Sobi Capital Markets Day



November 2013

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Forward Looking Statements

In order to utilize the 'Safe Harbor' provisions of the United States Private Securities Litigation Reform Act of 1995, Swedish Orphan Biovitrum 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. 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.

An International Healthcare Company Dedicated to Rare Diseases

Strategic Priorities

1. **Near-term** focus on growth in key therapeutic areas, with sustainable positive cash flow from operations.
2. **Medium-term** investments to ensure successful commercialization of our late-stage pipeline.
3. **Long-term** growth will come organically and through acquisitions in key therapeutic areas.

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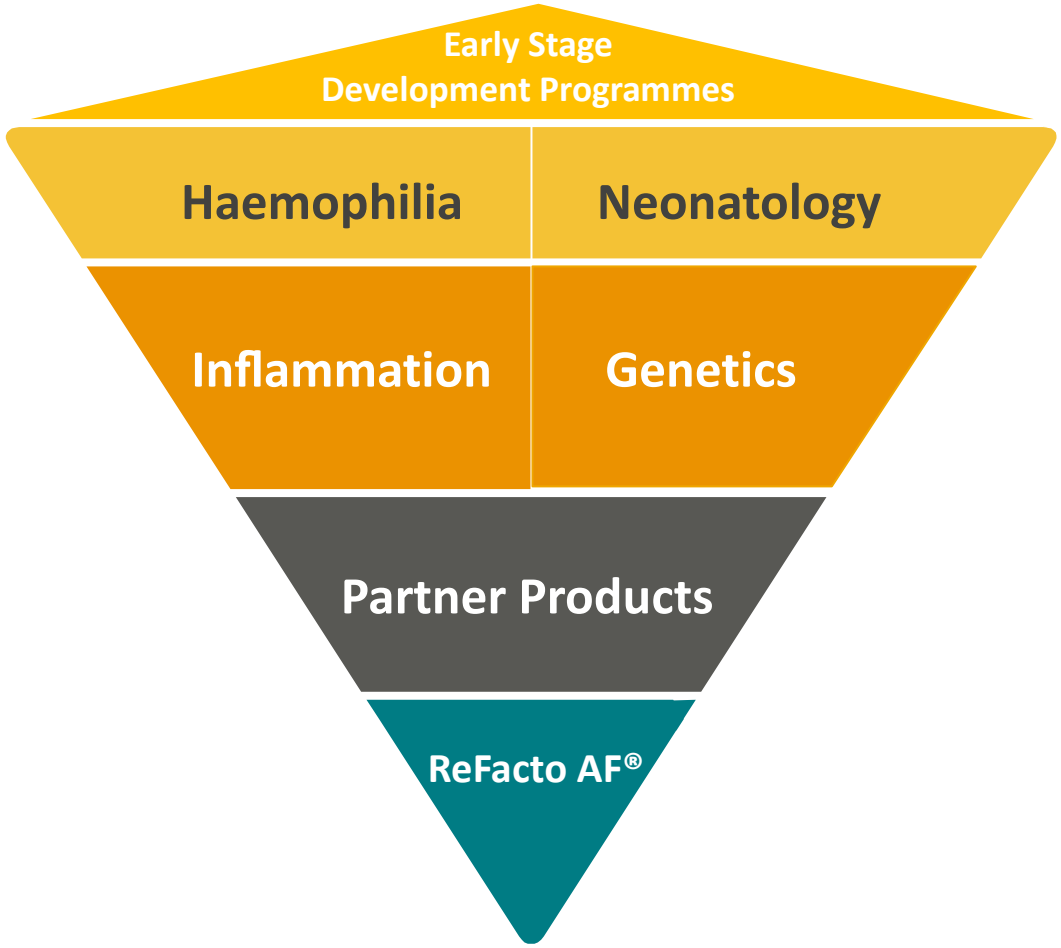
A Diverse, Growing Business Platform



Medium term investments to support commercialisation of the late stage Pipeline

Continued focus on growth in key Therapeutic Areas

An integrated solution for commercialisation of niche and specialty products

Stable contribution to revenues from drug production and royalties

What Is Special About Rare Diseases?

1. Drugs which really work.

   EFFECT SIZE

2. Drugs which work in every patient treated.

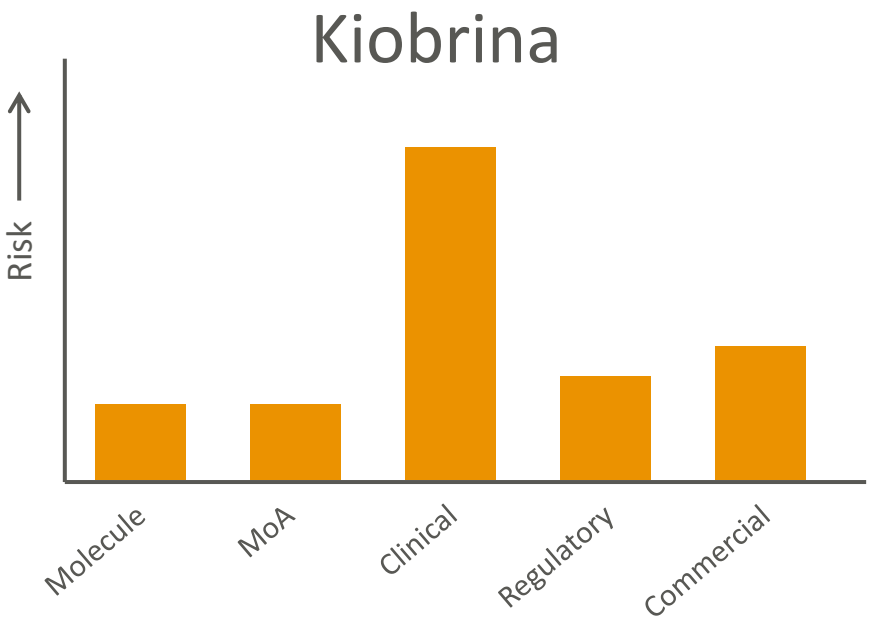
   RESPONSE RATE

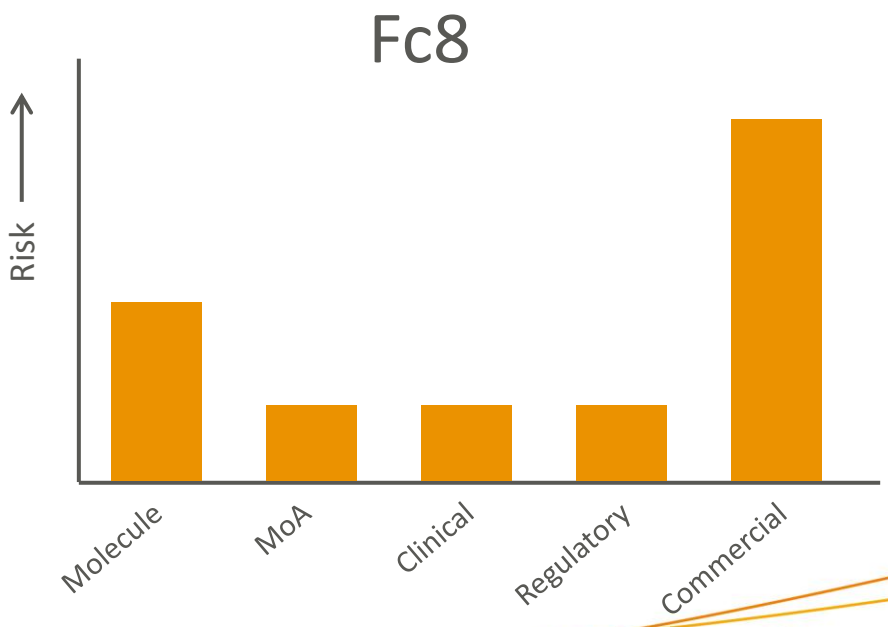
3. Drugs which deliver sustainable value.

   OUTCOMES IN LIFE

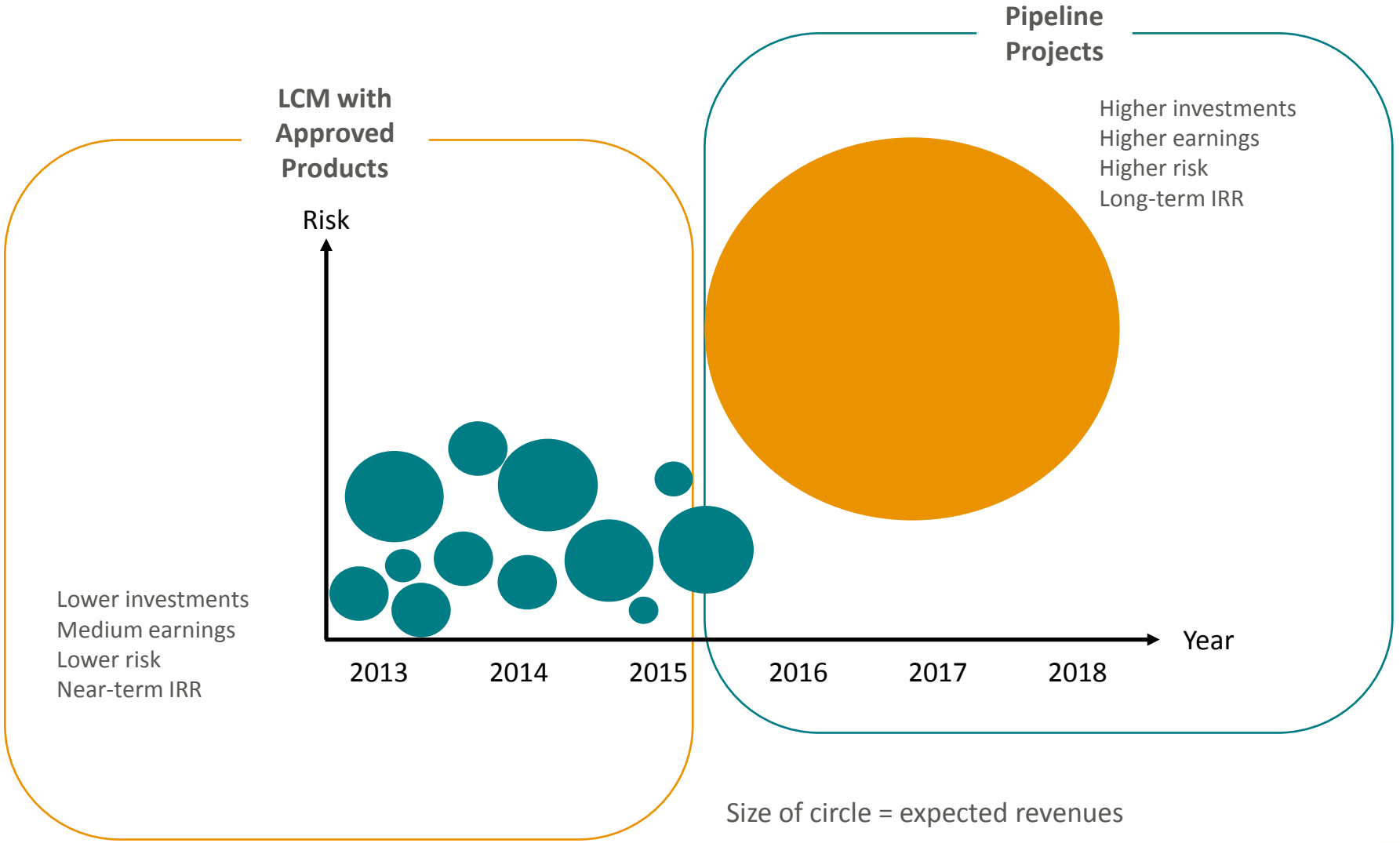
Mitigating Risk in Drug Development

1. **Molecule** – What is known about the candidate?
2. **Mechanism** – How will it achieve its effect? Potency + Specificity
3. **Clinical** – How established is the clinical design and endpoints? Connected to MoA?
4. **Regulatory** – How do the regulators understand value and risk for # 1- 3?
5. **Commercial** – Does the market exist? Who is, or will be there with you?





