increased competition
- Safety appears to rank higher in Europe than US
- Europe is a more complex landscape
- Sobi is well prepared for a change in landscape

<sup>1</sup> Represents treated moderate and severe haemophilia A

<sup>2</sup> EHL category includes Elocta, Adynovi, Jivi, and Esperoct

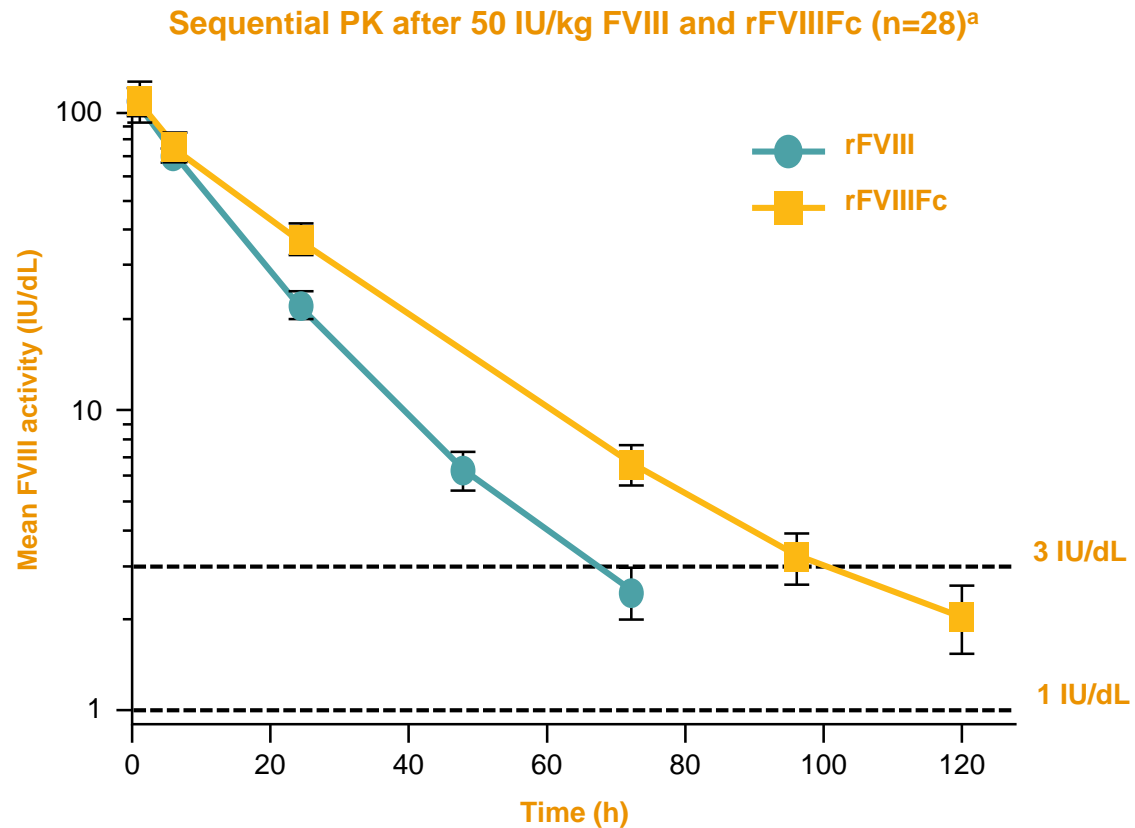
<sup>3</sup> Expect prophylaxis usage to grow to 80 per cent of moderate and severe patients over long term

# Elocta experience across age groups and clinical situations



1. Mahlangu et al. *Blood* 2014 2. Young et al. *J Thromb Haemost* 2015 3. Nolan et al. *Haemophilia* 2016 4. Konkle et al. EAHAD 2019 Poster P039 5. Su et al. ISTH 2017 Poster PB-1783 6. Quon et al. *Haemophilia* 2017 7. Oldenburg et al. EAHAD 2019 Poster P158 8. Oldenburg et al. *Haemophilia* 2018 9. Oldenburg et al. ISTH 2017 Poster PB946 10. Mahlangu et al. *Thromb Haemost* 2016

# A-LONG: rFVIII Fc and its prolonged haemostatic protection

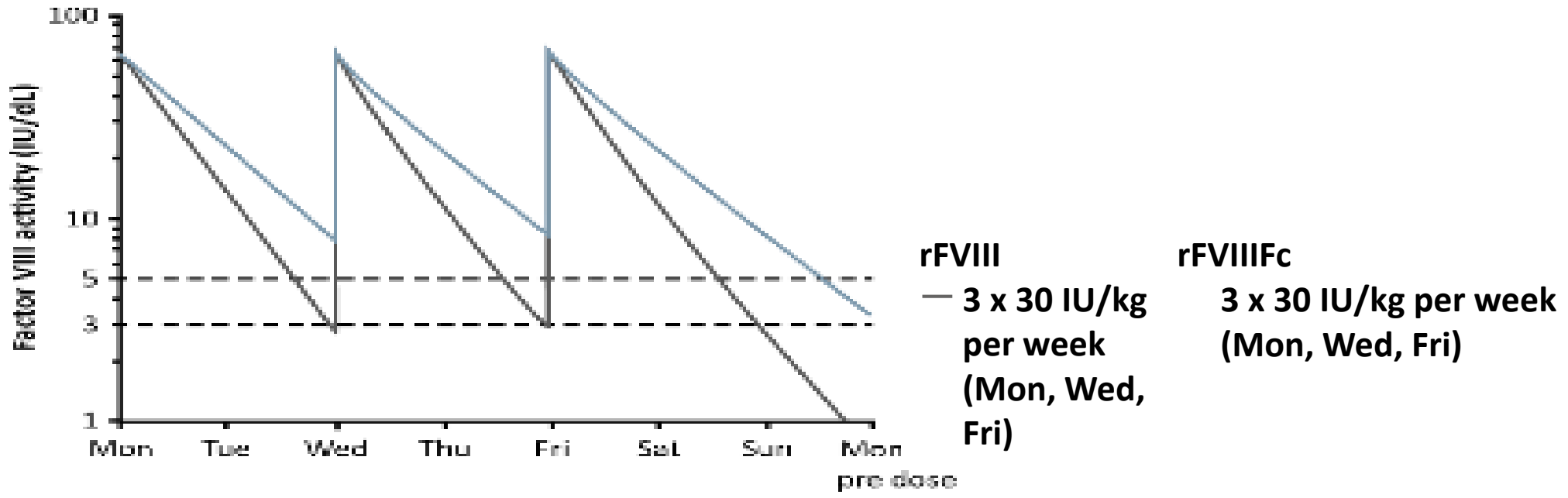


Compared with FVIII, rFVIII Fc showed on average:

- **33% lower clearance<sup>b</sup>**  
(2.0 versus 3.0 mL/h/kg<sup>c</sup>)
- **56% higher AUC<sup>b</sup>**  
(51.2 versus 32.9 IU x h/dL per IU/kg<sup>c</sup>)
- **1.5-fold longer half-life**  
(19.0 versus 12.4 hrs<sup>c</sup>)
- **1.5-fold longer time to 1 and 3 IU/dL (%)**

A Sampling up to 72 hours for rFVIII and up to 120 hours for rFVIII Fc  
 B Calculated from Mahlangu et al. Blood 2014  
 C p<0.001  
 SOURCE: Mahlangu et al. Blood 2014

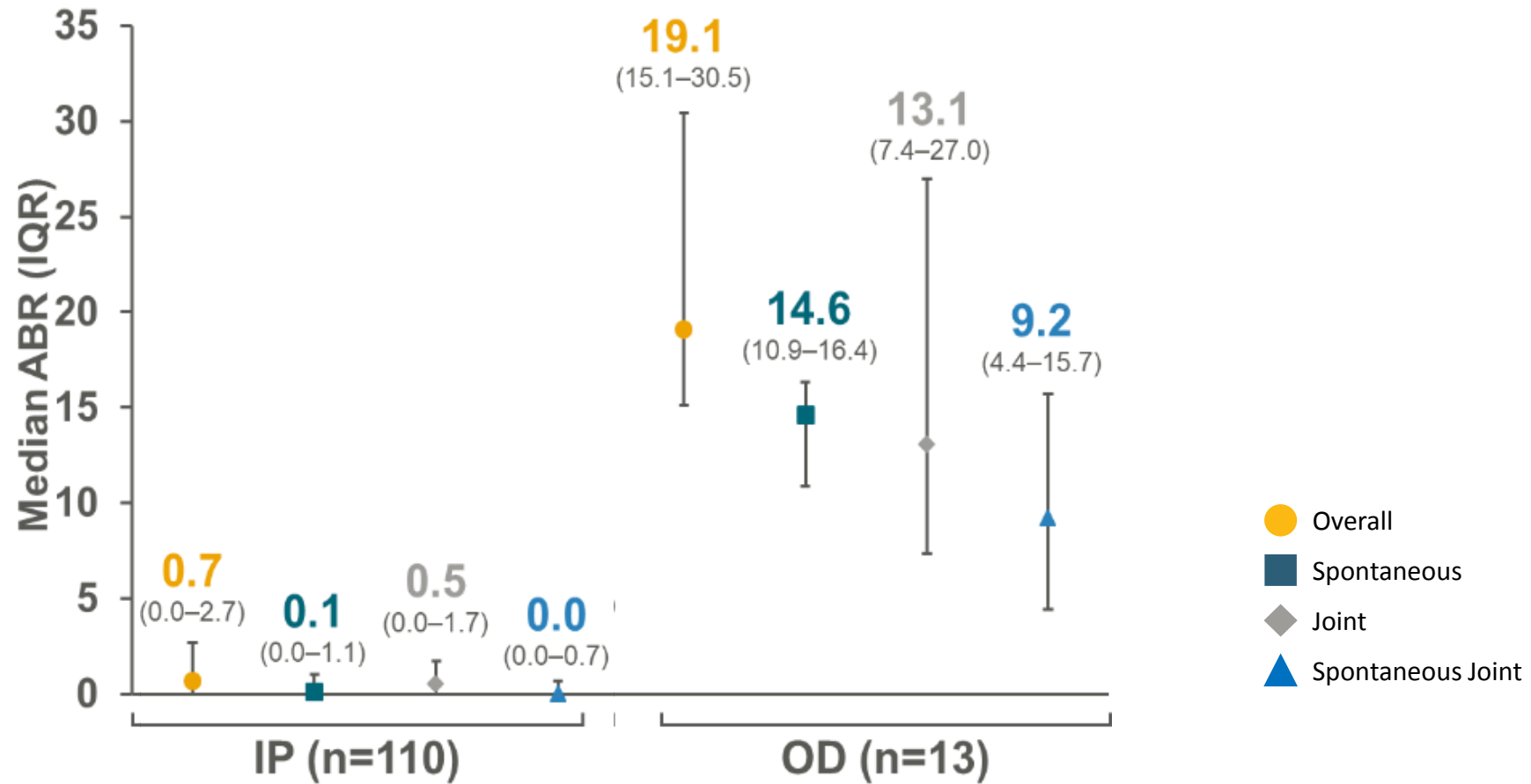
# Improved patient protection with individual dosing



Injections/week	=
Weekly factor consumption	=
Factor VIII level	↑↑↑

1 Simulations shown are an example for rFVIII Fc only, and are based on a hypothetical 73 kg adult patient with typical PK parameters  
SOURCE: Adapted from Berntorp et al. Haemophilia 2016

# Elocta: Individualising therapy improves patient outcomes



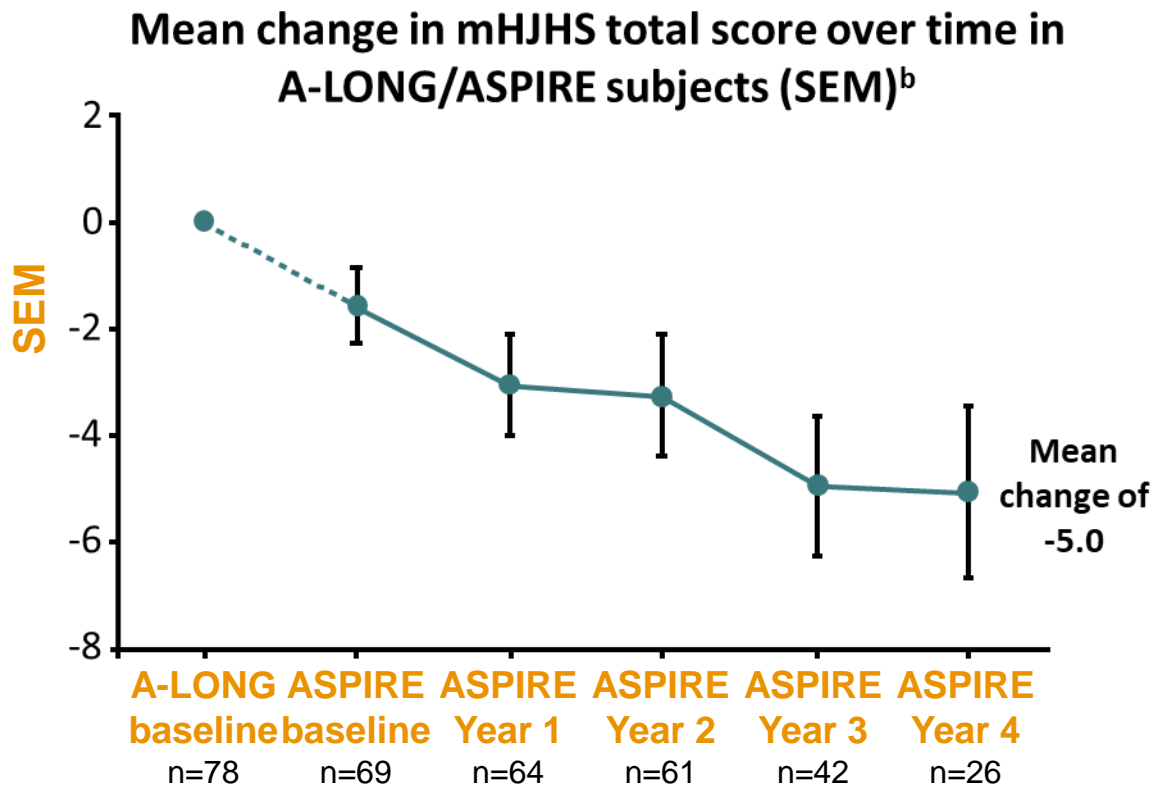
IP: Individualised prophylaxis

IQR: Interquartile range

OD: On-demand treatment

SOURCE: Adapted from Nolan et al. ASH 2018 Poster 1192

# Continuous improvement in joint health score after long-term Elocta prophylaxis



Total score (mean)

**A-LONG ASPIRE ASPIRE ASPIRE ASPIRE ASPIRE**  
**baseline baseline Year 1 Year 2 Year 3 Year 4**  
 n=78 n=69 n=64 n=61 n=42 n=26