Balancing Risk + Allocation of Capital



R&D Pipeline 2013

Indication	Project	Partner	Pre-Clin.	Phase I	Phase II	Phase III	Launch
CAPS	Kineret	sobi					
Hemophilia A	rFVIIIFc	biogen idec					
Hemophilia B	rFIXFc	biogen idec					
Improve growth in preterm infants	Kiobrina	sobi					
Oral Mucositis in Head & Neck Cancer	Kepivance	sobi					
Hereditary Tyrosinemia Type 1	Orfadin Liquid	sobi					
Hereditary Tyrosinemia type 1	Orfadin 20mg capsule	sobi					
Alkaptonuria	Orfadin	AKU alkaptonuria society					
Complement –mediated disease	SOBI002	AFFIBODY					
ERT	SOBI003	sobi					
IL-1-driven disease	IL-1 Affibody	AFFIBODY					

Pipeline Projects

LCM with Approved Products

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Hemophilia Update

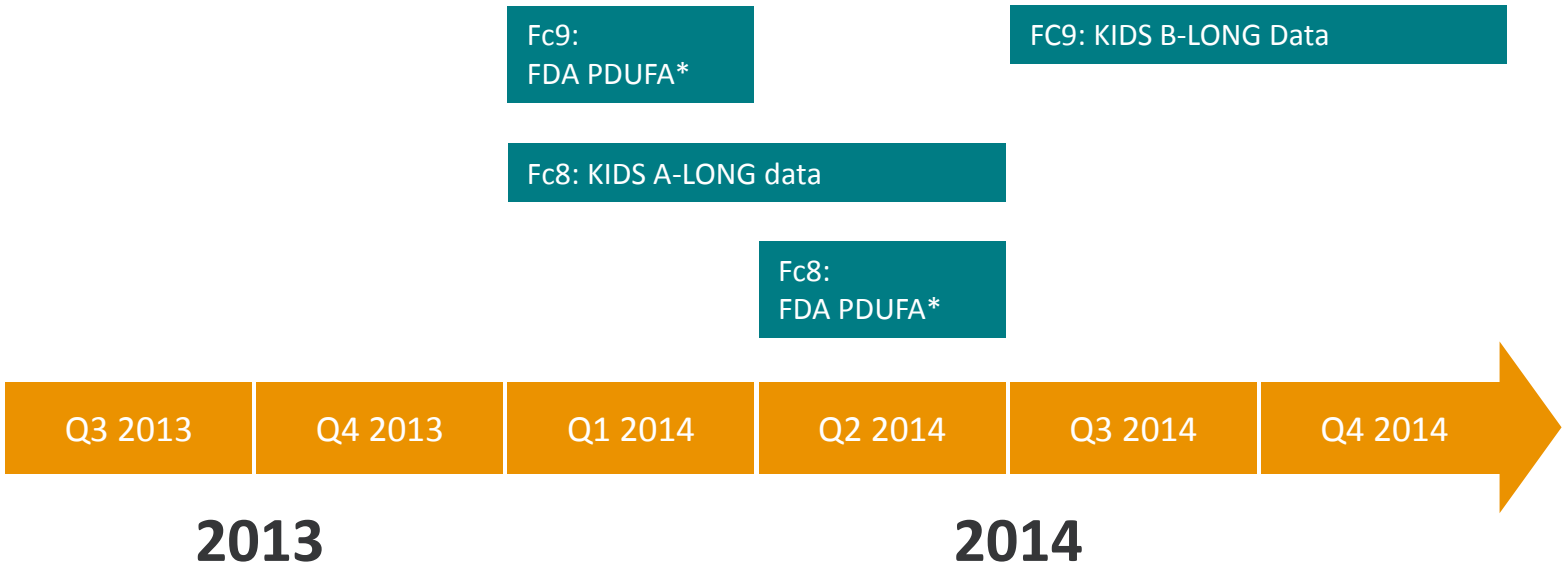
Hemophilia

- rFIXFc PDUFA est. 1Q 2014
  - KIDS B-LONG data 2H 2014
- rFVIIIFc PDUFA est. 2Q 2014
  - KIDS A-LONG data 1H 2014

→Biogen Idec Hemophilia Event

→TBD

Hemophilia Timeline 2013 – 2014



**Dates are consensus estimates based on initial filing*

Agenda

1.	Introduction	Geoffrey McDonough
2.	Late Stage Programs	Birgitte Volck
	Kiobrina	Kristina Timdahl
	Q + A	
	Break	
3.	Early Stage Projects	Stephen James
	SOBI002	Patrik Strömberg
	Q + A	
4.	Close	Geoffrey McDonough

Late Stage Portfolio

Birgitte Volck, M.D., Ph.D.
Senior Vice President, Chief Medical Officer

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Birgitte Volck, M.D., Ph.D.

- 2012- **Sobi** Senior Vice President, Chief Medical Officer
- 2007-2012 **Amgen** Regional and HQ
- 2004-2007 **Genzyme** Nordic & BELux
- 2001-2004 **Pharmexa** Biotech DK HQ
- 2000-2001 **Aventis** DK affiliate
- 1991-2000 MD **CPH University**

  PhD **CPH University**

  » Arthritis and Biomarkers

How We Think About Development

- Full integrated medical approach across the entire lifecycle of products
- Orientation to and alignment with patient access, commercial organization and affiliates
- Unified medical platform for countries and HQ

→

- Informs evidence generating filing/line extension and access enabling strategies
- Country oriented partner in patient and customer centric strategies
- Medical : Commercial peer leadership with balanced investment and priorities

Building capacity and focused efforts in support of patient & customer focused commercialization

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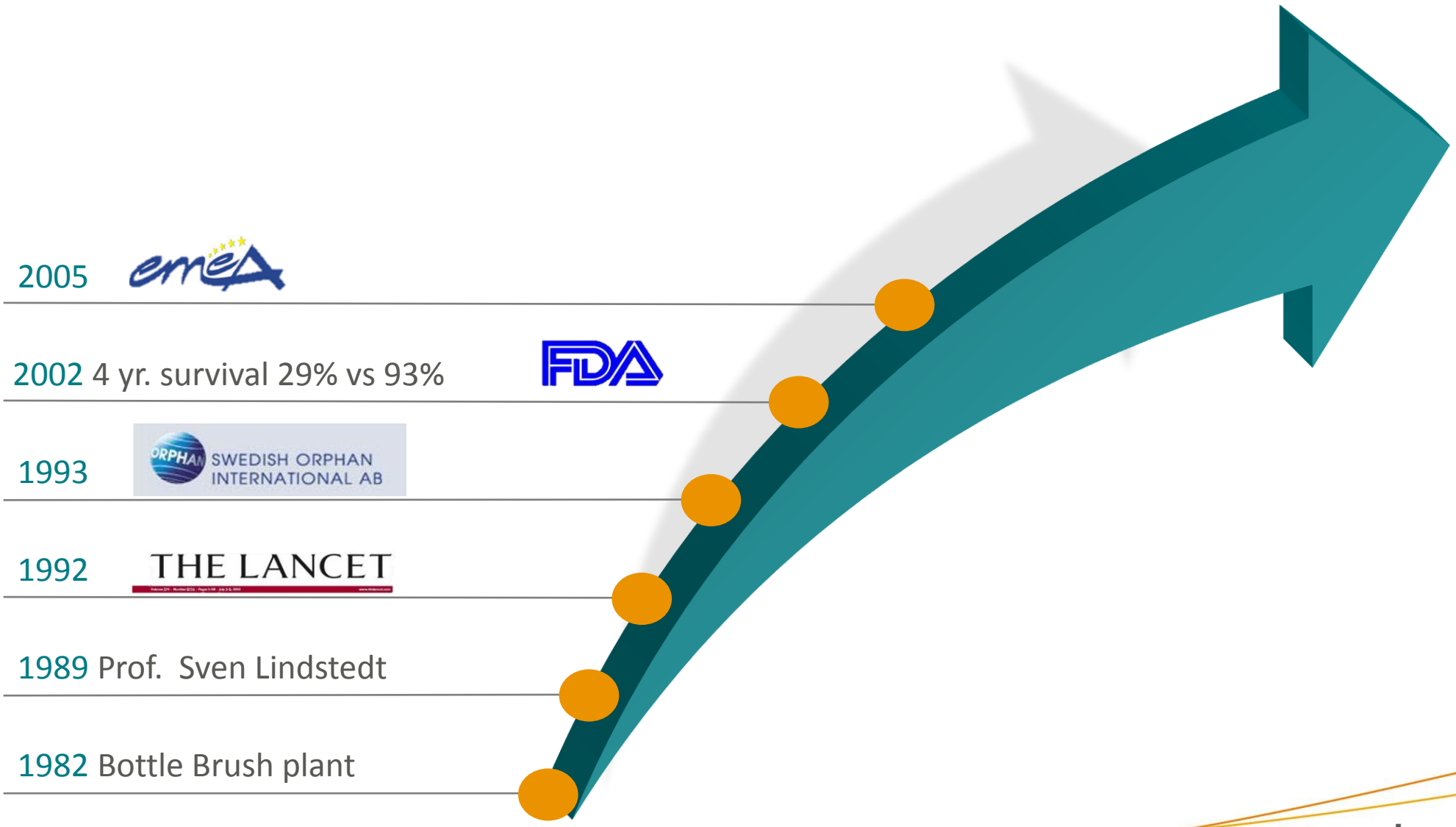
A Rare Journey: 30 Years With Orfadin

Our Legacy in Rare Diseases



Principles of Development & Medical
Informed by the Patient Journey

Diagnosis + Treatment

Disease Management

Outcomes Development

Optimizing Care & Advancing the Science

Undiagnosed Patient

- Symptoms
- Awareness
- Testing
- Diagnosis + Staging
- Treatment

Ongoing Mgt.

Monitoring

Data Capture

Health System Access

Outcomes Reporting

Commercial & Patient Access

Medical + Scientific Affairs

Research Biology and Process Development

PV Regulatory Clin Ops Biostat DM

Guiding Principles: best integrity, ethics, scientific and technical standards

Value Dossier

- Revised Treatment Guidelines
- Physicians Publications
- Label Updates
- Identification of Unmet Medical Need

We Pursue Novel Approaches in Development

Partnering Through Early and Continous Dialogue

STATE OF THE ART

nature publishing group

VOLUME 91 NUMBER 3 | MARCH 2012 | www.nature.com/cpt

Open

[1]European Medicines Agency, London, UK; [2]MIT Center for Biomedical Innovation, Cambridge, Massachusetts, USA; [3]MIT Department of Political Science, Cambridge, Massachusetts, USA; [4]MIT Division of Engineering Systems, Cambridge, Massachusetts, USA; [5]Agence Français de Sécurité Sanitaire des Produits de Santé, Saint Denis, France; [6]Department of Population Medicine, Harvard Medical School, Boston, Massachusetts, USA; [7]Novartis Vaccines & Diagnostics, Cambridge, Massachusetts, USA; [8]National Institute for Health and Clinical Excellence, London, UK; [9]Commonwealth Fund, New York, New York, USA; [10]AstraZeneca, London, UK; [11]Bristol-Myers Squibb, New York, New York, USA; [12]Singapore Health Sciences Authority, Singapore, Singapore; [13]Health Canada, Ottawa, Ontario, Canada; [14]US Food and Drug Administration, Silver Spring, Maryland, USA; [15]Johnson & Johnson, New Brunswick, New Jersey, USA; [16]Canadian Agency for Drugs and Technologies in Health, Ottawa, Ontario, Canada; [17]Aetna, Hartford, Connecticut, USA; [18]Pfizer, New York, New York, USA; [19]Friends of Cancer Research, Washington, DC, USA; [20]Ohio Northern University Raabe College of Pharmacy, Ada, Ohio, USA. Correspondence: K Oye (oye@mit.edu)

Adaptive Licensing: Taking the Next Step in the Evolution of Drug Approval

H-G Eichler[1,2], K Oye[2,3,4], LG Baird[2], E Abadie[5], J Brown[6], CL Drum[2], J Ferguson[7], S Garner[8,9], P Honig[10], M Hukkelhoven[11], JCW Lim[12], R Lim[13], MM Lumpkin[14], G Neil[15], B O'Rourke[16], E Pezalla[17], D Shoda[18], V Seyfert-Margolis[14], EV Sigal[19], J Sobotka[20], D Tan[12], TF Unger[18] and G Hirsch[2]

Traditional drug licensing approaches are based on binary decisions. At the moment of licensing, an experimental therapy is presumptively transformed into a fully vetted, safe, efficacious therapy. By contrast, adaptive licensing (AL) approaches are based on stepwise learning under conditions of acknowledged uncertainty, with iterative phases of data gathering and regulatory evaluation. This approach allows approval to align more closely with patient needs for timely access to new technologies and for data to inform medical decisions. The concept of AL embraces a range of perspectives.