21.6 19.8 19.5 18.9 19.2 19.5

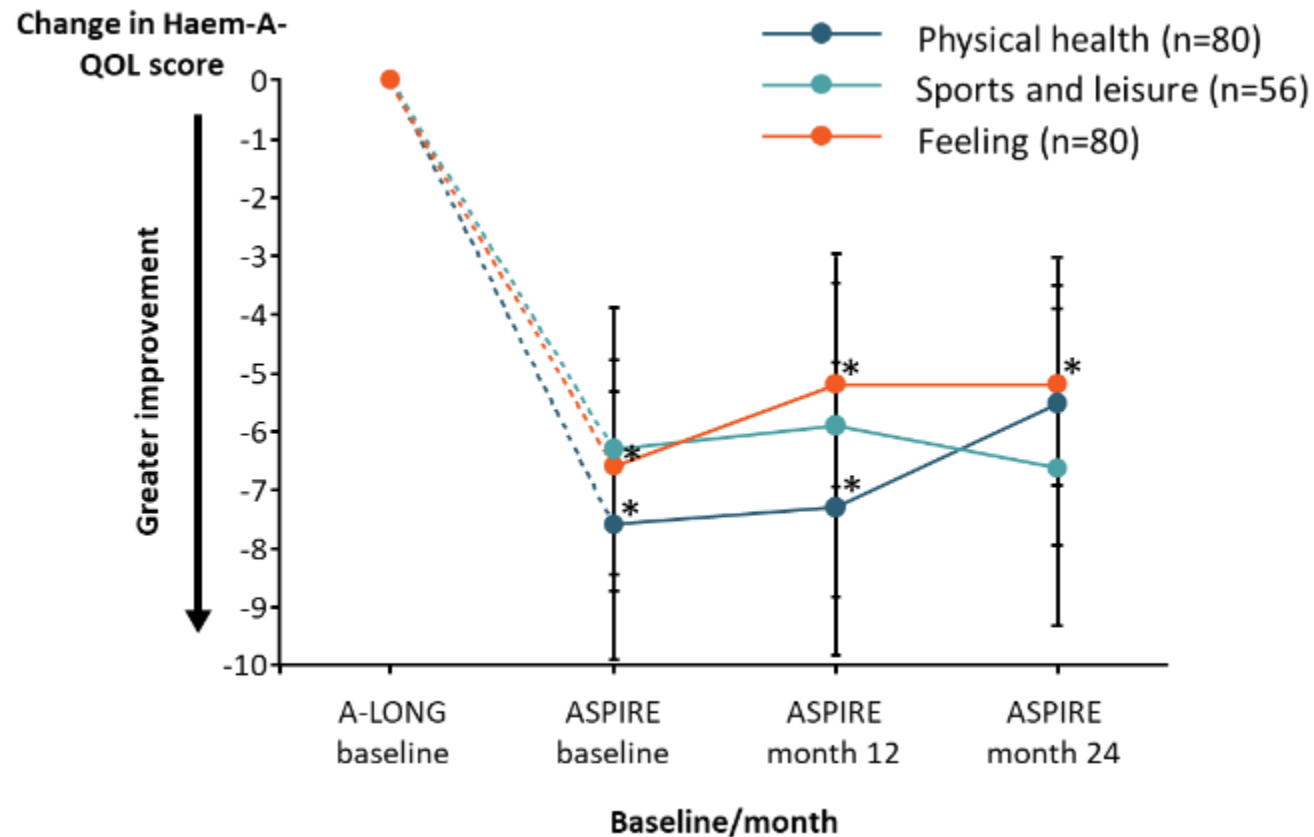
- Assessed using modified Haemophilia Joint Health Score in adolescents and adults
- **Benefits were seen despite pre-existing target joints and also in patients with severe arthropathy**
- **mHJHS components with the greatest improvement were swelling, range of motion and strength**
- Post-hoc analysis

NOTE: As of second ASPIRE interim data cut (8 December 2014); Number of subjects listed were those who were always on prophylaxis and had baseline mHJHS/HJHS from A-LONG/Kids A-LONG and at least one assessment in ASPIRE at a major assessment visit. Dashed line indicates variable follow-up time between A-LONG to ASPIRE baseline, median: 8.3 months

SOURCE: Adapted from Oldenburg et al. EAHAD 2019 Poster P158, Oldenburg et al. Haemophilia 2018, Oldenburg et al. ISTH 2017 Poster PB946 and Nolan et al EAHAD 2019

# Improved quality of life in patients on Elocta prophylaxis<sup>a,1</sup>

Improved health scores “Sports & Leisure,” “Physical Health” and “Feeling” in adult subjects (≥17 yrs) vs. A-LONG baseline<sup>a,1</sup>



\*p<0.01; Error bars stand for standard error of the mean <sup>a</sup>As of third ASPIRE interim data cut (11 January 2016)  
 1. Adapted from Su et al. ISTH 2017 Poster PB-1783



# Summary – Elocta: Features and outcomes



- Elocta represents an innovative treatment option, with demonstrated **efficacy** and a well-established **safety** profile for people with haemophilia A<sup>1-3</sup>



- Elocta is the first and only FVIII using Fc technology** to achieve **half-life extension via a natural recycling pathway**, and which **might convey other immunomodulatory properties** that are currently being investigated<sup>4,5</sup>



- Elocta has demonstrated **long-term joint protection**, **0 median spontaneous joint bleeds**, **99.6% of target joints resolved** and **continuous improvements in HJHS**<sup>6-8</sup>



- Confidence with Elocta can be supported by **8 years of clinical experience** and **over 4 years of real-world experience** where Elocta demonstrated a consistent long-term safety profile<sup>1-4</sup>



- Elocta is indicated across **all clinical settings** and in **all age ranges**<sup>2,3</sup>



- Elocta can be **easily measured with a variety of assays** for routine management of treatment as well as for any other need<sup>9</sup>

HJHS: Haemophilia Joint Health Score

1. Nolan et al. Haemophilia 2016 2. Eloctate USPI 3. Elocta SmPC 2019 4. Shapiro Expert Opin Biol Ther 2013 5. Oldenburg et al Haemophilia 2018 6. Oldenburg et al. EAHAD 2019 P158 7. Nolan et al. ASH 2019 P1192 8. Konkle et al. EAHAD 2019 P039 9. Sommer et al. Haemophilia 2014

# How we will continue to grow

## Our sources of business, our value proposition

- In future replacement factors will remain dominant
  - The natural solution, with corresponding safety
  - This is a highly conservative market, safety conscious
- Evolution of standards of care
  - Prophylaxis remains key focus for treaters and truly achieving Zero bleeds (all bleeds)
  - Value of prophylaxis over on demand increasingly recognised by payer community when backed with data
  - Inhibitor management remains a key unmet medical need
- People with Haemophilia are all individuals
  - Personalised treatment is needed as a result, intensified to enable people to live beyond their haemophilia
  - Providing patients with certainty, enabling psychological and physical freedom
  - Only replacing the missing factor enables this



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Immunology

A small white circle.

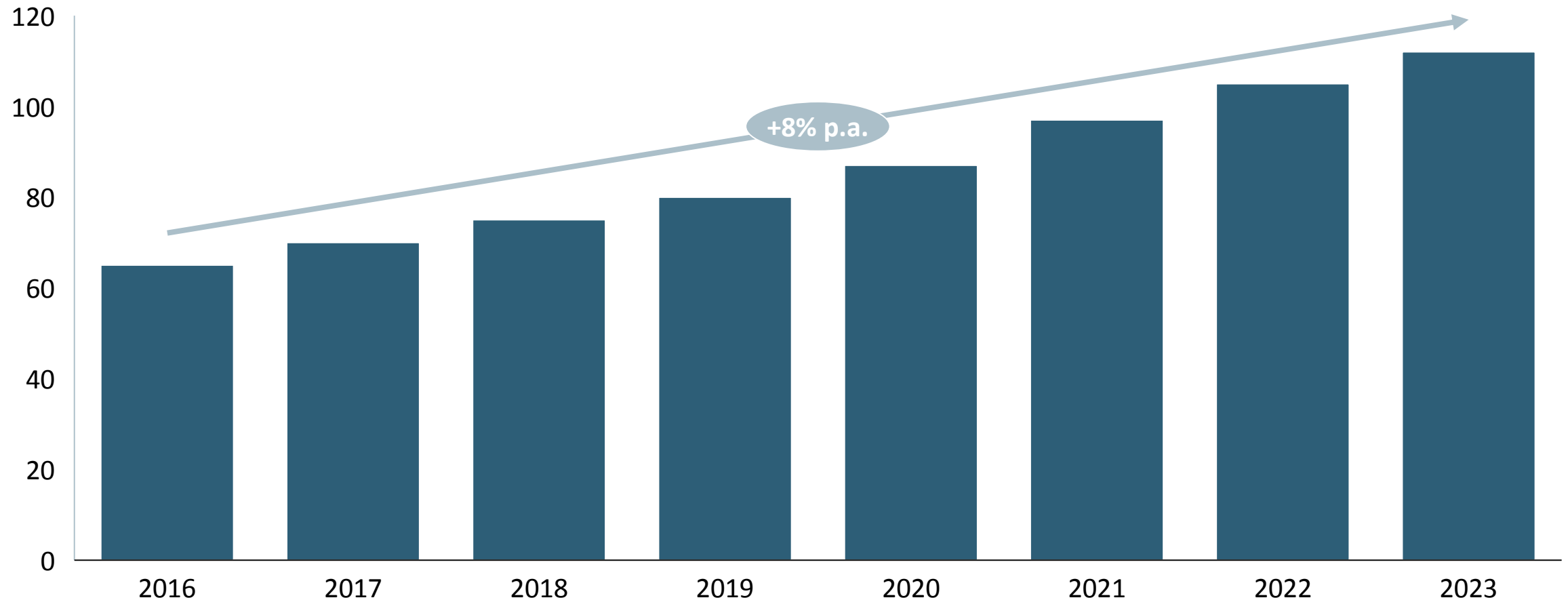
**Norbert Oppitz**  
Head of Specialty Care

# Why Immunology will drive Sobi's future

- 1 We have deep understanding within Immunology**  
Immunology is at the core of what we do  
Kineret: extensive expertise in commercialisation and mining new indications
- 2 The immunology market is poised to grow to total USD 113 B by 2023, with immuno-oncology becoming an attractive segment**
- 3 Emapalumab and Synagis will allow us to establish a significant platform in Immunology**

# Immunology drug market projected to display solid growth at a CAGR of 8% from 2016 to 2023

Global immunology drug sales, USD billions



Sobi currently has three strong assets in immunology





Synagis



# Introduction to RSV and Synagis



## What is respiratory syncytial virus?

- Seasonal viral infection causes ~57,000 hospitalisations annually in the US in children under 5
- A leading global cause of death in children under five years of age (~ 50,000)
- Can develop into potentially life-threatening bronchiolitis or pneumonia, particularly in premature babies and those with heart or lung diseases
- No treatment currently available, so prevention during RSV season (~October – May) is important for susceptible babies



## What is Synagis (palivizumab)?

- Seasonal immunoprophylaxis, not vaccine, that is the only marketed product to protect against RSV
- Infants typically receive 5 monthly injections during RSV season
- Eligibility for treatment limited to premature babies or children with heart or lung disease<sup>1</sup>
- Approved in 1998
- Global standard of care for RSV prevention and the only approved therapy to prevent RSV
- Synagis has protected ~3 million babies globally

<sup>1</sup> A history of premature birth ( $\leq 35$  weeks gestational age) and who are 6 months of age or younger at the beginning of the RSV season; Bronchopulmonary dysplasia (BPD) that required medical treatment within the previous 6 months and who are 24 months of age or younger at the beginning of the RSV season; Haemodynamically significant congenital heart disease (CHD) and who are 24 months of age or younger at the beginning of the RSV season  
SOURCE: US CDC, US FDA

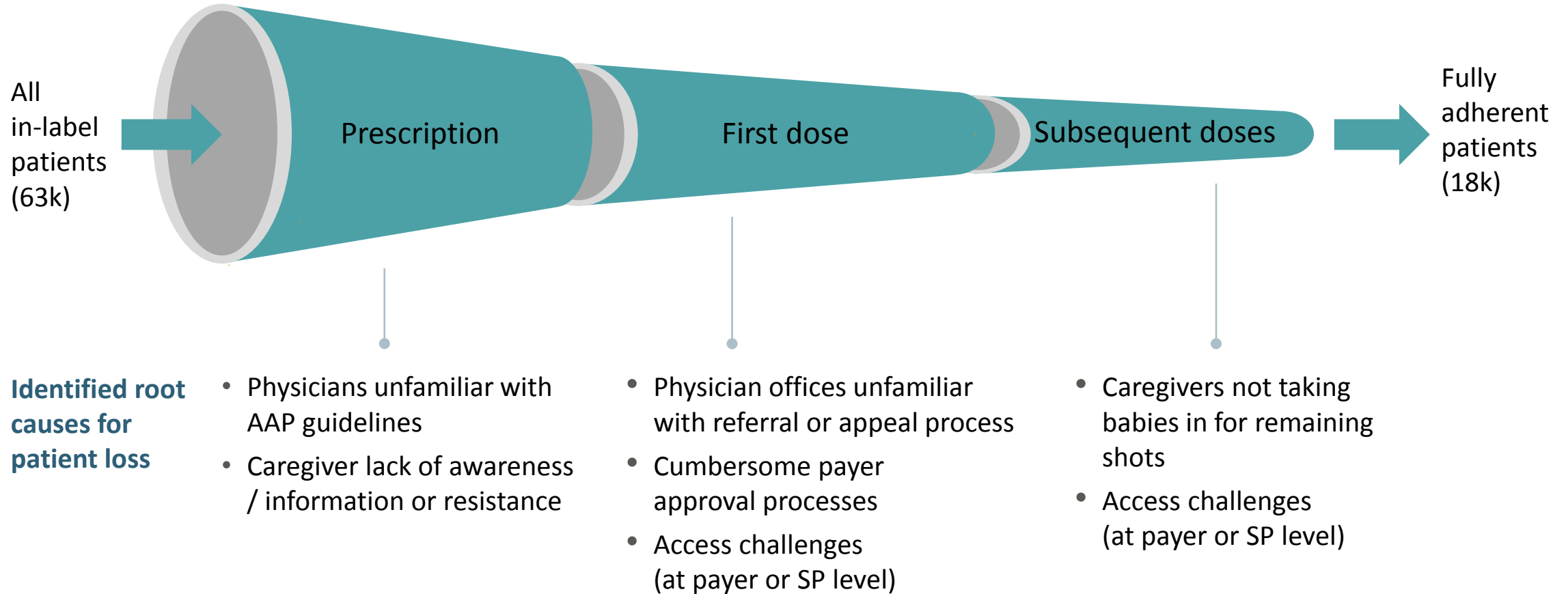
## Synagis integration is going well

- 135/135** FTE offers accepted. Employees transferred on Day 1
- 16** Integration workstreams managed by a central Integration Management Office
- 100%** of TSA tracking towards successful cutover, with first wave transitioning 30 June
- 35+** new employees already hired to support Synagis with more planned before the 2019/2020 season
- 9.5+ /10** Average self-rating from surveyed employees about working at Sobi

**“The integration was seamless. The priority we have is to continue to protect the babies which we have been able to do without distractions.”**

–Employee who joined Sobi from AZ

# Large number of pre-term babies eligible for Synagis not currently receiving treatment



# 2019 Synagis brand plan guided by three priorities

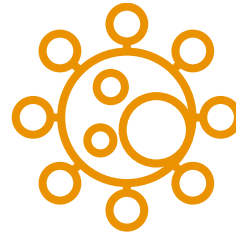
A



## Secure Synagis access for <29wGA and CHD/CLD patients

- Ensure all stakeholders are educated on the critical need for RSV protection in this patient population
- Streamline administrative processes to limit unintended patient drop-off

B



## Activate all in-label patient populations at risk of contracting RSV

- Present recent data on increased RSV hospitalisations to emphasise the consequences of RSV contraction

C



## Leverage clinical data to deepen engagement with external stakeholders

- Utilise KOLs and up-to-date clinical studies to highlight the evidence-based value proposition of Synagis
- Deploy a comprehensive advocacy plan that uses a diverse portfolio of data-driven materials to engage all key audiences relating to RSV and Synagis

A large orange circle with a bite taken out of its top-left corner, and a smaller solid orange circle above it to the left. The text is centered within the larger circle.

**Gamifant  
(emapalumab)**

# Gamifant addresses a high unmet medical need in HLH



**HLH is a rare but dramatic health crisis** that presents as a heterogeneous syndrome of rapidly progressive, life-threatening disease

**~200**

Patients with primary HLH in the US and EU (2023 estimate)

**~4,200**

Patients with secondary HLH (2023 estimate)



- High fever
- Infection
- Rash



- Hyperferritinemia
- Coagulation defects
- Severe cytopenia



- Hepatosplenomegaly
- Liver impairment
- Jaundiced appearance

# Two types of HLH: primary and secondary<sup>1-4</sup>

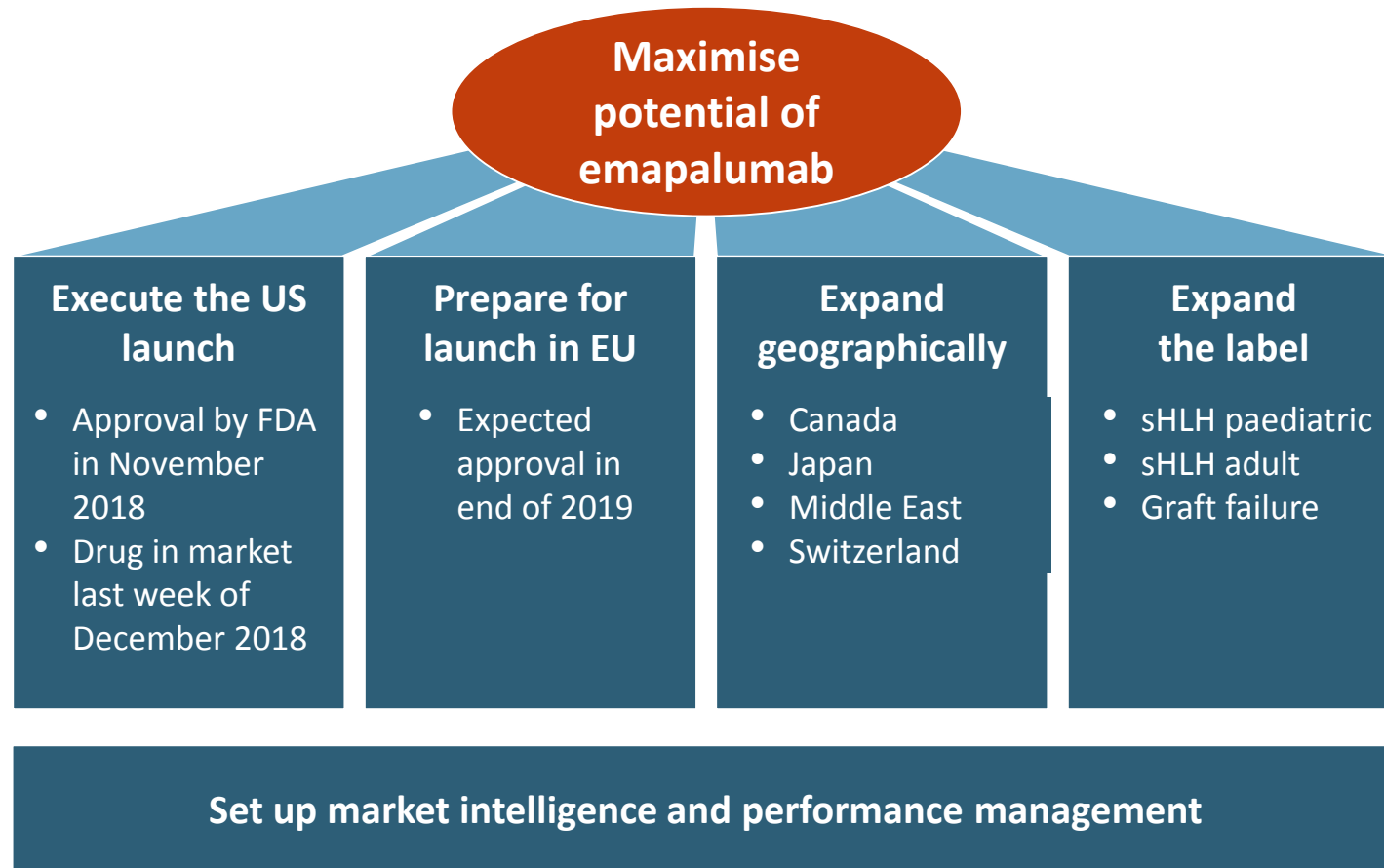
## Primary (pHLH)

- Genetic mutations cause primary HLH
- Can be suspected on the basis of family history
- Patients are more frequently infants or children
- An infection is often the trigger of the disease

## Secondary (sHLH)

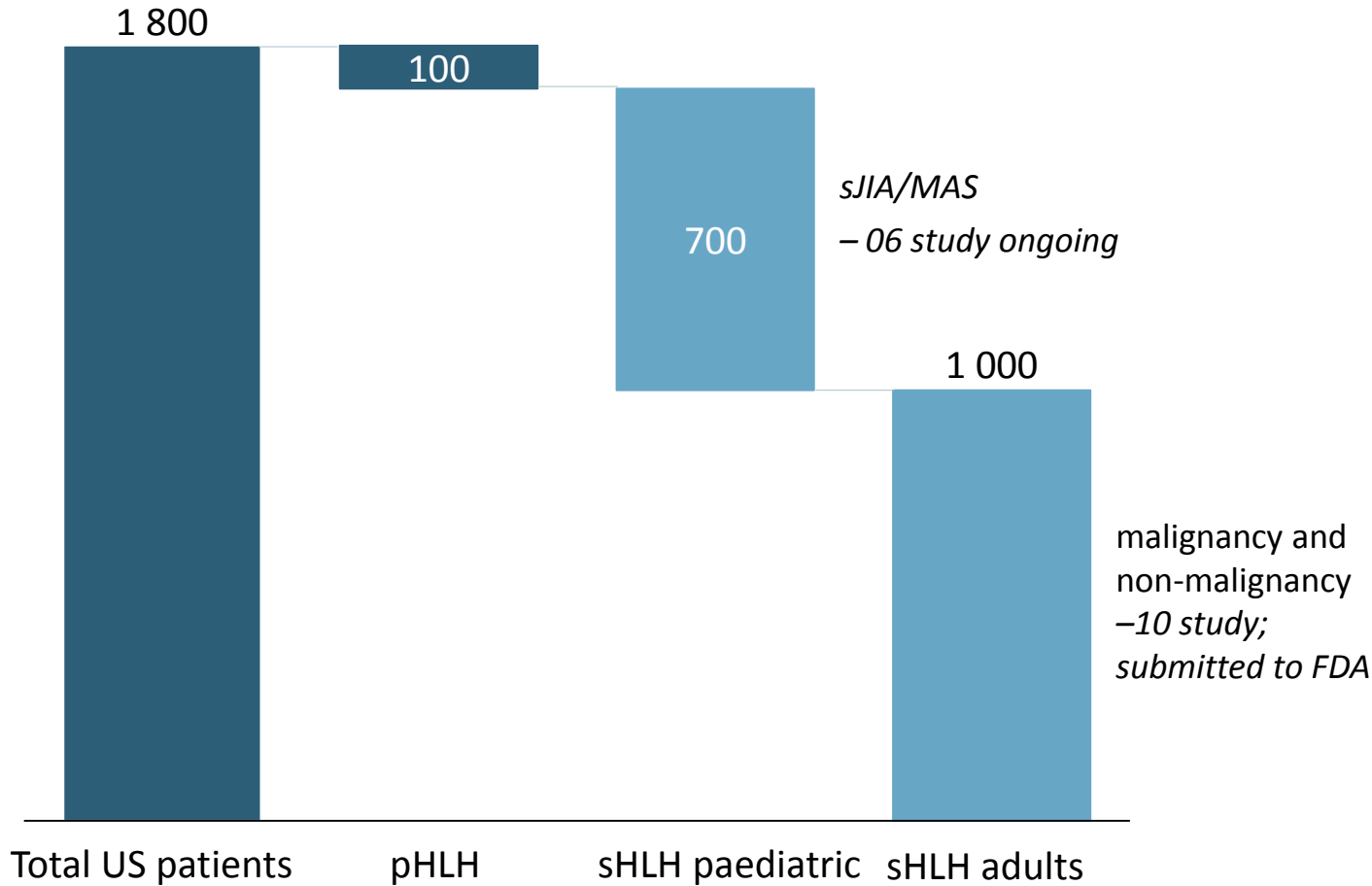
- Also called acquired HLH
- Can occur at any age
- Causes include:  
Infections, autoimmune/inflammatory diseases, malignancies

# Expansion strategy for emapalumab - promising start in Q1





# Emaplumab – significant potential beyond primary HLH



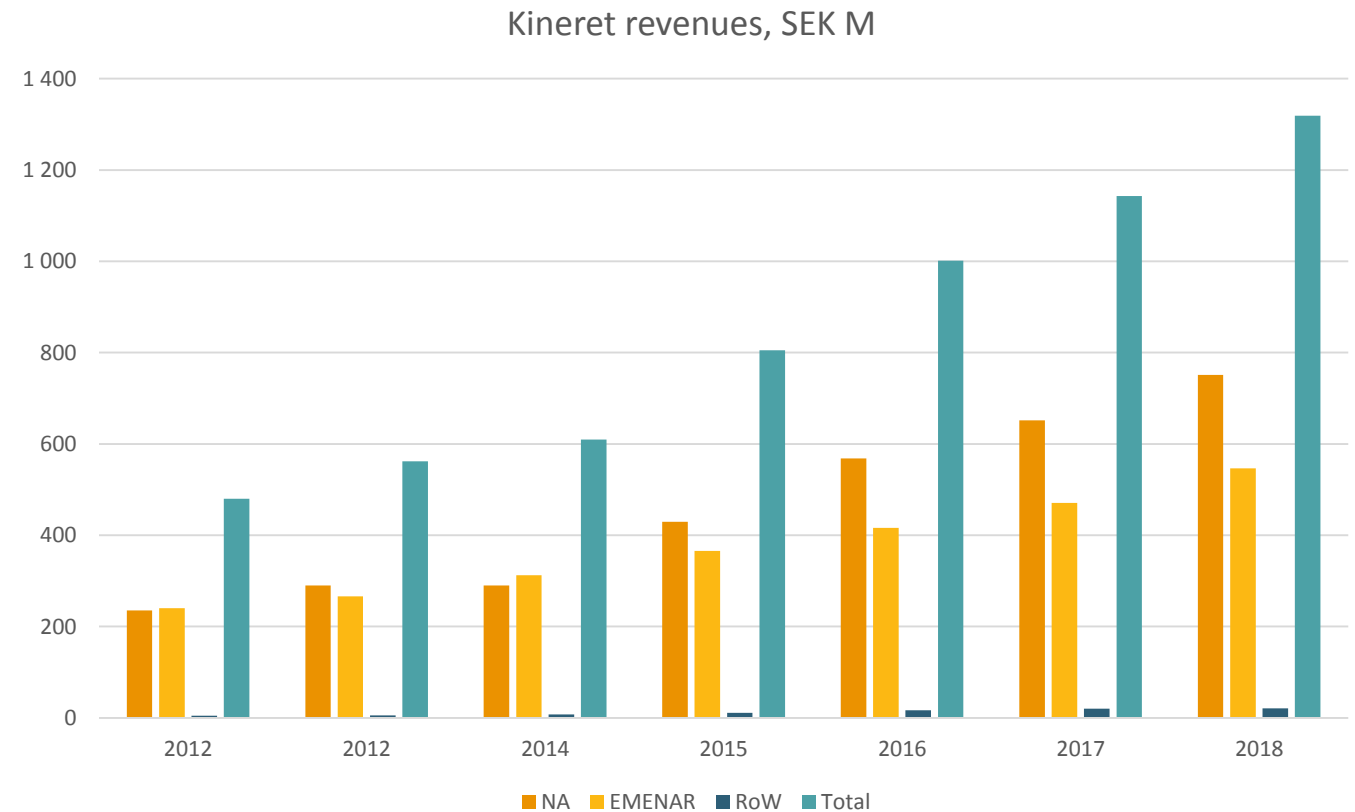
1. Significant economic opportunity
2. High unmet medical needs
3. Studies to unlock opportunities on the way or submitted