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A Rare Journey: 30 Years With Orfadin

Our Legacy in Rare Diseases

2013 International filings /oral suspension/ 20 mg

DevelopAKUre

2012 Pioneering Corporate-Academic-Public Collaboration

2005 emea

2002 4 yr. survival 29% vs 93% FDA

1993 ORPHAN SWEDISH ORPHAN INTERNATIONAL AB

1992 THE LANCET

1989 Prof. Sven Lindstedt

1982 Bottle Brush plant

Patient voice inspires our commitments

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AKU
alkaptonuria society

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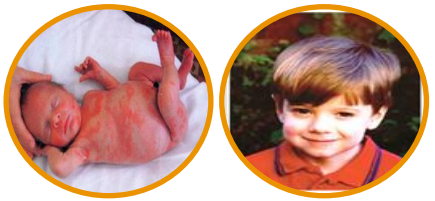
Kineret for CAPS & NOMID – A Rare Journey



Clinical study management, data analysis, study report

FDA pre-meeting

FDA pre-submission meeting

Kineret Pediatric Investigation Plan Approval (EU)

FDA Approval NOMID

2010 | **2011** | **2012** | **2013**

Orphan Drug Designation US

Scientific Advice EU

Filing US

Filing EU

CHMP Positive Opinion - CAPS

Cryopyrin Associated Periodic Syndromes (CAPS)
Neonatal onset Multisystem Inflammatory Disease (NOMID)

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R&D Pipeline 2013

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CAPS	Kineret	sobi					
Hemophilia A	rFVIIIFc	biogen idec					
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Improve growth in preterm infants	Kiobrina	sobi					
Oral Mucositis in Head & Neck Cancer	Kepivance	sobi					
Hereditary Tyrosinemia Type 1	Orfadin Liquid	sobi					
Hereditary Tyrosinemia type 1	Orfadin 20mg capsule	sobi					
Alkaptonuria	Orfadin	AKU alkaptonuria society					
Complement –mediated disease	SOBI002	AFFIBODY					
ERT	SOBI003	sobi					
IL-1-driven disease	IL-1 Affibody	AFFIBODY					

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Kepivance – Head and Neck Cancer

Birgitte Volck, M.D., Ph.D.
Senior Vice President, Chief Medical Officer

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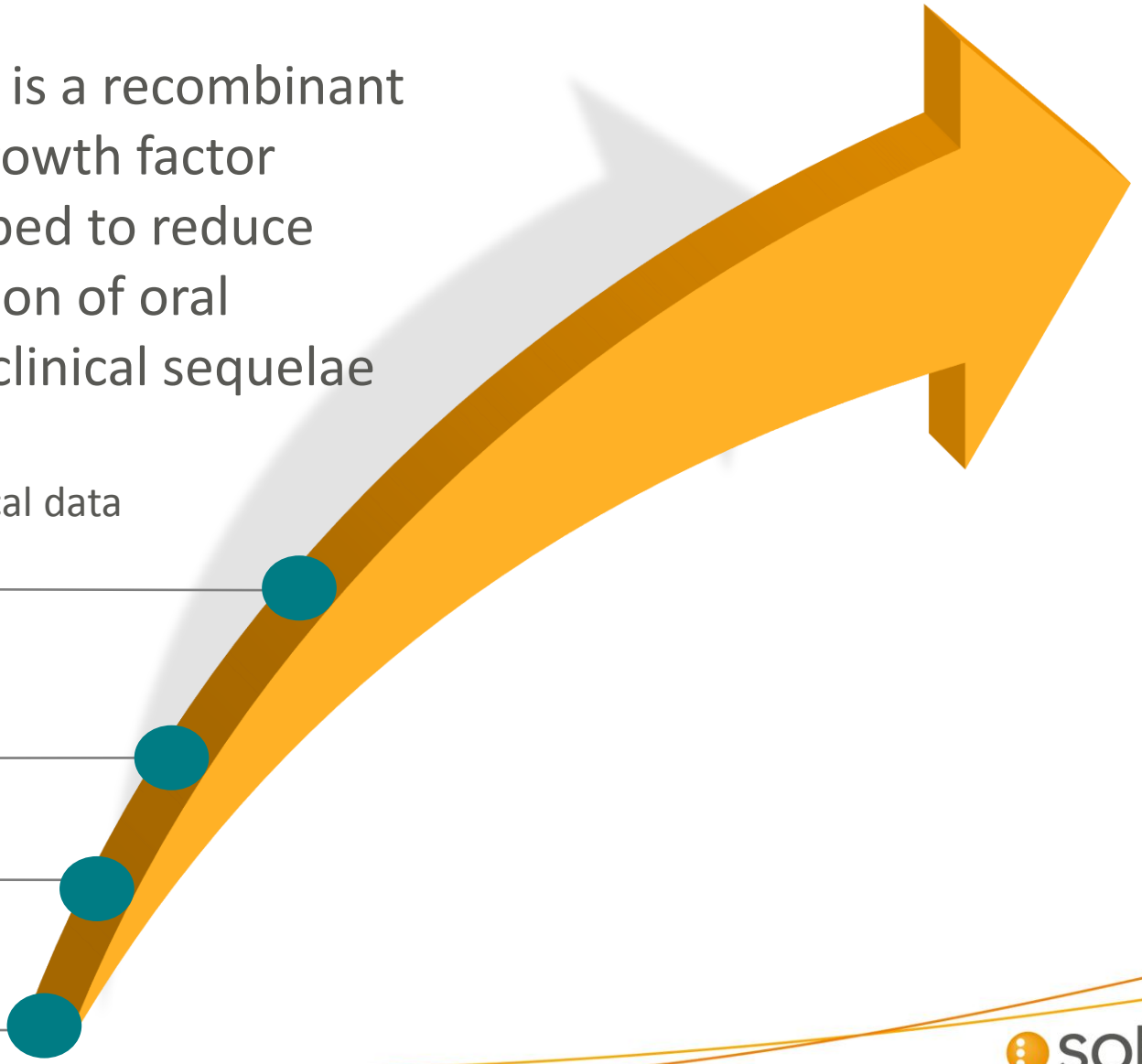
Kepivance Background

- Kepivance (palifermin) is a recombinant human keratinocyte growth factor
- Palifermin was developed to reduce the severity and duration of oral mucositis and related clinical sequelae



2013 rights to additional clinical data for Kepivance from Amgen

2008 proprietary product, acquired from Amgen

2005 EMEA

2004 FDA

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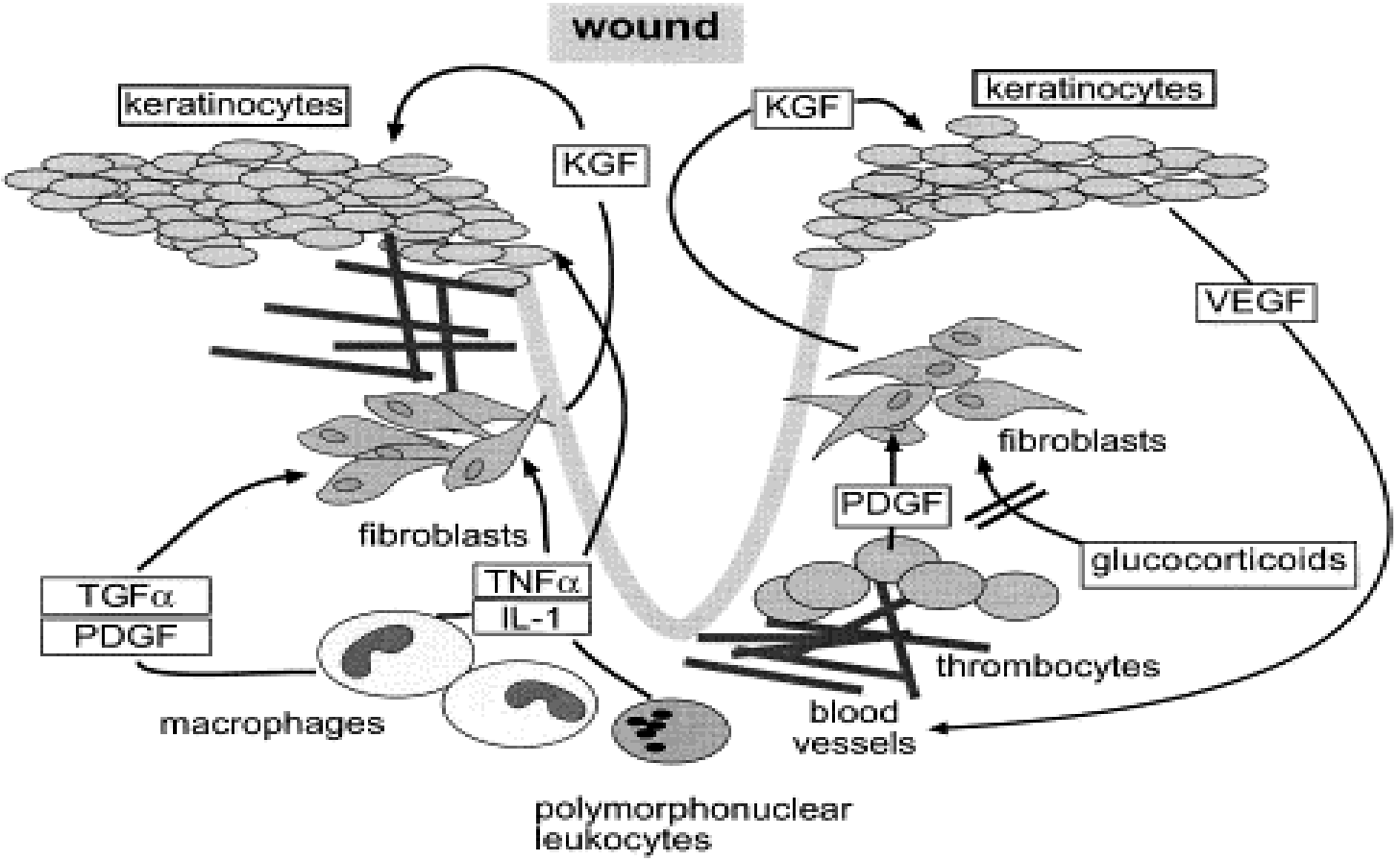
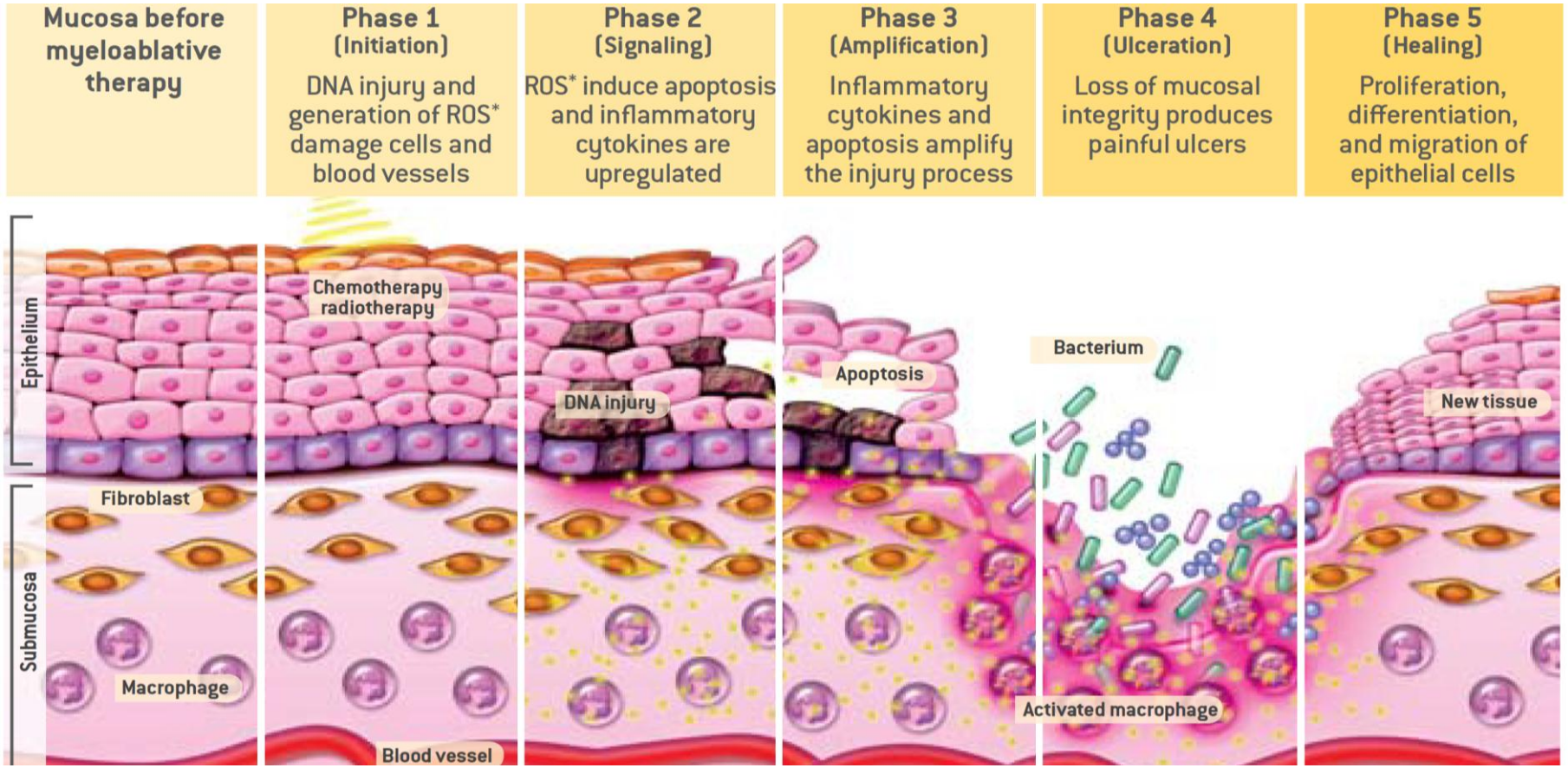
Keratinocyte Growth Factor (KGF)

KGF is an endogenous protein in the
fibroblast growth factor (FGF) family stimulating epithelial cells



Kepivance increases epithelial thickness and enhances recovery after injury



Adapted from Sonis

* ROS=reactive oxygen species, chemically reactive molecules containing oxygen like oxygen and peroxides

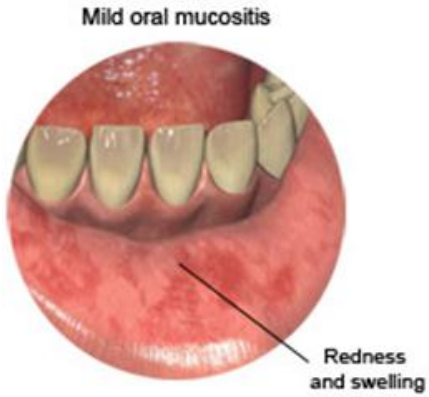
Severe Oral Mucositis – A Frequent Treatment Complication of Certain Cancer Therapy