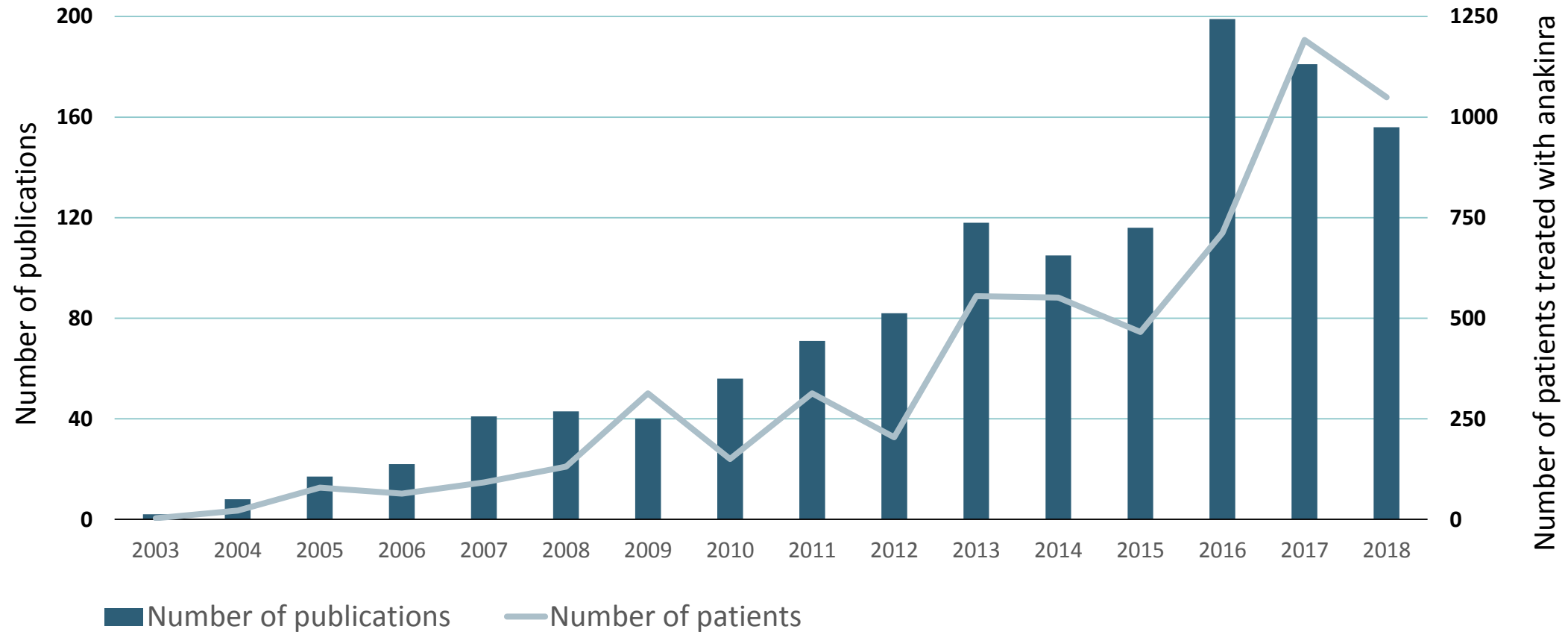
Kineret

# Kineret – a great growth story

- Launched in US 2001 and EU 2002
  - EU: RA, CAPS and Still's disease
  - US: RA and NOMID
- Sobi acquired Kineret from Amgen in 2008, first full-year sales in 2009



# Increased scientific interest in anakinra



RA trials and other RA publications not included

Approximate numbers (some redundancy in patient reports across publications)

# Many possible indications for Kineret beyond the current label

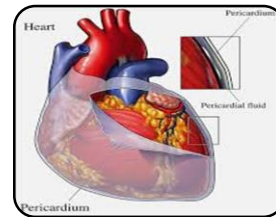
## Kineret label so far ...



### Currently approved

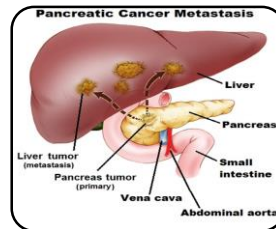
- Rheumatoid arthritis (RA)
- Neonatal-onset multisystem inflammatory disease (NOMID)
- Cryopyrin-associated periodic syndrome (CAPS)
- Still's disease (EMA approval)

## Additional indications being considered



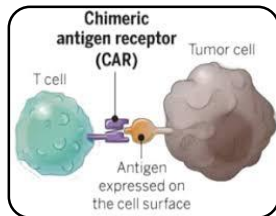
### Idiopathic Recurrent Pericarditis (IRP)

- Syndrome in which the sack that surrounds the heart (pericardium) gets inflamed.
- Recurrence of pericarditis occurred in 9 (90%) of the 10 patients randomized to placebo and in 2 (18.2%) of the 11 patients randomized to anakinra



### Pancreatic Ductal Adenocarcinoma (PDAC)

- Metastatic cancer associated with poor prognosis
- Anakinra 100 mg QAD in combination with FOLFIRINOX in patients with metastatic PDAC showed overall survival of 17.4 months



### Chimeric antigen receptor T-cell therapy (CAR-T) cell therapy-associated toxicities

- Very active space including Novartis (Kymriah) and Gilead (Yescarta)
- IL-1 blockade, but not IL-6 blockade, protects mice from delayed lethal neurotoxicity

1 86% of all Kineret use in adults is off-label in an Italian study: Vitale et al., 2016. 2 IRP = Idiopathic recurrent pericarditis. 3 PDAC = pancreatic ductal adenocarcinoma, i.e. the most common form of pancreatic cancer.

4 CRC = colorectal carcinoma

SOURCE: Sobi, McKinsey

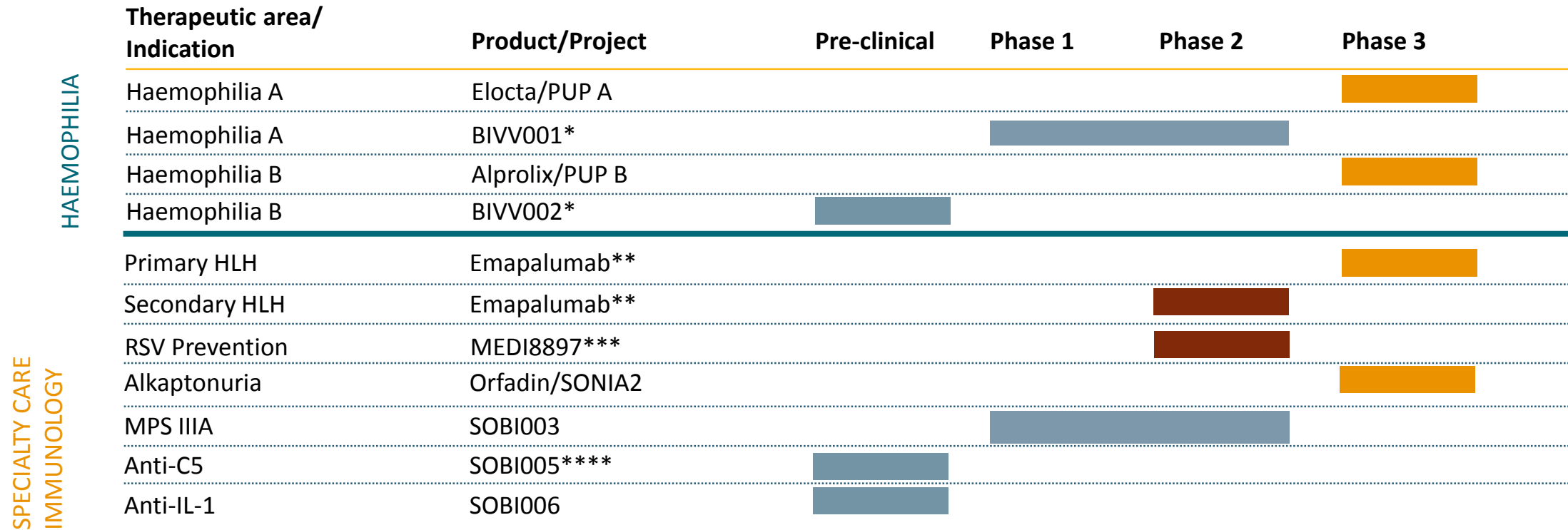


A large white bubble with a small notch at the bottom right, containing the text "R&D" in orange. A smaller white circle is positioned to the right of the bubble's top edge.

R&D

**Milan Zdravkovic**  
Head of R&D, Chief Medical Officer

# A rare disease R&D pipeline with increasing value



\* Sanofi development programmes, Sobi has elected to add programmes to the collaboration agreement but not yet opted-in

\*\* Global licensing agreement with Novimmune

\*\*\* Participate in 50 per cent of the future earnings in the US


\*\*\*\* Divested; progress related milestones and royalties



A large orange graphic element on the left side of the slide. It features a small solid orange circle at the top left, and a larger orange shape below it that is roughly circular but has a jagged, bite-like edge on its right side. The text "Haemophilia" and "BIVV001" is centered within this larger shape.

Haemophilia

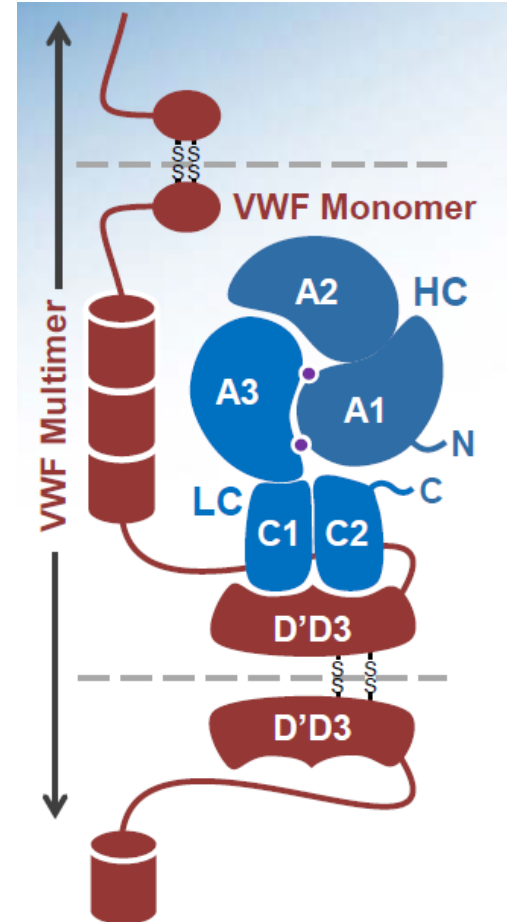
BIVV001

A background image of a smiling man with a grey beard and balding head, wearing a dark wetsuit. He is holding a surfboard under his arm and has his arms raised in a celebratory gesture. The background is a bright, hazy outdoor setting, possibly a beach or a boat deck.

***BIVV001 is a Sanofi programme  
Sobi has elected to add BIVV001 to the collaboration  
agreement with Sanofi but has not yet opted in.***

# The effect of VWF on FVIII half-life<sup>1-3</sup>

- In circulation, >95% of FVIII is bound to VWF, which stabilises and protects FVIII from degradation
- In particular the **D'D3 region of VWF** interacts with the **C1/C2 region of FVIII**
- But VWF also seems to be responsible for limiting the half-life extension of approved EHL FVIII molecules
- FVIII-VWF interaction couples FVIII to the VWF clearance pathway
- The circulating half-life of VWF thereby sets the limit for the FVIII half-life



# BIVV001: Combining D'D3 and XTEN to rFVIII Fc fusion to break the VWF ceiling

## XTEN insertions<sup>1</sup>:

- Hydrophilic sequences comprised of natural amino acids
- Provide protection, increase half-life

## Covalent linkage to the D'D3 domain of VWF:

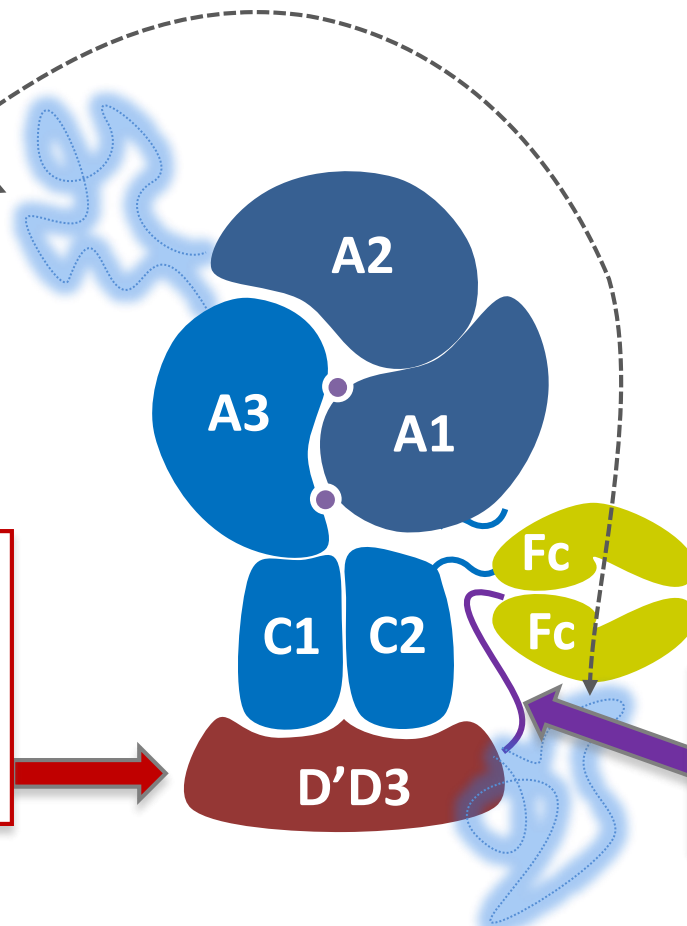
- Prevents binding to endogenous VWF, decoupling from VWF-mediated clearance<sup>2</sup>
- Confers partial protection from degradation to FVIII normally afforded by VWF<sup>2</sup>

## Based on rFVIII Fc domain:

- Extends half-life through FcRn-mediated recycling pathway<sup>3,4</sup>

## Thrombin-cleavable linker:<sup>2</sup>

- Enables release of D'D3 upon FVIII activation



rFVIII Fc-VWF-XTEN

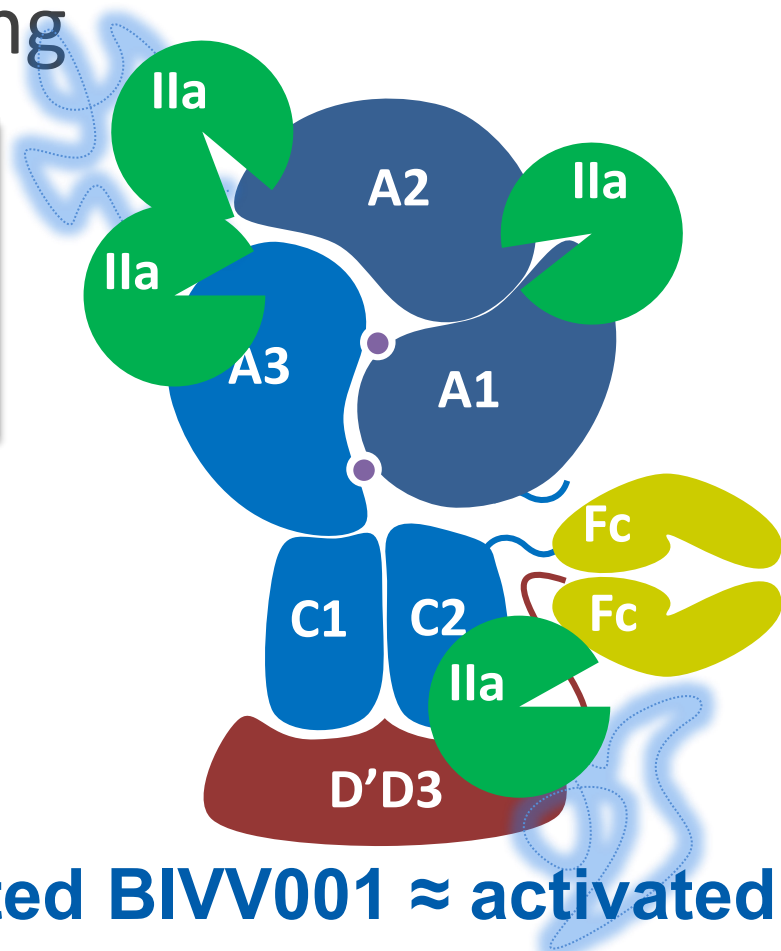
BIVV001 is an investigational product that has not been approved for use

1. Podust et al. J Control Release 2016 2. Adapted from Liu et al. WFH 2016 Oral Presentation 3. Roopenian & Akilesh. Nat Rev Immunol 2007

4. Shapiro. Expert Opin Biol Ther 2013 5. Patarroyo-White et al ISTH 2015

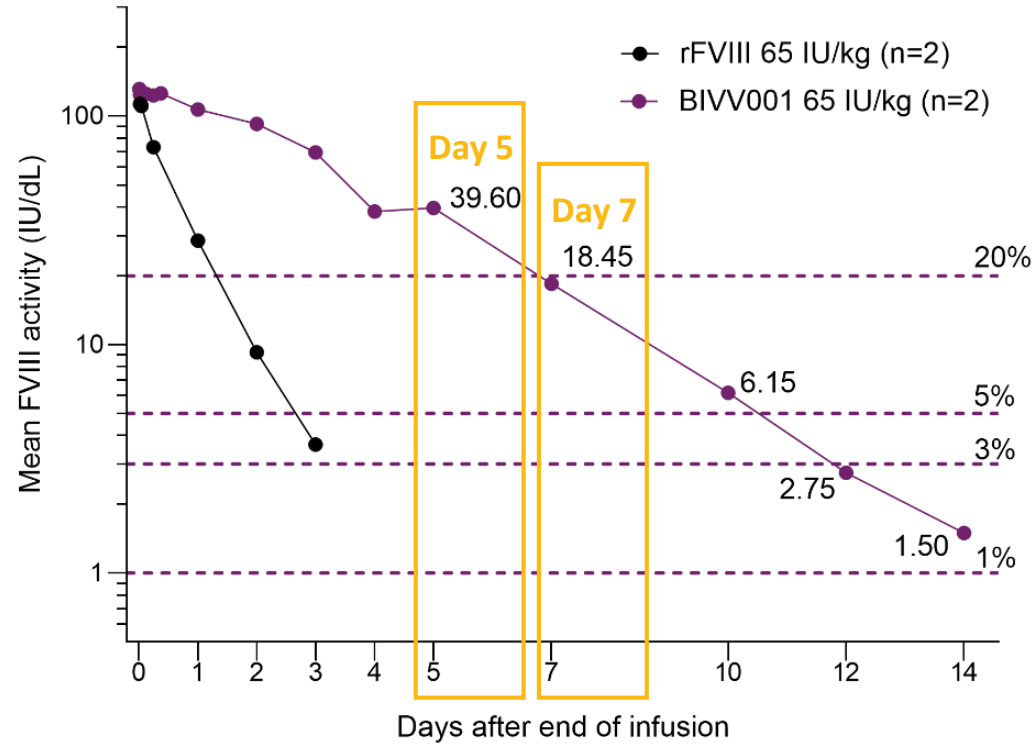
# BIVV001: Combining D'D3 and XTEN to rFVIIIFc fusion to break the VWF ceiling

- Upon thrombin activation:**
- Removes B domain XTEN
  - Disrupts D' D3 interaction
  - Removes D' D3/XTEN
  - **Results in same molecule as activated rFVIIIFc**



**activated BIVV001 ≈ activated rFVIIIFc**  
**BIVV001**

# BIVV001: Single 65 IU/kg dose extends FVIII half-life to 44h and shows 18% activity post-infusion (N=2)<sup>1,a</sup>




*The average FVIII activity post-infusion at 5 days was 40% and at 7 days was 18%*

PK parameter	BIVV001 (n=2) <sup>b</sup>	rFVIII (n=2) <sup>b</sup>
$t_{1/2}$ (h)	<b>43.76</b> [42.05–45.55]	<b>16.98</b> [16.15–17.84]
$C_{max}$ (IU/dL)	132.10 [117.2–148.9]	114.55 [93.4–140.5]
$AUC_{0-inf}$ (h x IU/dL)	<b>11894</b> [9442–14982]	<b>1958</b> [1527–2510]
MRT (h)	73.13 [71.77–74.51]	17.75 [16.63–18.95]
CL (mL/h/kg)	0.55 [0.43–0.69]	3.30 [2.57–4.23]
IR (IU/dL per IU/kg)	2.02 [1.80–2.27]	1.74 [1.42–2.14]



<sup>a</sup>As of Interim data cut 2 <sup>b</sup>Values are geometric means [range] FVIII activity determined by the one-stage clotting assay 1. Konkle et al. ASH 2018

A close-up photograph of a young girl with dark hair, laughing heartily. Her eyes are closed, and her mouth is wide open, showing her teeth. The background is a soft, out-of-focus outdoor setting with light filtering through trees.

**Emapalumab (Gamifant) is approved in the US for the treatment of adult and paediatric (newborn and older) patients with primary haemophagocytic lymphohistiocytosis (HLH) with refractory, recurrent or progressive disease or intolerance with conventional HLH therapy**

**Full prescribing information available on:**

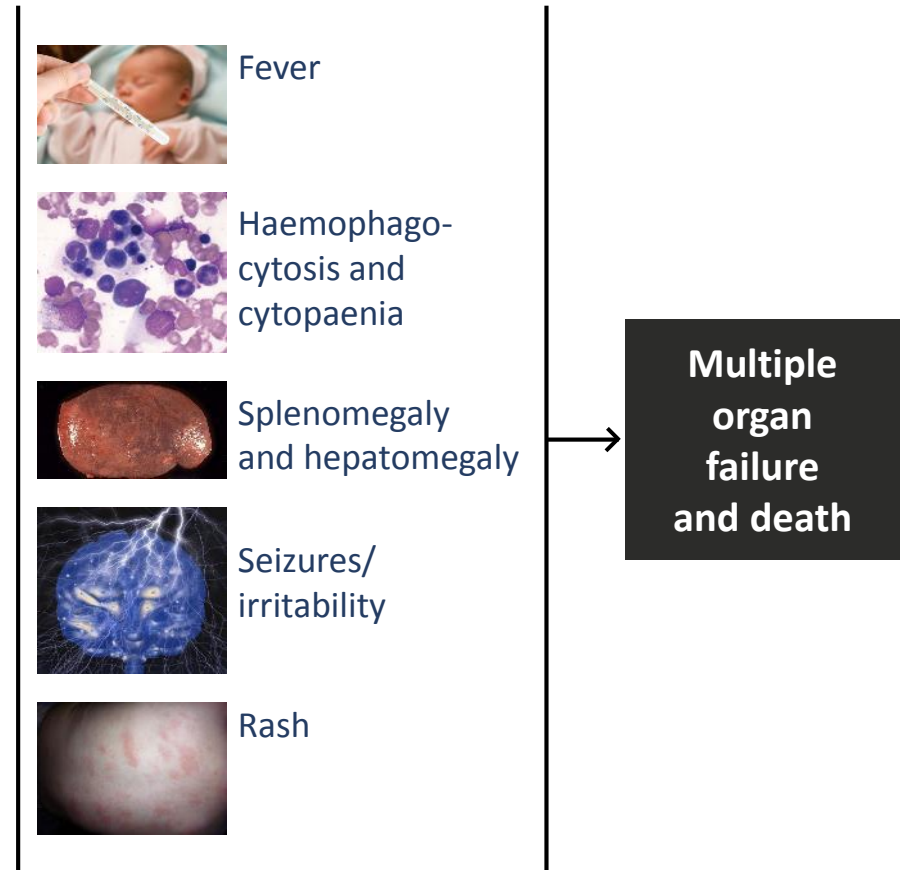
**<https://gamifant.com/pdf/Full-Prescribing-Information.pdf>**

A large, bright orange circular graphic with a white, irregular shape cut out of its right side. It is positioned on the right side of the slide, overlapping the girl's image.

**Immunology**  
**Emapalumab**

# Haemophagocytic lymphohistiocytosis (HLH)

- HLH is a clinical syndrome of hyperinflammation, driven by high interferon (IFN)- $\gamma$  production, characterized by severe hyperferritinaemia, fever, severe cytopenia, coagulation defects, organomegaly (spleen and liver), liver function impairment, and infections
- It occurs as a familial autosomal recessive disorder (i.e., primary HLH) or as an acquired, reactive condition (i.e., secondary HLH)
- Untreated HLH syndrome is lethal



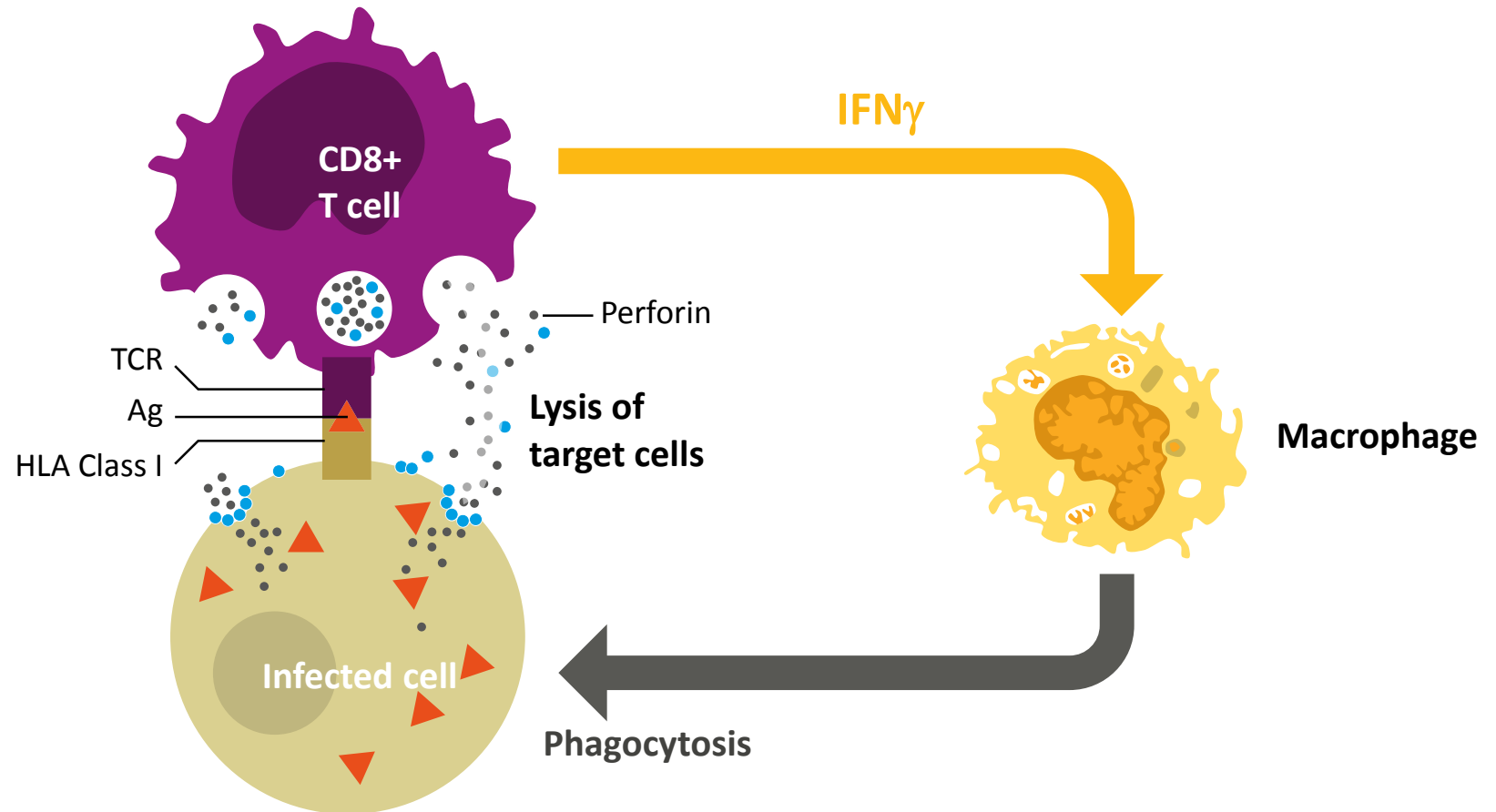




# Defect in killing by cytotoxic T cells leads to elevation of IFN $\gamma$ and severe inflammation<sup>1-2</sup>

## Normal cytotoxic function

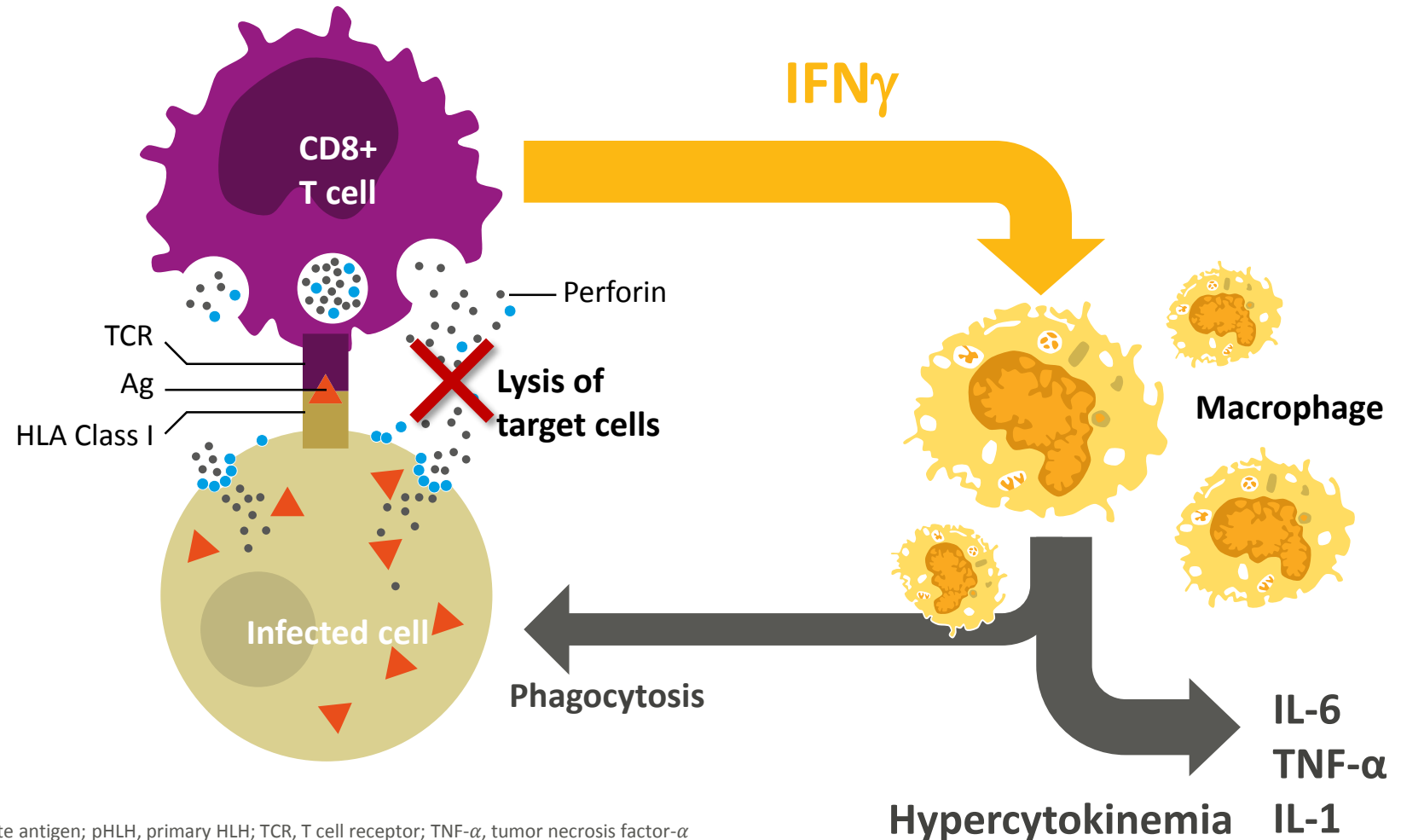
During a normal immune response, infected cells present antigen to CD8+ T cells, inducing activation and cytotoxic response that aims to kill the infected cells by release of perforin and granzymes. Simultaneously, upon activation cytotoxic CD8+ T cells secrete IFN $\gamma$ , activating macrophages.