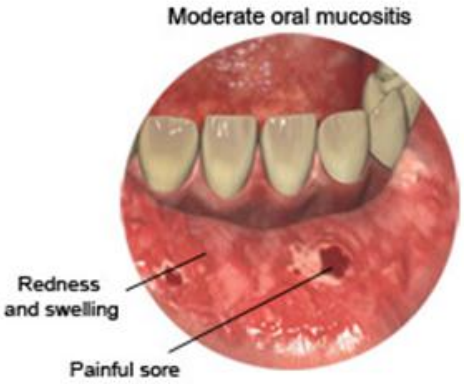
Severe OM

- **Breakdown of oral mucosa results in inflammation, pain, and often treatment and activity limiting disability**
- **Tumor location and radiation field the most predictive risk factors**

Clinical manifestations and treatment approaches

• **Pain**	→	Narcotic analgesics
• **Malnutrition/ Weight Loss**	→	PEG feeding tubes and Hospitalization
• **Dehydration**	→	IV fluids
• **Hemorrhage**	→	Emergency treatment
• **Infections**	→	Anti-infectives





Reference to the symptoms: Miller et al Cancer 47:207-214,1981

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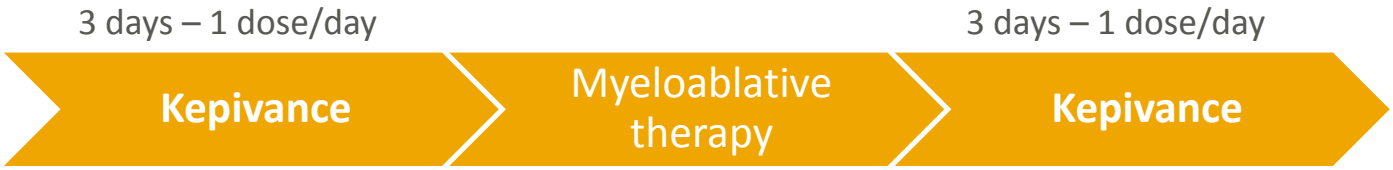
Current Indication:
Bone Marrow Transplantation

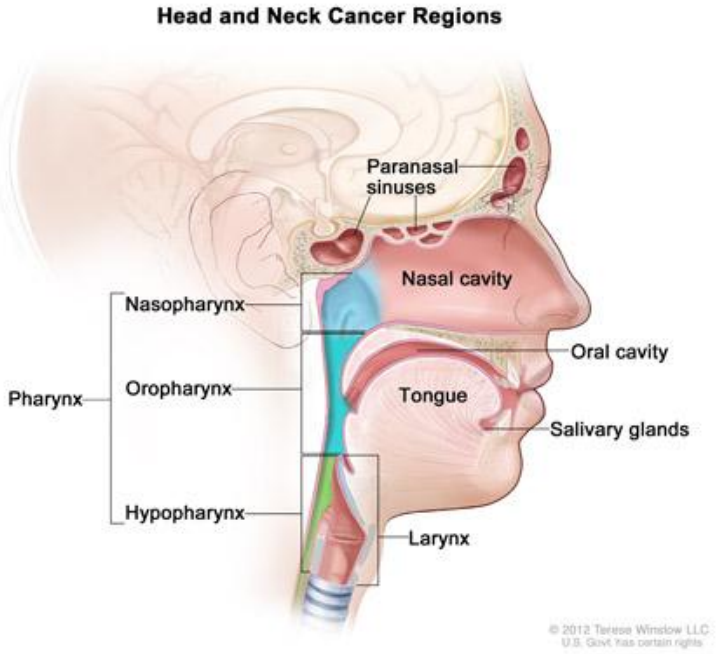
Kepivance is indicated to decrease the incidence and duration of severe oral mucositis in patients with hematologic malignancies receiving myelotoxic therapy requiring hematopoietic stem cell support

There are approximately 10,000 – 15,000 addressable patients in the US each year

Kepivance is administered as an intravenous bolus injection



Proposed Indication: Head and Neck Cancers



- 52,500 new cases of Head and Neck cancer in US 2013
  - Approximately 40% with advanced disease

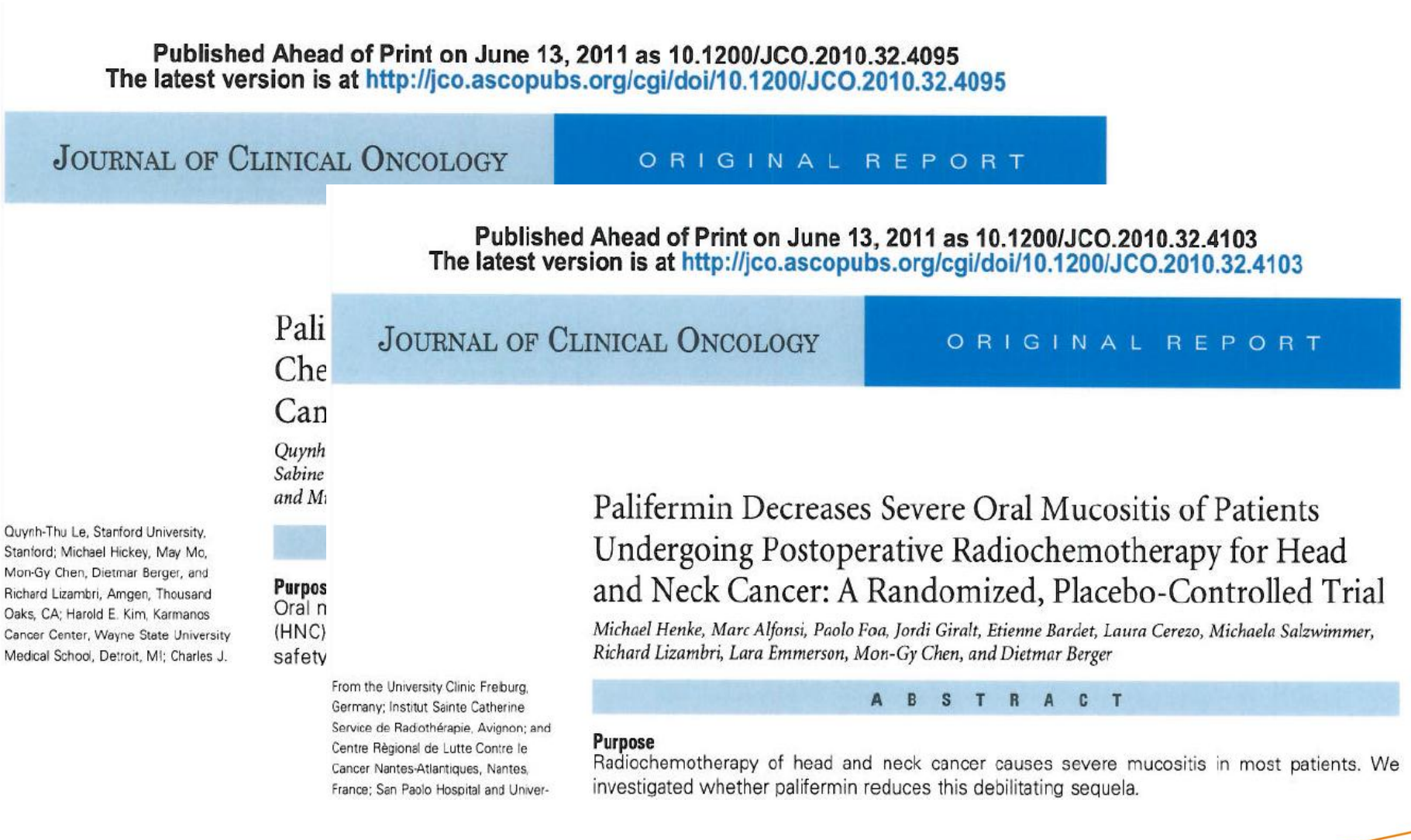
Head and Neck Cancer US Incidence

Oral Cavity	Oropharynx / Hypopharynx	Larynx / Hypolarynx	Nasopharynx & Other
~30%	~30%	~25%	~15%

- RadioChemoTherapy
  - Standard treatment for unresected locally advanced patients and for high risk resected patients
  - ~ 70-75 % of Head and Neck cancer patients

FDA Reported and Published Results

Two Pivotal H&N Cancer Studies



Published Ahead of Print on June 13, 2011 as 10.1200/JCO.2010.32.4095
The latest version is at http://jco.ascopubs.org/cgi/doi/10.1200/JCO.2010.32.4095

JOURNAL OF CLINICAL ONCOLOGY ORIGINAL REPORT

Quynh-Thu Le, Stanford University, Stanford; Michael Hickey, May Mo, Mon-Gy Chen, Dietmar Berger, and Richard Lizambri, Amgen, Thousand Oaks, CA; Harold E. Kim, Karmanos Cancer Center, Wayne State University Medical School, Detroit, MI; Charles J.

Published Ahead of Print on June 13, 2011 as 10.1200/JCO.2010.32.4103
The latest version is at http://jco.ascopubs.org/cgi/doi/10.1200/JCO.2010.32.4103

JOURNAL OF CLINICAL ONCOLOGY ORIGINAL REPORT

Palifermin Decreases Severe Oral Mucositis of Patients Undergoing Postoperative Radiochemotherapy for Head and Neck Cancer: A Randomized, Placebo-Controlled Trial

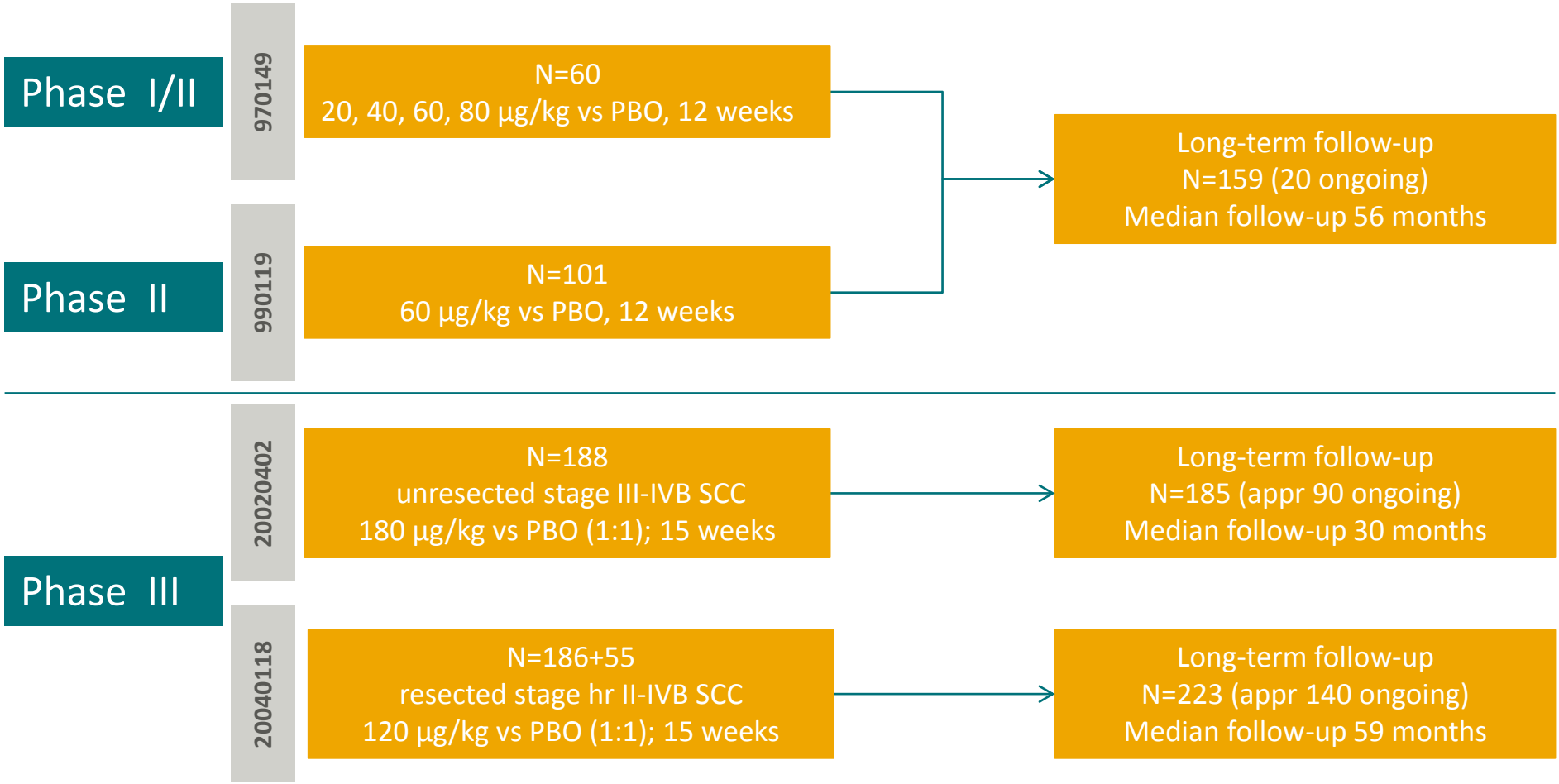
Michael Henke, Marc Alfonsi, Paolo Foa, Jordi Giralt, Etienne Bardet, Laura Cerezo, Michaela Salzwimmer, Richard Lizambri, Lara Emmerson, Mon-Gy Chen, and Dietmar Berger