# Defect in killing by cytotoxic T cells leads to elevation of IFN $\gamma$ and severe inflammation<sup>1-2</sup>

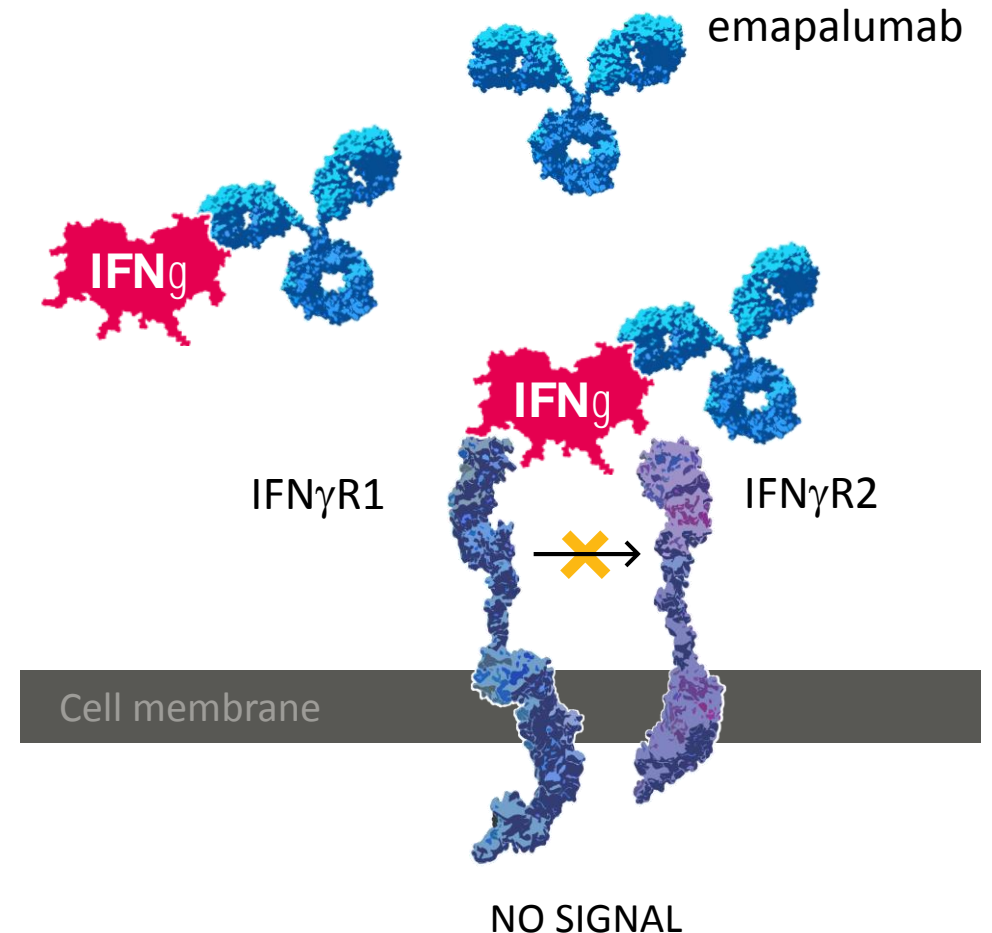
## Defective cytotoxic function

In pHLH, a defect in the cytotoxic activity of CD8+ T cells and NK cells results in a failure to lyse infected cells. This results in increase secretion of IFN $\gamma$ , elevated activation of macrophages, and hyper-cytokinaemia that results in the signs and symptoms of HLH.

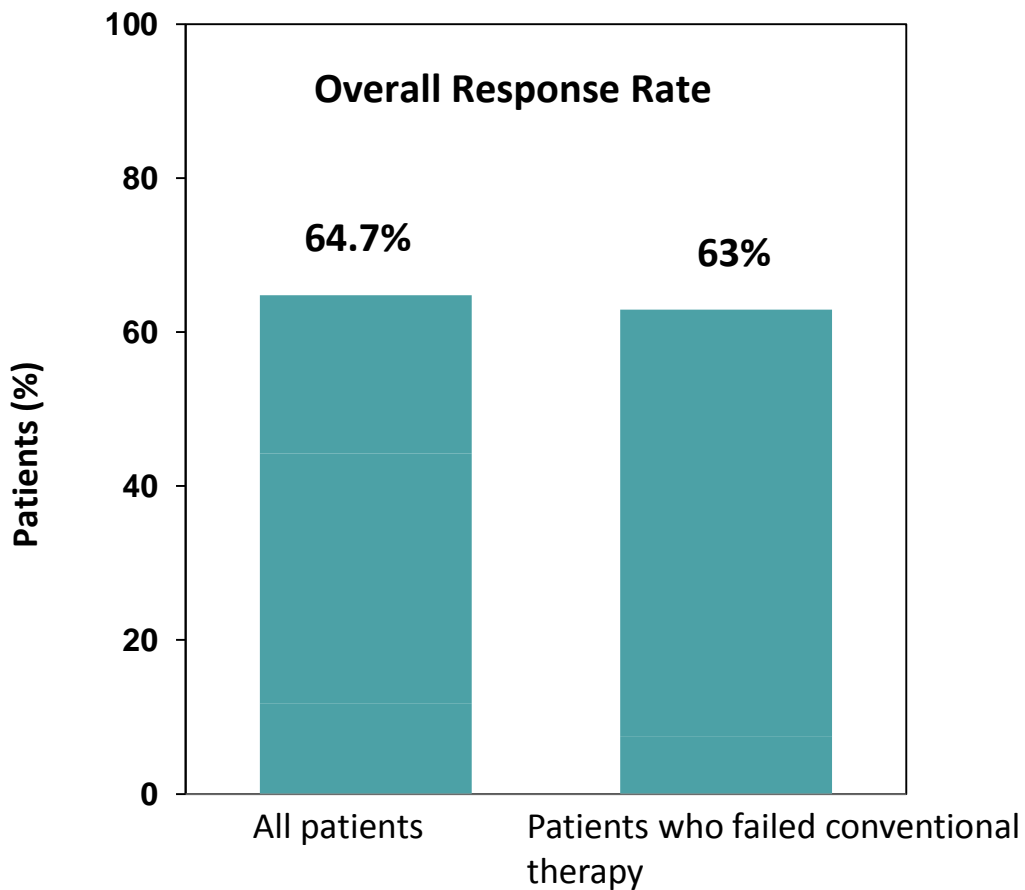


# Emapalumab: anti-IFN $\gamma$ antibody

- Emapalumab is a high affinity, fully human IgG1 anti-IFN $\gamma$  monoclonal antibody (mAb) that binds to soluble and receptor-bound forms of IFN $\gamma$
- When IFN $\gamma$  binds to its receptors, it results in dimerisation and activation of signalling that results in the transcription of genes that encode inflammatory molecules
- Emapalumab binds to IFN $\gamma$  preventing binding to its receptors and the expression of inflammatory cytokines



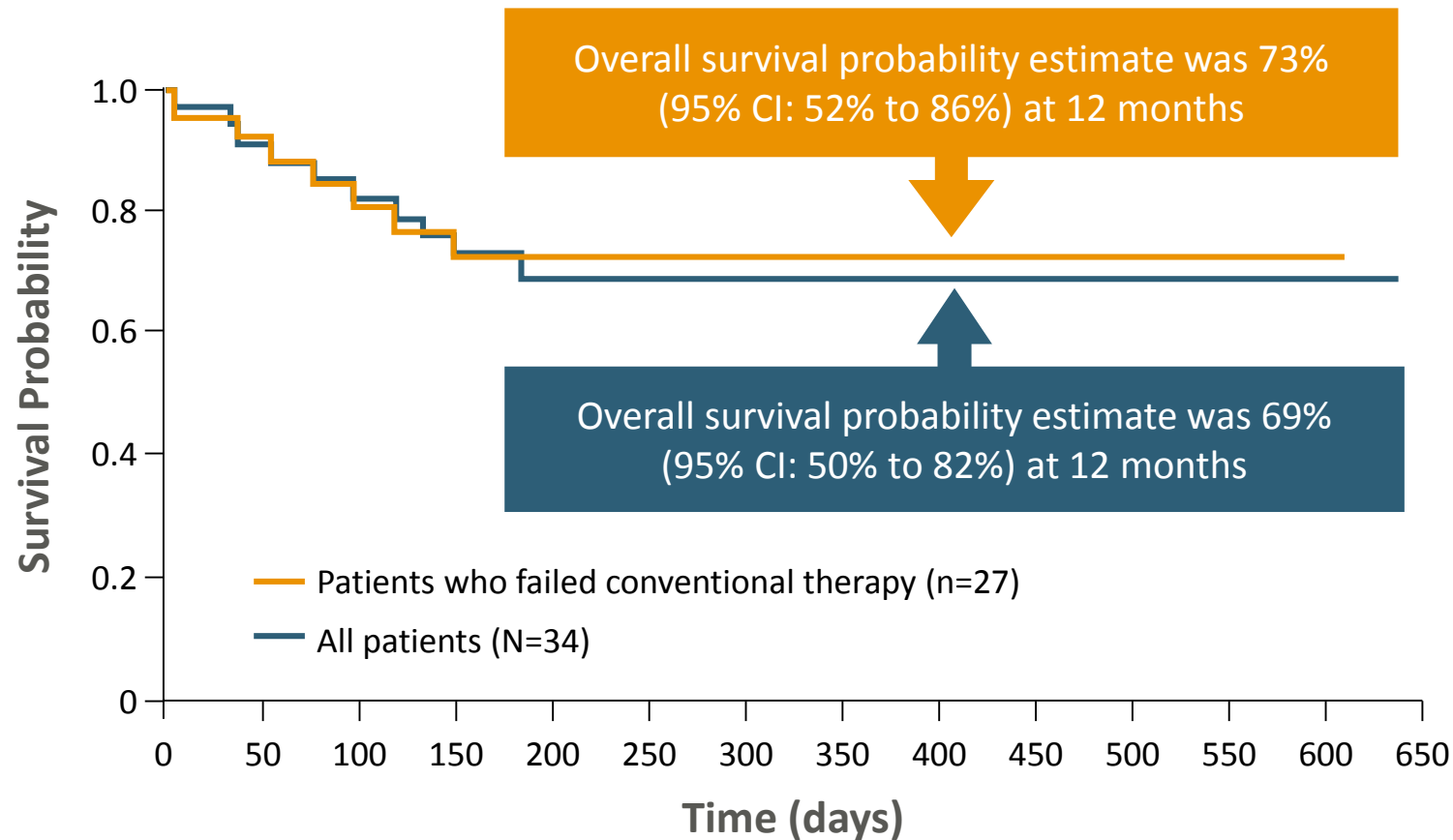
# Emapalumab clinical data in primary HLH: In patients failing conventional therapy, 63% responded to emapalumab



- The primary efficacy endpoint of study NI-0501-04 was the Overall Response Rate (ORR) at end of treatment
- Overall response was evaluated using an algorithm based on objective clinical and laboratory parameters
- Primary efficacy endpoint of the study was met: ORR was significantly higher than the pre-specified null hypothesis of 40%

# Overall survival

– secondary endpoint

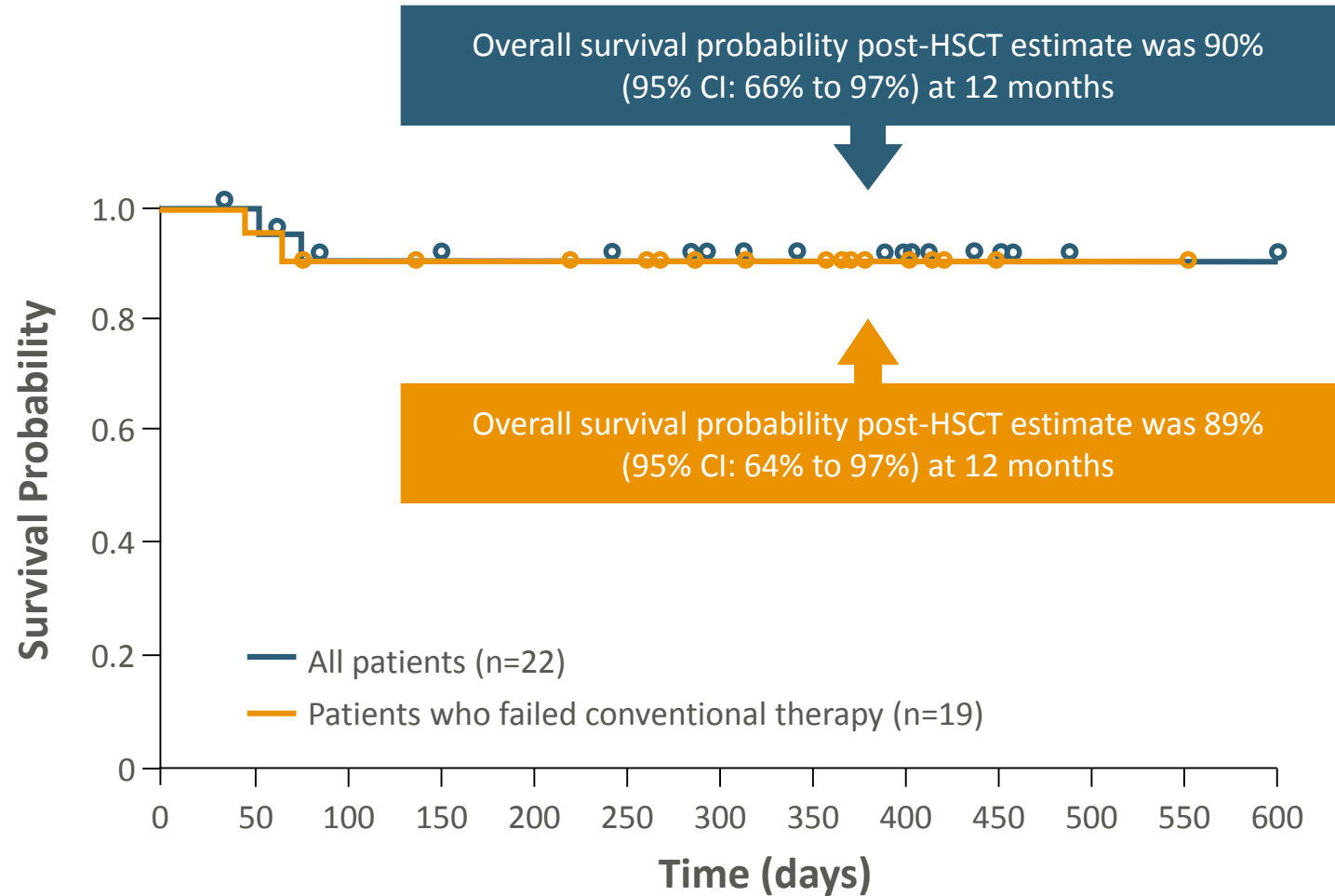


Among patients who failed conventional therapy, 20/27 patients were alive at last observation\*

Among all treated patients, 24/34 patients were alive at last observation\*

\* Last observation was defined as up to 1 year after HSCT or after last emapalumab infusion

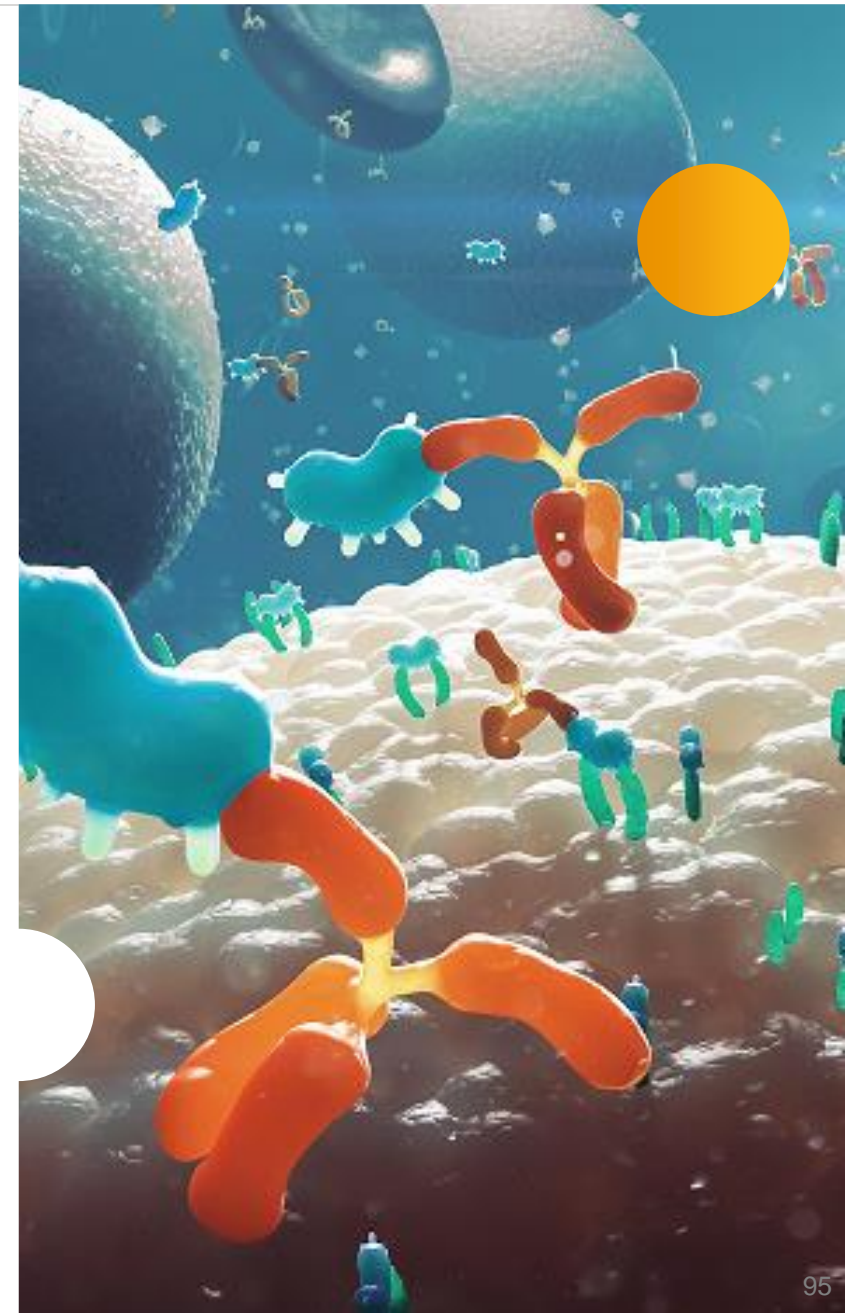
# Survival post-HSCT — secondary endpoint



2 patients died after HSCT due to septic shock and respiratory failure (one experienced primary graft failure)

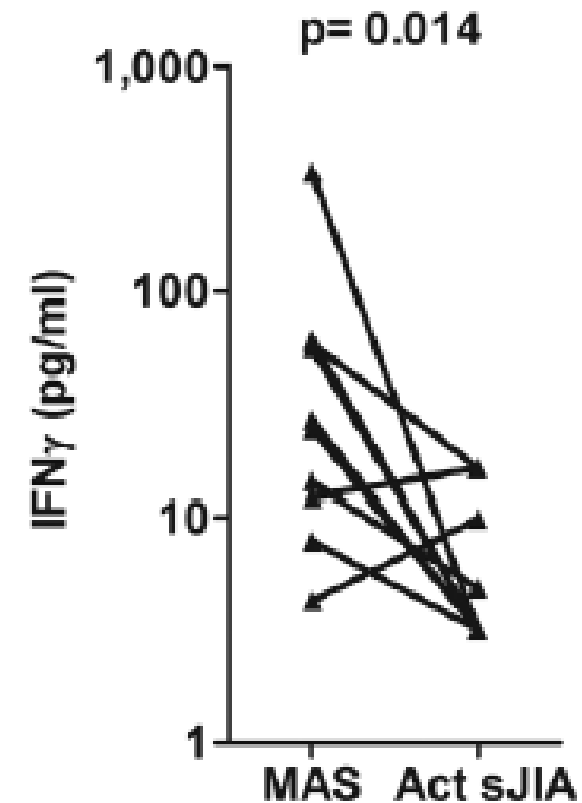
# 2019 R&D investments in emapalumab

- In 2019 we will make investments into clinical activities:
- secondary HLH in children with autoimmune Systemic Juvenile Idiopathic Arthritis (sJIA) Developing Macrophage Activation Syndrome
- adult patients with malignancy and non-malignancy induced secondary HLH (in planning)
- preemptive treatment of graft failure in children undergoing hematopoietic stem cell transplantation (in planning)



# Clinical study in secondary HLH in children with autoimmune Systemic Juvenile Idiopathic Arthritis (sJIA) developing Macrophage Activation Syndrome is supported by pre-clinical and clinical data

- Phase 2 study in patients < 18 years with sJIA patients with MAS having shown inadequate response to high-dose glucocorticoid treatment to evaluate safety, tolerability, pharmacokinetics and efficacy
- Sample size: 10 patients
- Total treatment duration is 4 weeks
- Starting dose of emapalumab 6 mg/kg

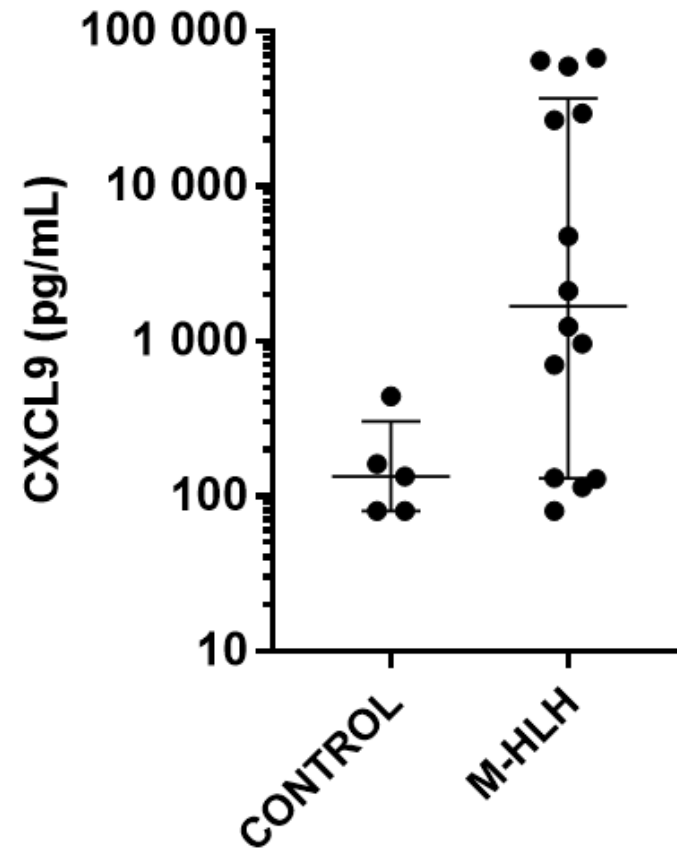




# Adult patients with sHLH have a IFN-g signature

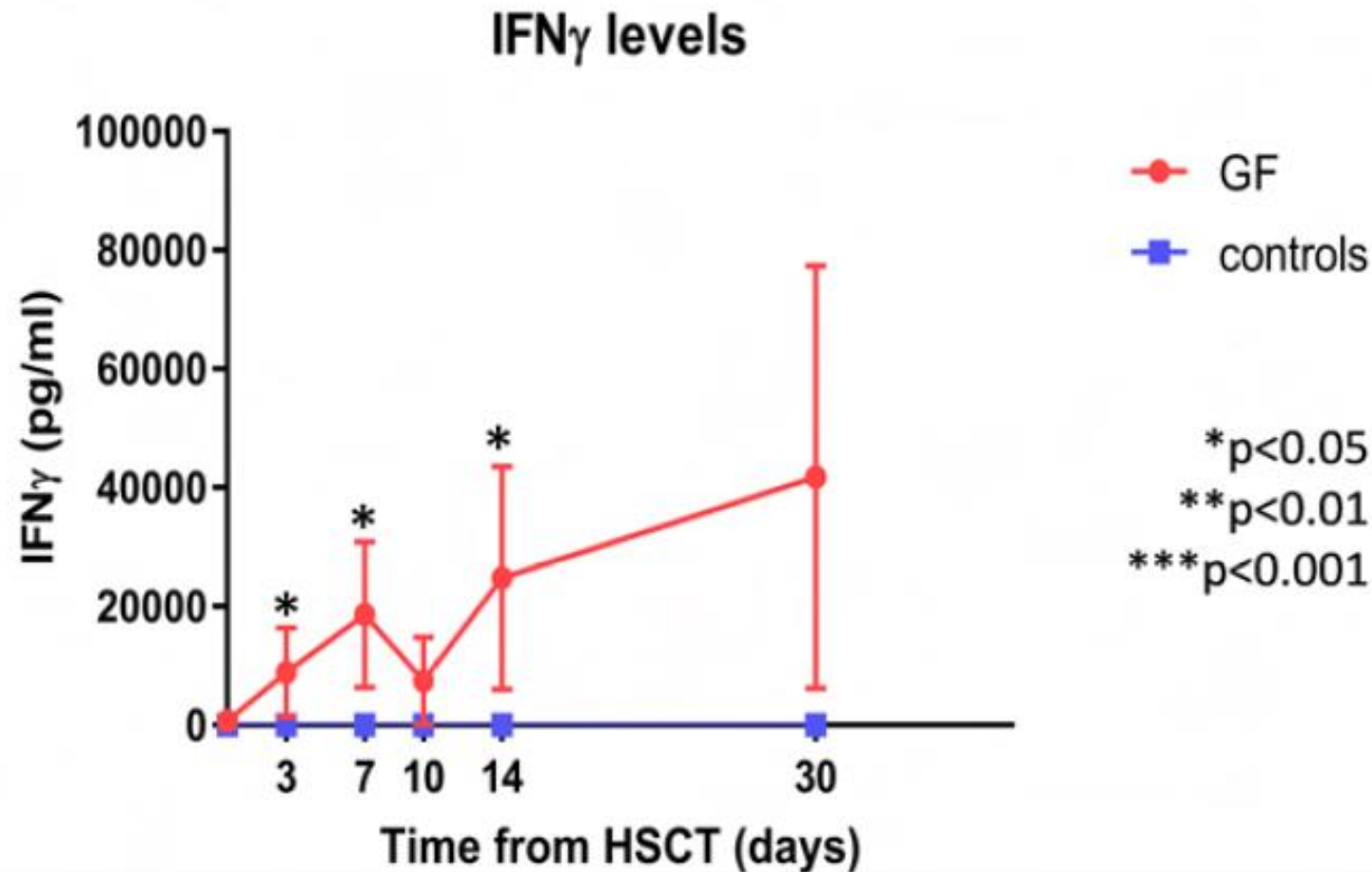
## Clinical study to be initiated in 2019

- A phase 2/3 study to evaluate the efficacy, safety, and pharmacokinetics of emapalumab in adult patients with secondary haemophagocytic lymphohistiocytosis
- Initial sample size (adaptive design): 10 patients in each of 2 strata (malignancy and non-malignancy associated HLH)
- Treatment duration will be variable depending on response
- Primary endpoint is at Week 4
- Drug regimen: emapalumab administered IV at an initial dose of 6 mg/kg



“Control” are pts diagnosed with malignancy only

Increased serum levels of IFN $\gamma$  seen in children experiencing graft failure  
 – Possibility for early diagnosis and intervention with targeted neutralisation of IFN $\gamma$