From the University Clinic Freiburg, Germany; Institut Sainte Catherine Service de Radiothérapie, Avignon; and Centre Règional de Lutte Contre le Cancer Nantes-Atlantiques, Nantes, France; San Paolo Hospital and Univer-

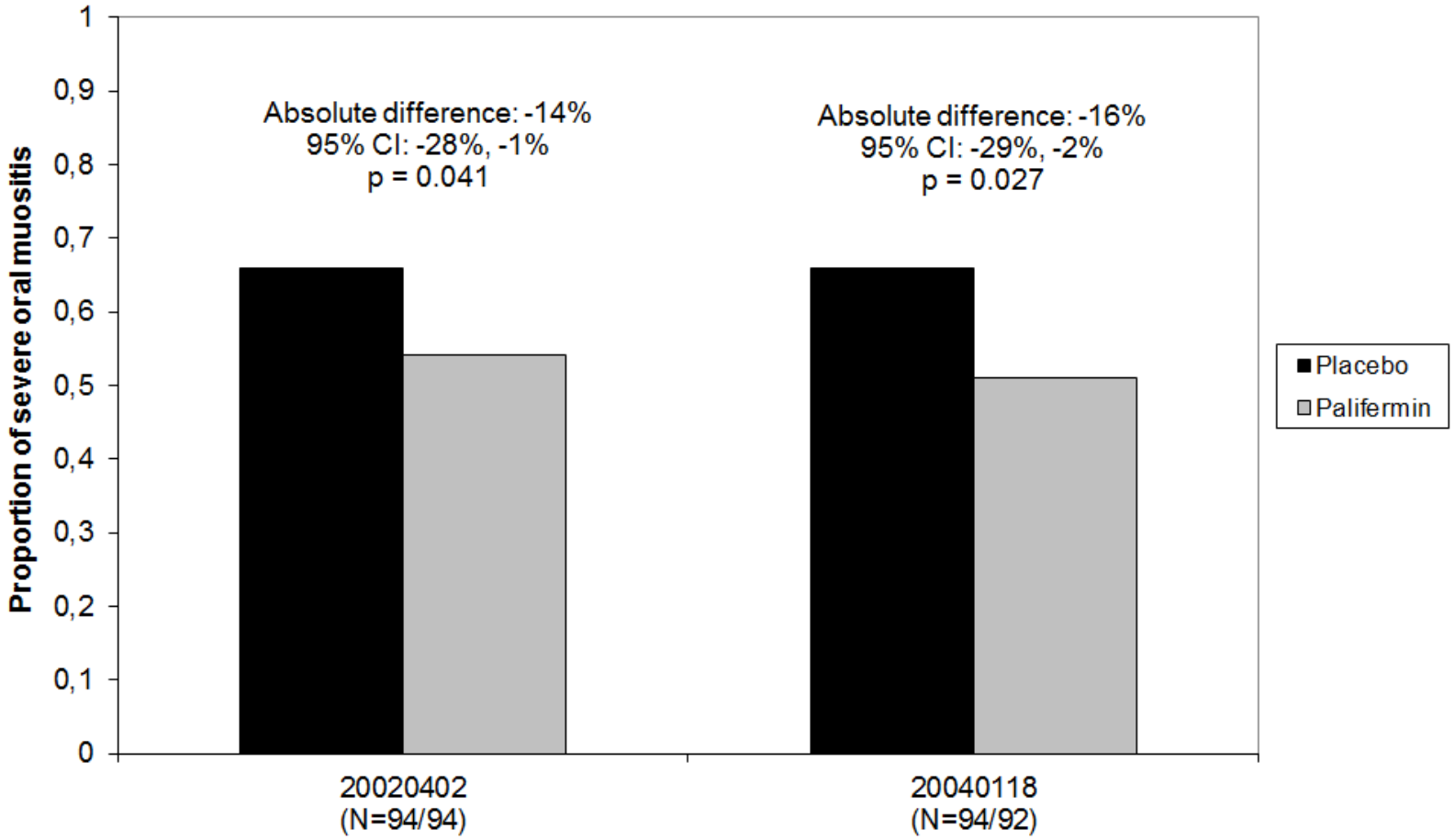
ABSTRACT

Purpose
Radiochemotherapy of head and neck cancer causes severe mucositis in most patients. We investigated whether palifermin reduces this debilitating sequela.

Kepivance Head and Neck Program



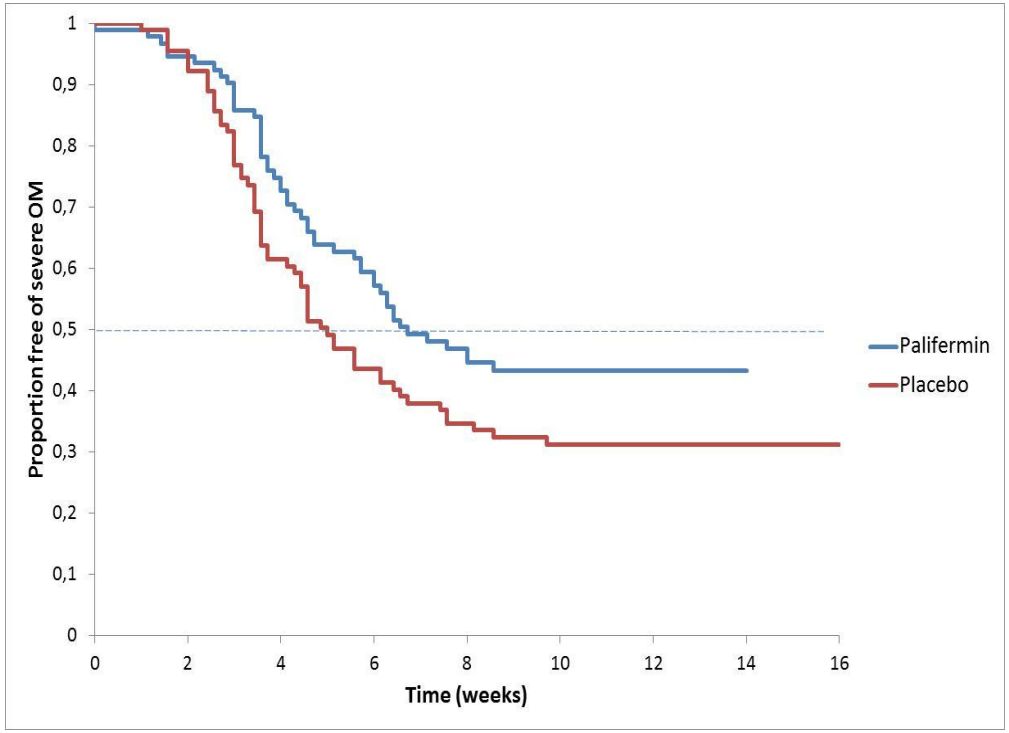
Primary Endpoint: Incidence of Severe Oral Mucositis (OM)*



*Grade 3 or 4 OM at least once during the acute evaluation phase (up to week 12-15)

Time to Severe OM (Days) (Protocol-specified Secondary Endpoint)

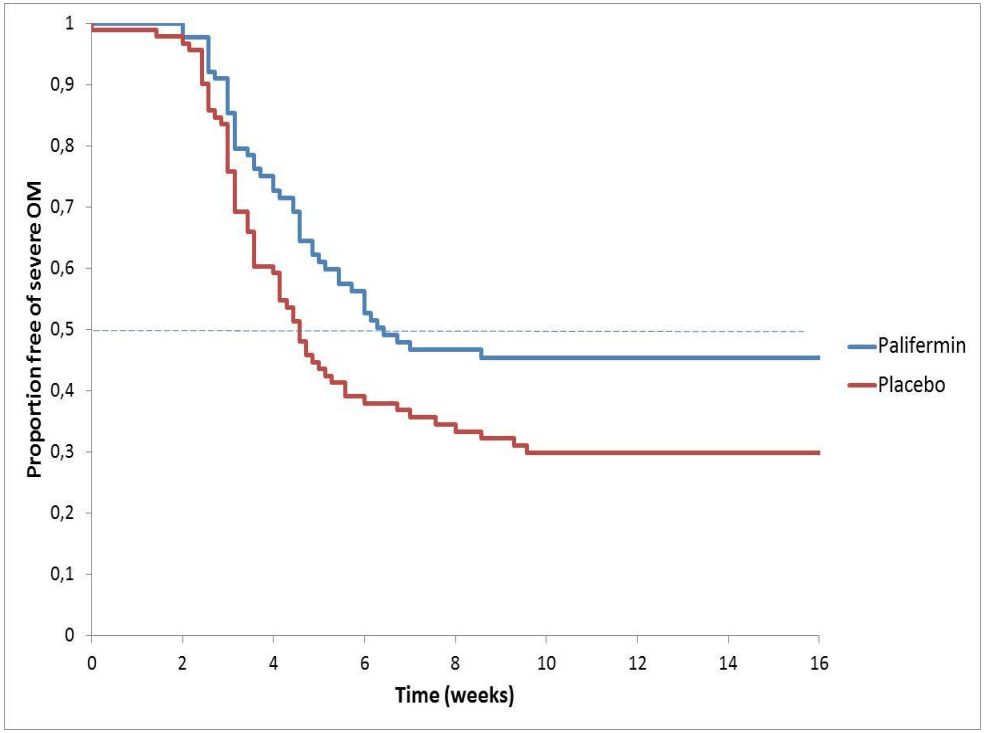
20020402



Median time to severe OM:

35 vs 47 days (raw p=0.026)

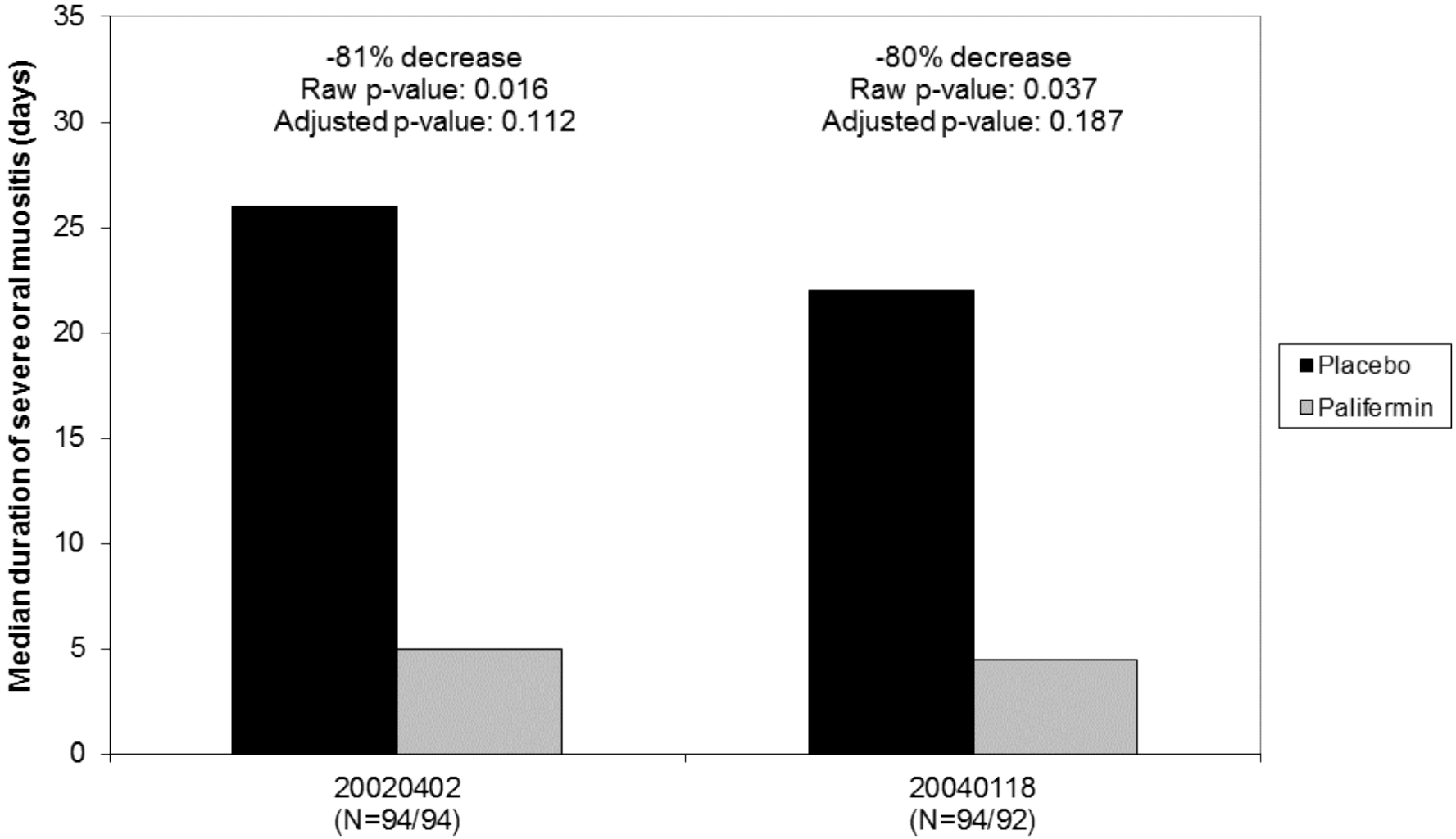
20040118



Median time to severe OM:

32 vs 45 days (raw p=0.022)

Secondary Endpoint: Median Duration (Days) of Severe OM



Short-term Safety Data: Summary of Adverse Events

	20020402		20040118	
	Placebo (N=91) n(%)	Palifermin (N=94) n(%)	Placebo (N=92) n(%)	Palifermin (N=93) n(%)
All adverse events (AEs)	85 (93)	92 (98)	89 (97)	91 (98)
Severe AEs	46 (51)	62 (66)	41 (45)	46 (49)
Serious AEs	25 (27)	35 (37)	51 (55)	31 (33)
Treatment-related AEs	10 (11)	33 (35)	10 (11)	27 (29)
Study discontinuation Due to AE	1 (1)	5 (5)	5 (5)	3 (3)
Study treatment discontinuation due to AE	5 (5)	6 (6)	5 (5)	11 (12)
Deaths during acute OM evaluation period*	3 (3)	7 (7)	1(1)	1 (1)

*Deaths occurring during the OM evaluation phase or within 30 days from the last dose of investigational product

Secondary Efficacy Endpoints
Adjusted and Unadjusted P-values

End Point	A (402)			B (118)		
	Kepivance® (n=94)	Placebo (n=94)	P-values	Kepivance® (n=92)	Placebo (n=94)	P-values
Duration of severe OM (days)	5	26	Raw: 0.016 Adj: 0.112	4.5	22	Raw: 0.037 Adj: 0.187
Time to onset of severe OM (days)	47	35	Raw: 0.026 Adj: 0.157	45	32	Raw: 0.022 Adj: 0.154
Total opioid analgesic (mg IV morphine equivalent)	283	498	Raw: 0.238 Adj: 0.684	61	171	Raw: 0.669 Adj: 0.789
Patient-reported MTS score (0-4)	1.74	1.92	Raw: 0.071 Adj: 0.285	1.46	1.60	Raw: 0.626 Adj: 0.789
Incidence of xerostomia (month 4)	67%	80%	Raw: 0.046 Adj: 0.231	76%	63%	Raw: 0.035 Adj: 0.187
Incidence of unplanned breaks in chemotherapy	52%	45%	Raw: 0.342 Adj: 0.684	30%	40%	Raw: 0.164 Adj: 0.654
Incidence of unplanned breaks in radiotherapy	15%	15%	Raw: 0.958 Adj: 0.958	15%	14%	Raw: 0.789 Adj: 0.789

Data shown as median or % of patients; p-values shown as non-adjusted (raw) or adjusted by the Hochberg's procedure

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Kepivance in Head and Neck Cancer
Our Approach 2013

- High prevalence of Oral Mucositis in Head and Neck cancer patients undergoing Radio-Chemotherapy has and large unmet medical need
- Recently acquired Kepivance data in Head and Neck cancer are compelling
  - Revisiting data assessment from for two completed pivotal phase III trials
- Additional post-hoc analysis suggests stronger treatment effect in primary and some secondary endpoints
- Favorable long-term safety follow-up
- Preparing to discuss the potential for a sBLA filing with the FDA

Kiobrina – a Pioneering Project in Neonatology

Kristina Timdahl, M.D.
Vice President, TA Head Medical, Neonatology

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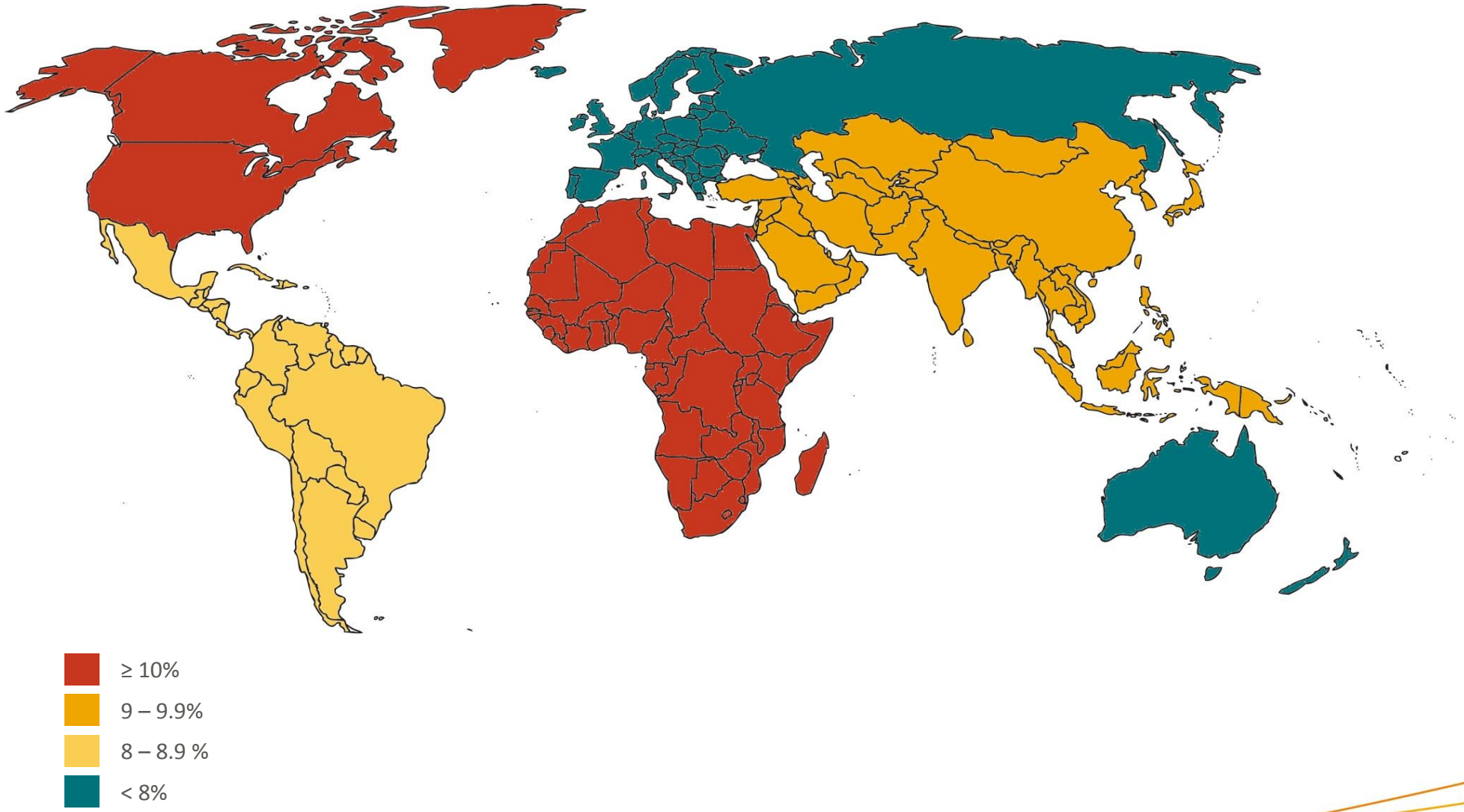
Kristina Timdahl, M.D.

- 2013- VP TA Head Medical Neonatology, **Sobi**
- 2008- Medical Director, Kiobrina **Biovitrum** and **Sobi**
- 2007-2008 Group Director ,Early Development
- 2003-2007 Global Senior Clinical Research Physician, **Astra Zeneca Neuroscience**
- 1998-2003 Medical Affairs Nordic affiliate, **Wyeth**
- 1992-1998 Physician internship ,General Practice, **Stockholm County Council**
- 1992 M.D. **Karolinska Institute**, Stockholm, 2006 Diploma in Pharmaceutical medicine , Stockholm

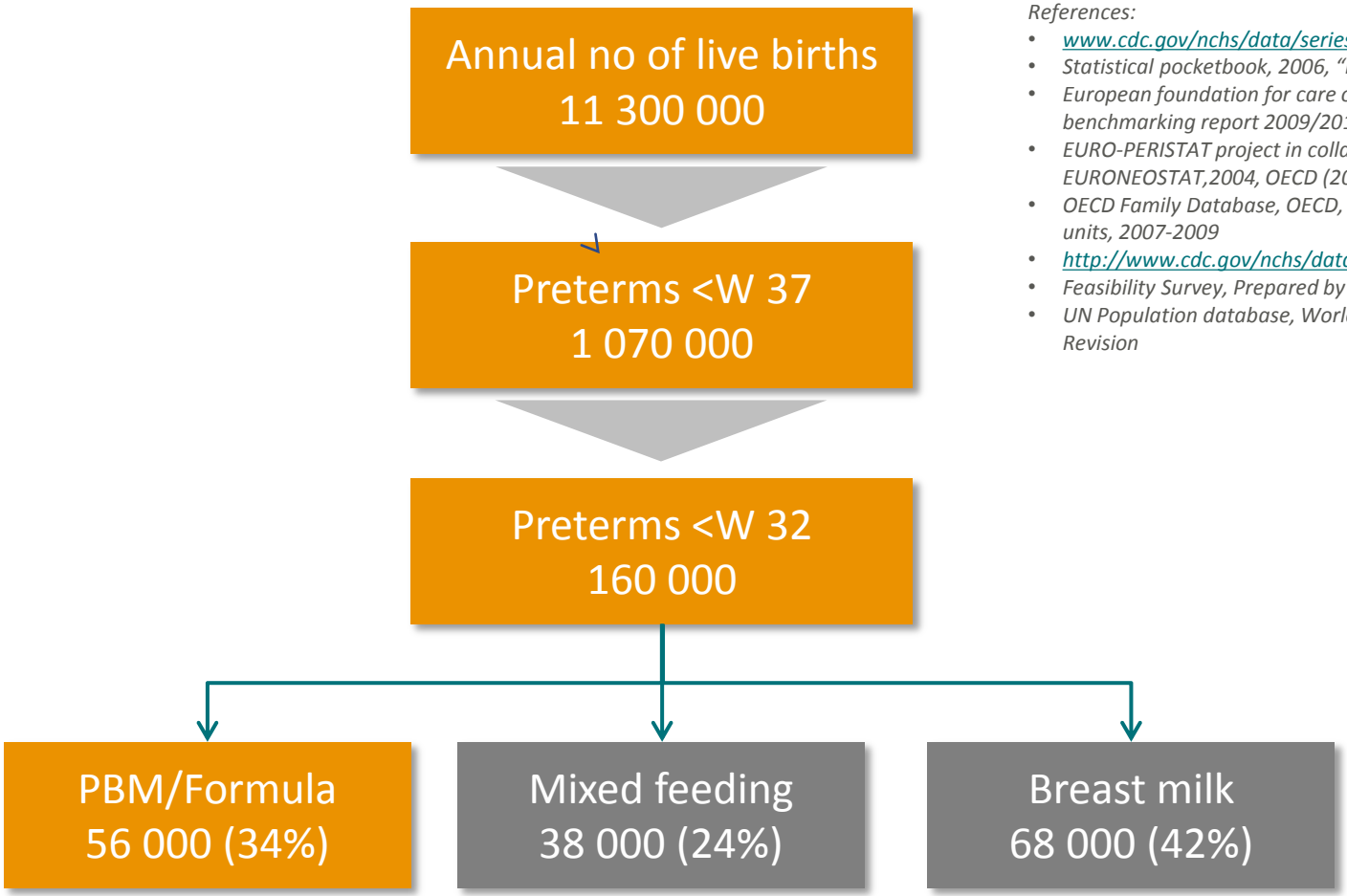
The Preterm Infant

Preterm Birthrates Are Increasing



Beck et al, OMS 2009

Number of Preterm Infants in Europe and US



References:

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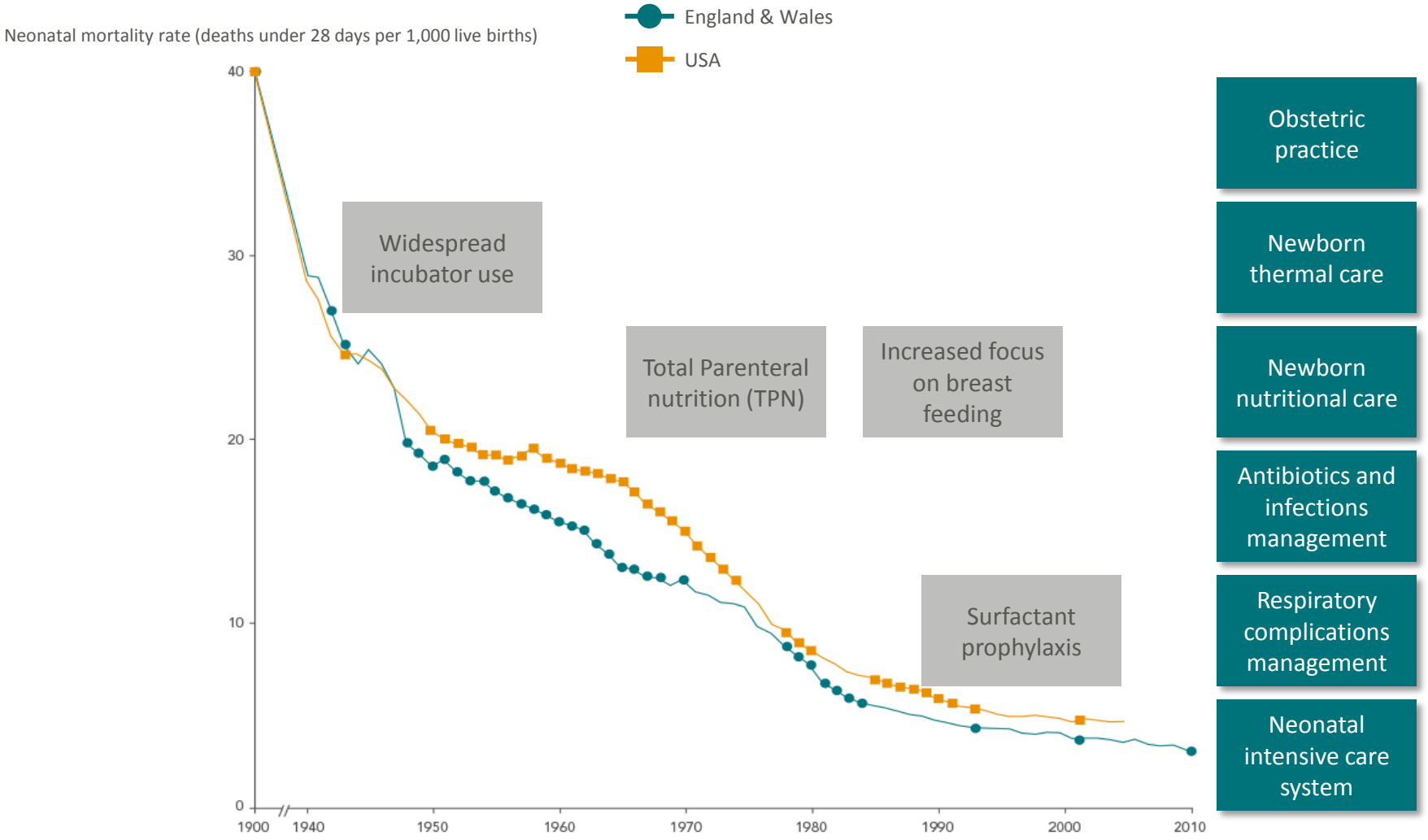
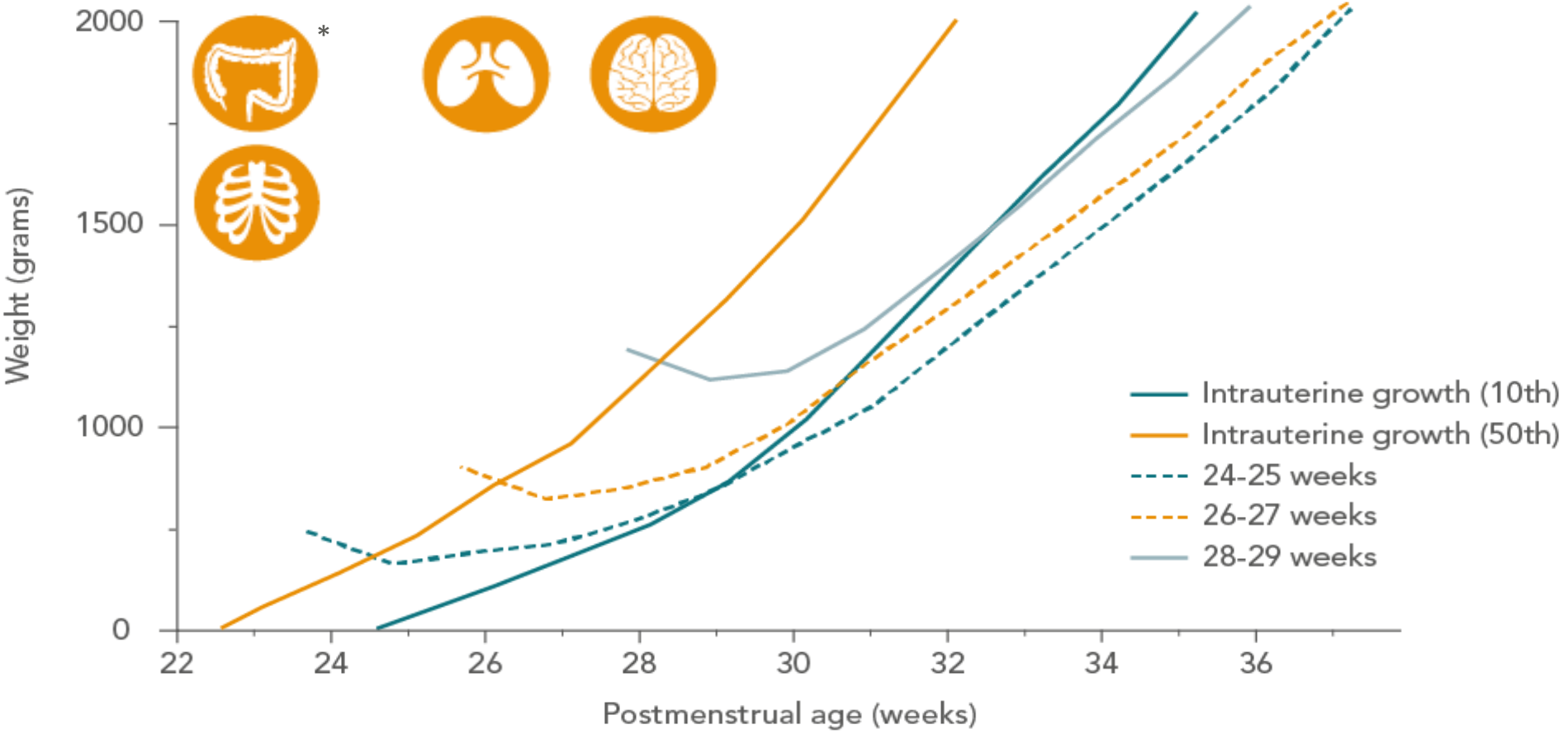
- *Statistical pocketbook, 2006, "Key figures on Europe"*
- *European foundation for care of the newborn infants, EU benchmarking report 2009/2010*
- *EURO-PERISTAT project in collaboration with SCPE, EUROCAT & EURONEOSTAT,2004, OECD (2011)*
- *OECD Family Database, OECD, Paris, Cyprus public maternity units, 2007-2009*
- *http://www.cdc.gov/nchs/data/series/sr_05/sr05_011e.pdf*
- *Feasibility Survey, Prepared by PPD for Biovitrum, 2010, Q21*
- *UN Population database, World Population Prospects, the 2010 Revision*

Advances in Neonatal Care Have Led to Dramatic Reductions in Mortality

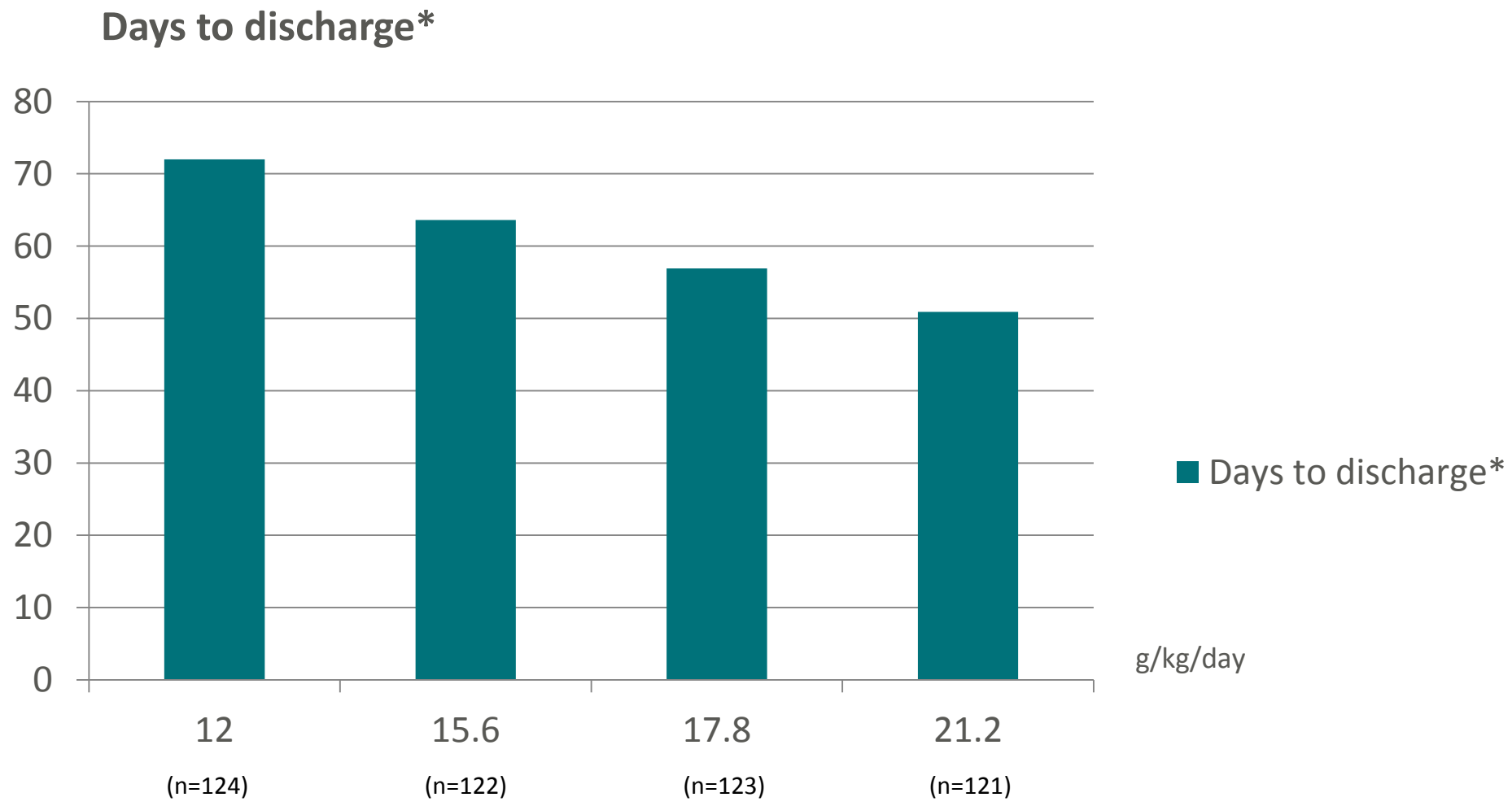


Preterm Infants Do Not Achieve Normal Growth



**The skeleton and internal organs begin to develop during the first trimester (Pilling, Elder et al. 2008)*
Ehrenkranz RA et al. Pediatrics 1999;104:280–289. Ehrenkranz RA et al. Pediatrics 2006;117:1253–1261

Duration of Hospital Stay and Growth



- Time from regaining birtweight to discharge ,transferred,age 120 days or reaching 2000g
- Ehrenkranz RA Pediatrics 2006

Short and Long-term Morbidity Remains High

- Respiratory disorder
- Retinopathy of prematurity (ROP)
- Brain injury
- Necrotizing enterocolitis
- Infections
- Poor growth

Early childhood outcome

- Impaired mental development
- Cerebral Palsy
- Visual problems and deafness

10 %

School-age outcome

- Behavioral problems
- Impaired cognitive functions
- Learning problems

40 %

Adult outcome?