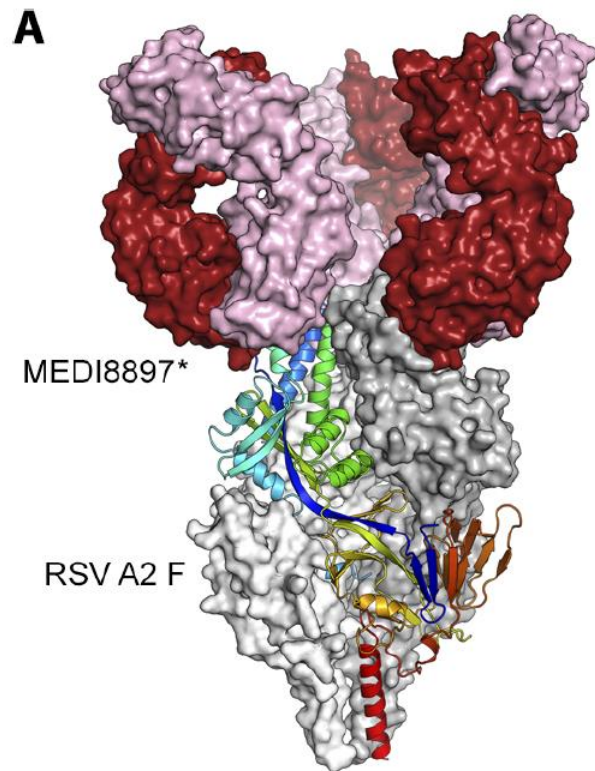
N=15/15

Immunology

MEDI8897

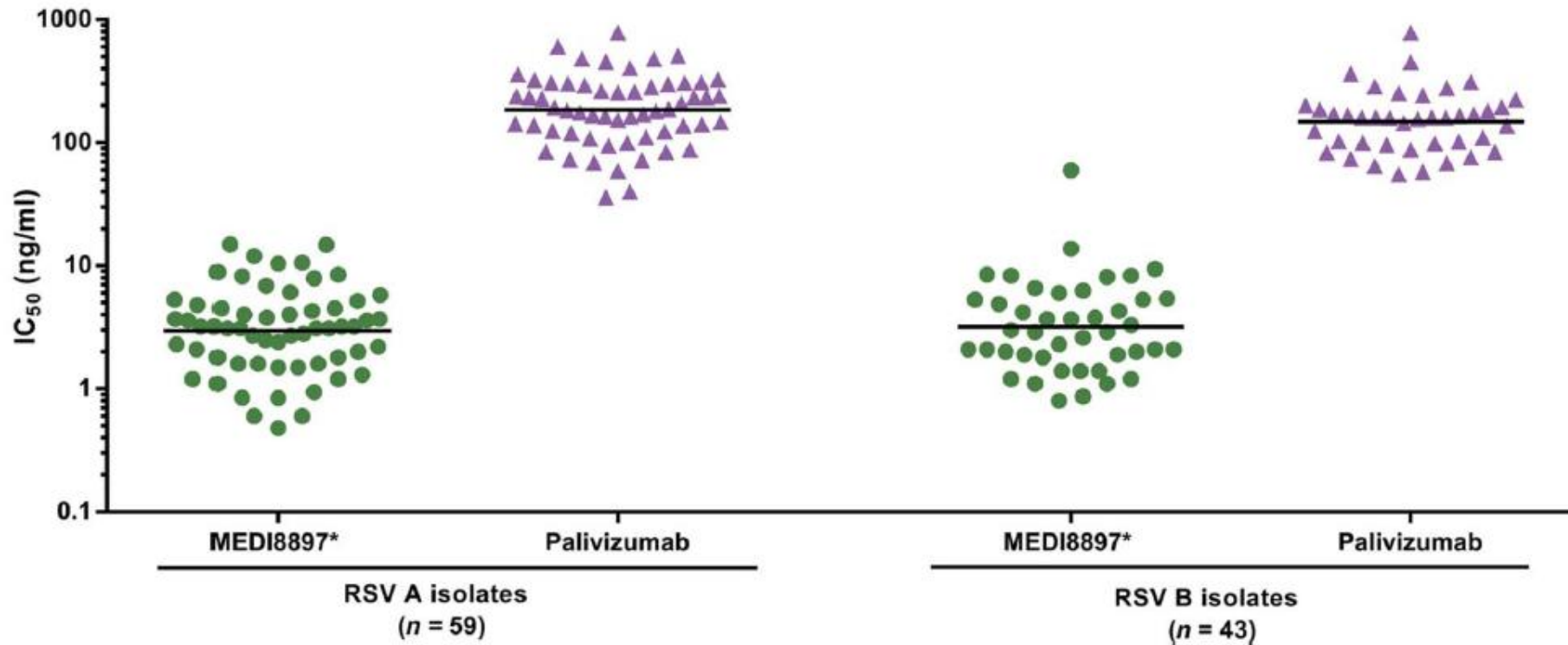


# MEDI8897: extended half-life anti-RSV F monoclonal antibody



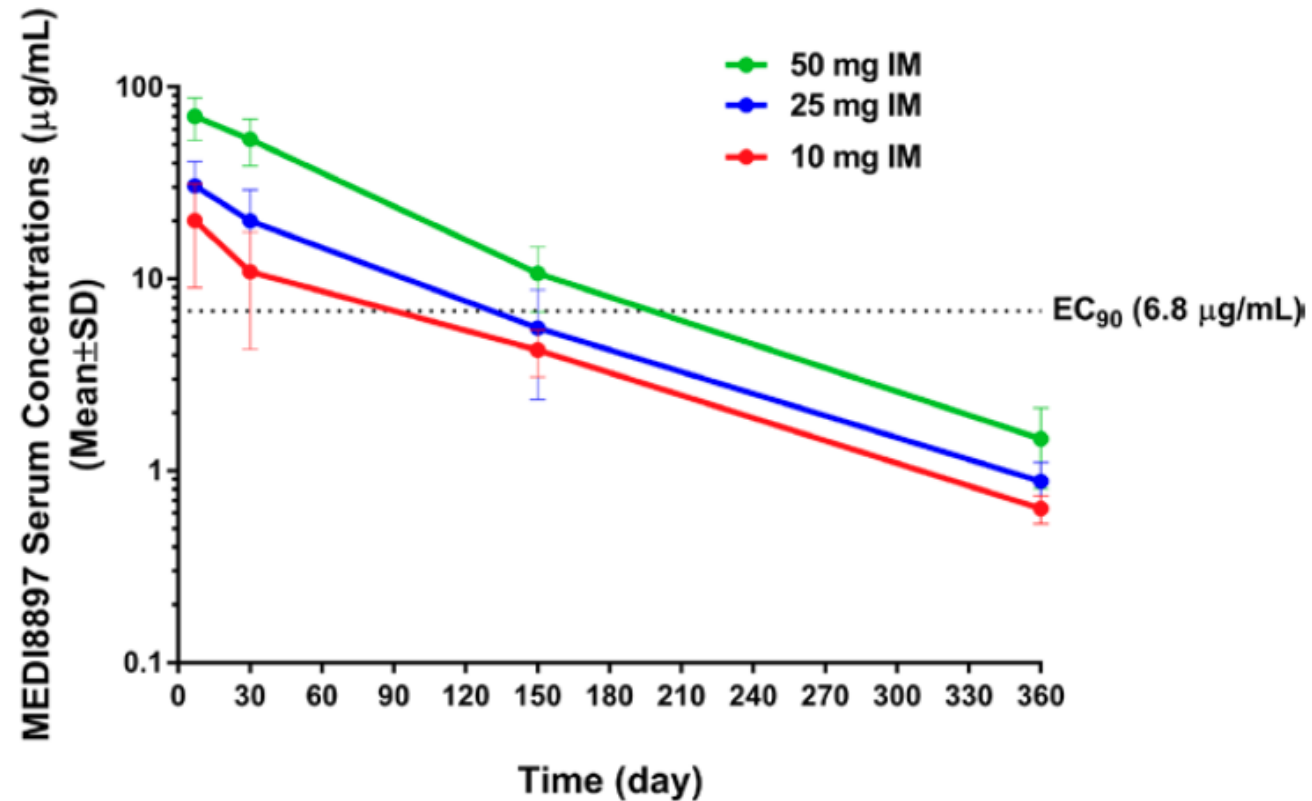
- Human antibody against RSV with greater potency than palivizumab in in-vitro and pre-clinical models
- Engineered to have an extended half-life thereby potentially enabling a single dose to cover an RSV season
- Received Fast Track Designation from the US FDA in 2015 and US FDA Breakthrough Therapy Designation in 2019
- Primary efficacy results for the phase 2b showed that the study met its primary endpoint, defined as a statistically significant reduction in the incidence of medically attended lower respiratory tract infection (LRTI) caused by reverse transcriptase polymerase chain reaction-confirmed RSV for 150 days after dosing
- The current development plan includes initiation of a phase 3 trial in healthy full-term and late pre-term infants

# MEDI8897 is 50-fold more active against RSV isolates in comparison to palivizumab (*in vitro*)



Zhu et al., Sci. Transl. Med. 9, eaaj1928 (2017)

# Data from healthy preterm infants supports single RSV-season dosing with MEDI8897



$t_{1/2}$  of MEDI8897 in infants was estimated to be 63–73 days. Palivizumab its 19–27 days  
*Pediatr Infect Dis J* 2018;37:886–892; *Antimicrob Agents Chemother.* 2012;56:4927–4936

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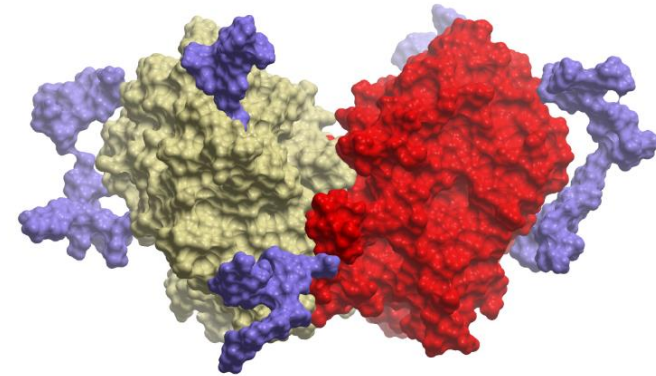
**Specialty Care**

A large, solid orange circle with a bite taken out of its top-right edge, positioned on the left side of the slide.

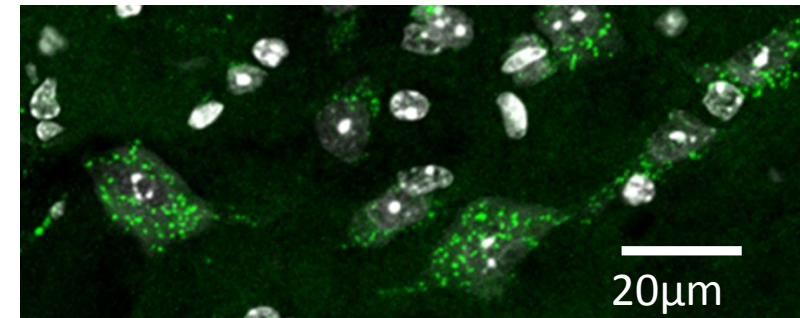
**SOBI003**

# SOBI003 for mucopolysaccharidosis IIIA (MPS IIIA)

- A rare systemic disease with a significant CNS component due to incomplete breakdown and lysosomal storage of heparan sulfate (HS)
- High morbidity and mortality
- Caused by mutations in gene for sulfamidase enzyme
- No treatment available for MPS IIIA
- SOBI003: a recombinant sulfamidase using proprietary Modifa™ technology with potential to meet unmet needs in MPS IIIA
- SOBI003 is effective in preclinical models of MPS IIIA
- Orphan Drug Designation in EU and US and Fast Track Designation in the US
- First in human study is ongoing – 2nd cohort initiated



SOBI003 - chemically modified recombinant human sulfamidase



Distinct intracellular SOBI003 fluorescence (green) indicates uptake into lysosomes in nerve cells in the CNS.





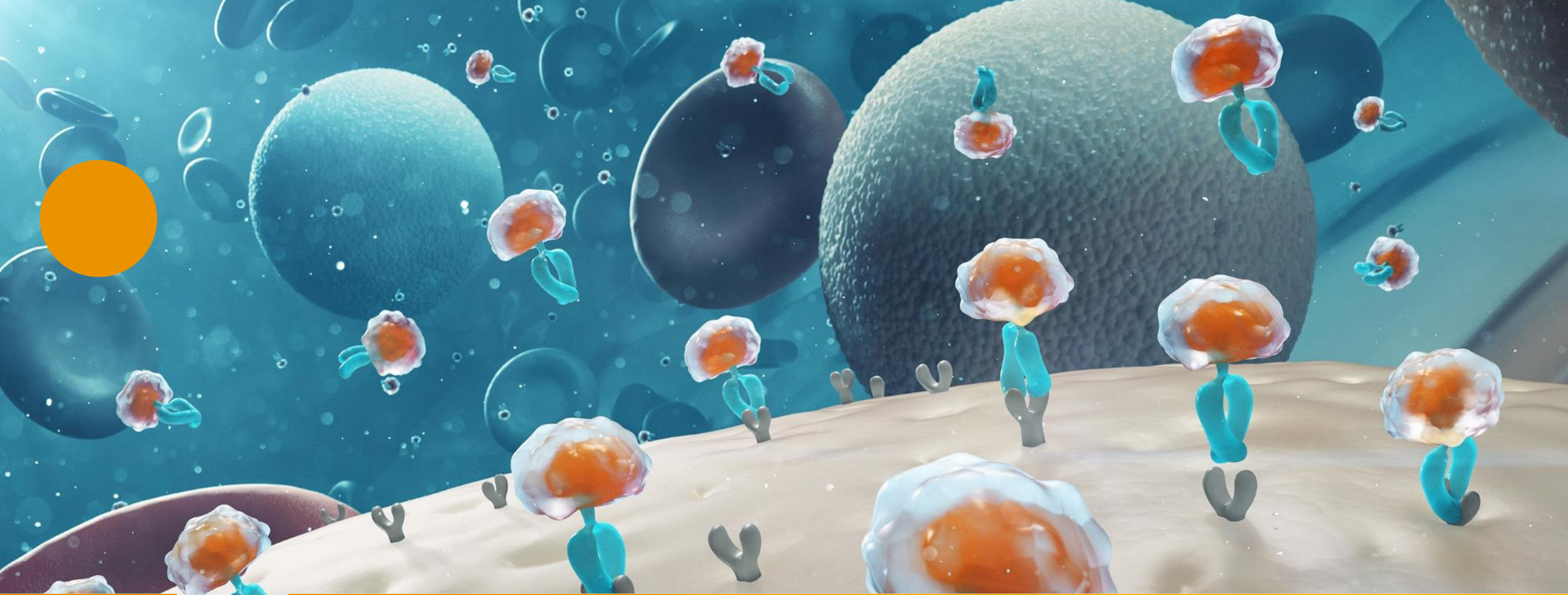
# Concluding remarks

**Guido Oelkers**  
CEO

# Key messages

- We are stronger than ever and have over the past two years made significant achievements
  - The business is on a whole new trajectory
- I see ample opportunity to take Sobi to the next level
  - Fundamentally attractive market
  - Best-in-class products on the market, well positioned for growth
  - Our rare disease R&D pipeline is increasing in value
  - We remain committed to M&A and there are many opportunities out there
- We remain committed to our strategic direction around four focus areas:
  - Drive Haemophilia penetration
  - Develop Specialty Care and Immunology
  - Grow US business and strengthen position in EMENAR
  - Strengthen R&D pipeline
- 2019 guidance remains unchanged; SEK 12.5-13.0 bn revenues, SEK 5.0-5.3 bn EBITA
- Sobi – Rare Strength





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rare **strength**