A reduction in the neonatal morbidity is a key factor in improving outcome

References: Vohr B 2000, Valcamonico 2007

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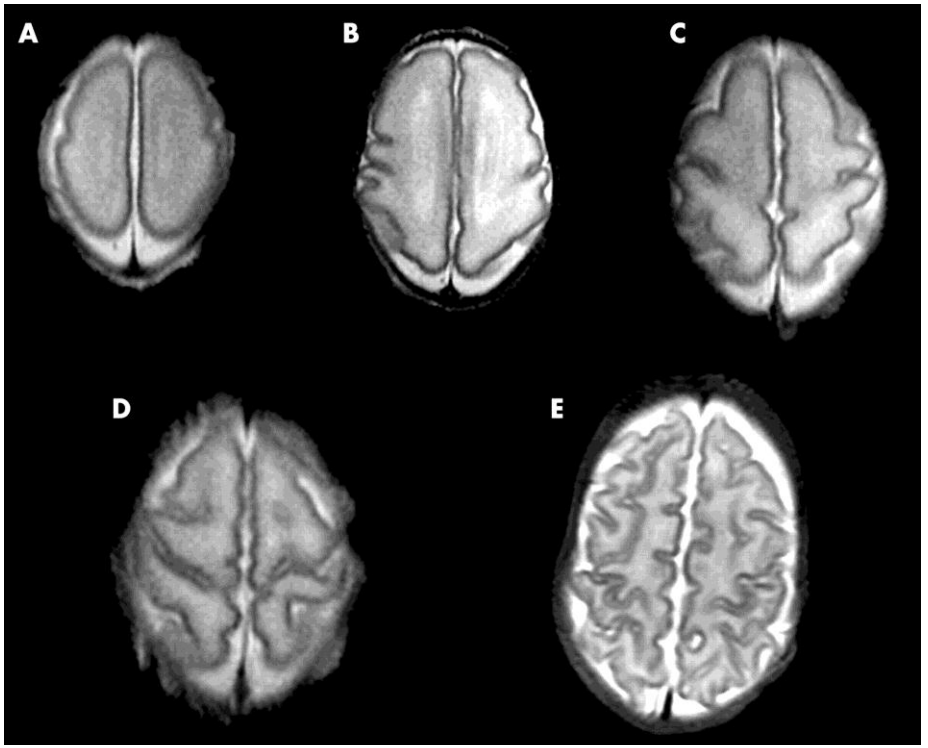
The 3rd Trimester Key for Neurodevelopment

- The brain is a fatty organ. Nutrition and accretion of LC-PUFAs (omega-3 fatty acids) important during the 3rd trimester
- LC-PUFAs important for brain and retina development
- Babies can't make LC-PUFAs. They must come from their nutrition which depends on absorbing and using them efficiently

MRI images of the brain developing between 25 – 39 weeks gestation



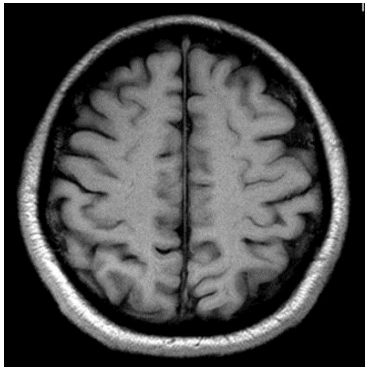
Adapted from Counsell S J et al.[4] (A.) 25 weeks; (B.) 28 weeks; (C.) 30 weeks; (D.) 33 weeks; (E.) 39 weeks.

References:
- *Volpe JJ 2009,Child Neurol 2009*
- *Lapillonne, J Pediatr 2013*
- *Lucas A, BMJ 1998*

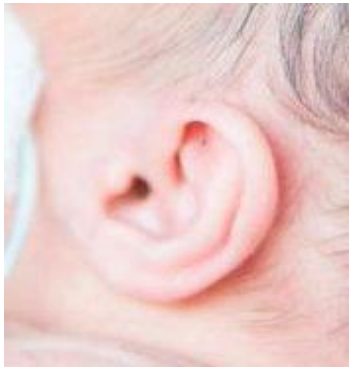
Prematurity Associated With Disability at 18-24 months

Cerebral Palsy

Mental retardation



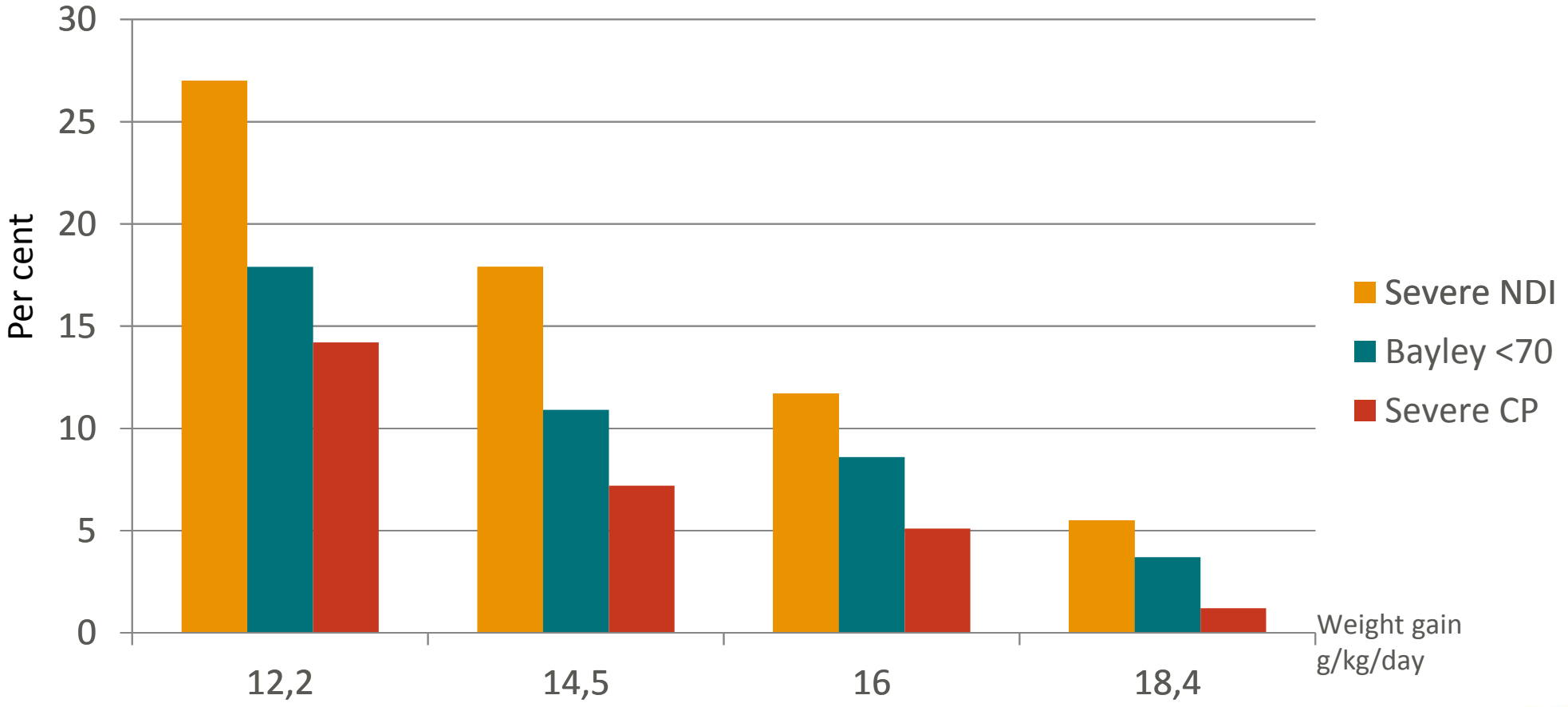
Hearing loss



Vision impairment

Growth Failure is Associated With Poor Neurodevelopment Outcome at 18-22 Months

As the rate of weight gain increase
the incidence of adverse outcomes decrease significantly



Reference: Growth and Neurodevelopmental Outcomes in Extremely Premature Infants
*Poindexter, Hinz, Langer, Ehrenkranz : new data from **PAS 2013***

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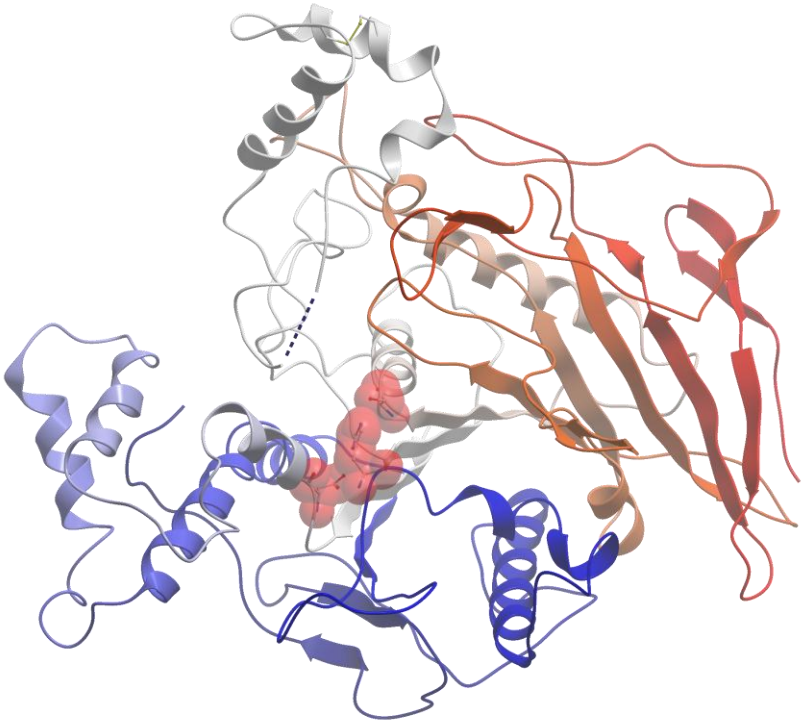
Fresh Breastmilk is Key for Growth & Development

- Composition of fresh breastmilk contains nutrients and several unique and essential bioactive components such as enzymes, cytokines and immune factors
- Since half of the nutritional energy requirement in newborns come from dietary lipids, their digestion and absorption must be very efficient

Bile Salt Stimulated Lipase (BSSL) is a Key Component of Fresh Breastmilk

- Bile salt stimulated lipase (BSSL) is an essential digestive enzyme in fresh breastmilk
- BSSL uniquely compensates for the immature pancreas of the newborn
- BSSL has the ability to hydrolyze all the major lipids that are important for energy and brain growth
- Pasteurized milk and formulas do not contain BSSL



References:

- *Howles PN, et al. Am J Physiol 1999*
- *Hurst NM. J Perinat Neonat Nurs 2007*
- *Lindquist S Curr Opin Clin Nutr Metab Care 2010*

Fresh Breastmilk is Associated With Better Cognitive Development in Preterm Infants

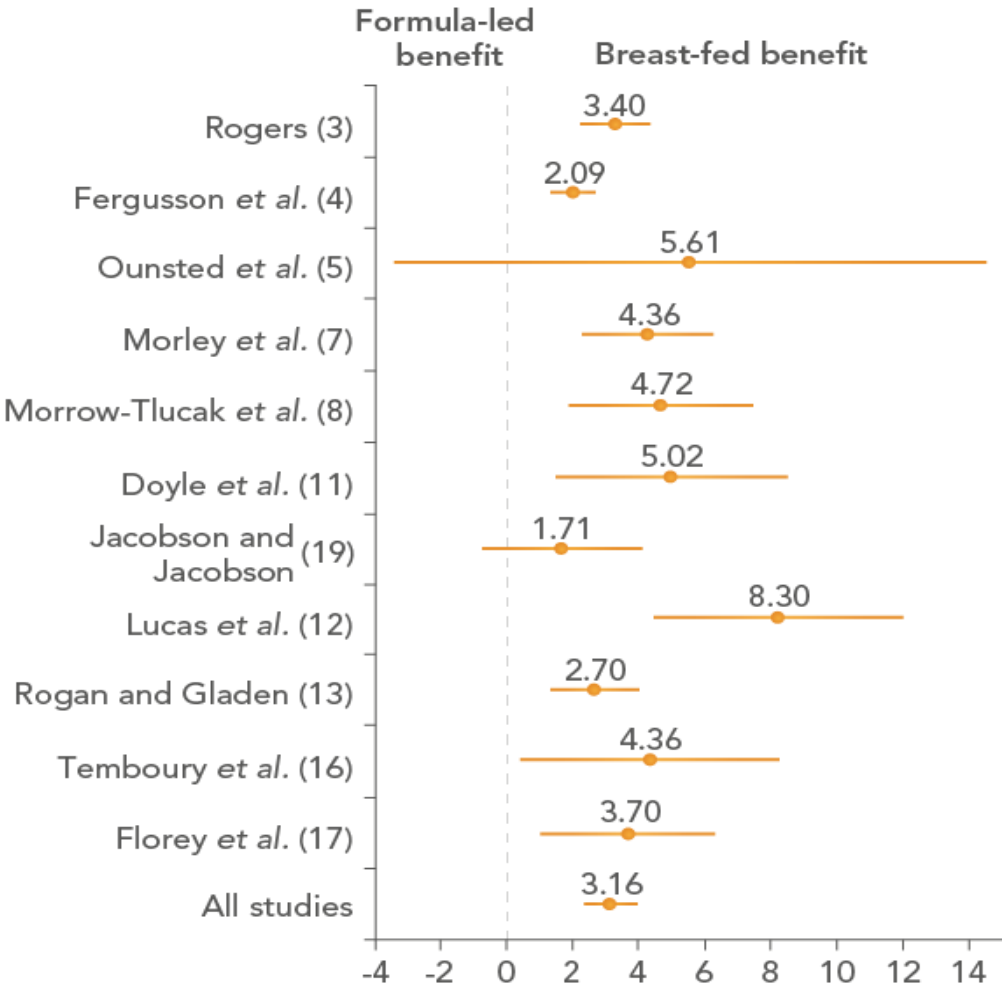


Figure 1. Effect of breast-feeding versus formula feeding on cognitive developmental score: covariate-adjusted mean differences for matched composite observations. (Adapted from Andersson 1999)

A meta-analysis of 11 studies revealed that fresh breastmilk is associated with significantly enhanced cognitive development scores compared to formula ($p<0.001$)

Cognitive function was significantly higher in breast-fed infants at 6-23 months of ages, and was stable across successive ages

References: Anderson JW, et al. Am J Clin Nutr 1999

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Our Question

What if we could restore BSSL activity in preterm infants
who do not receive fresh breastmilk?

Kiobrina – a Pioneering Project in Neonatology

Recombinant human bile-salt stimulated lipase (rhBSSL)

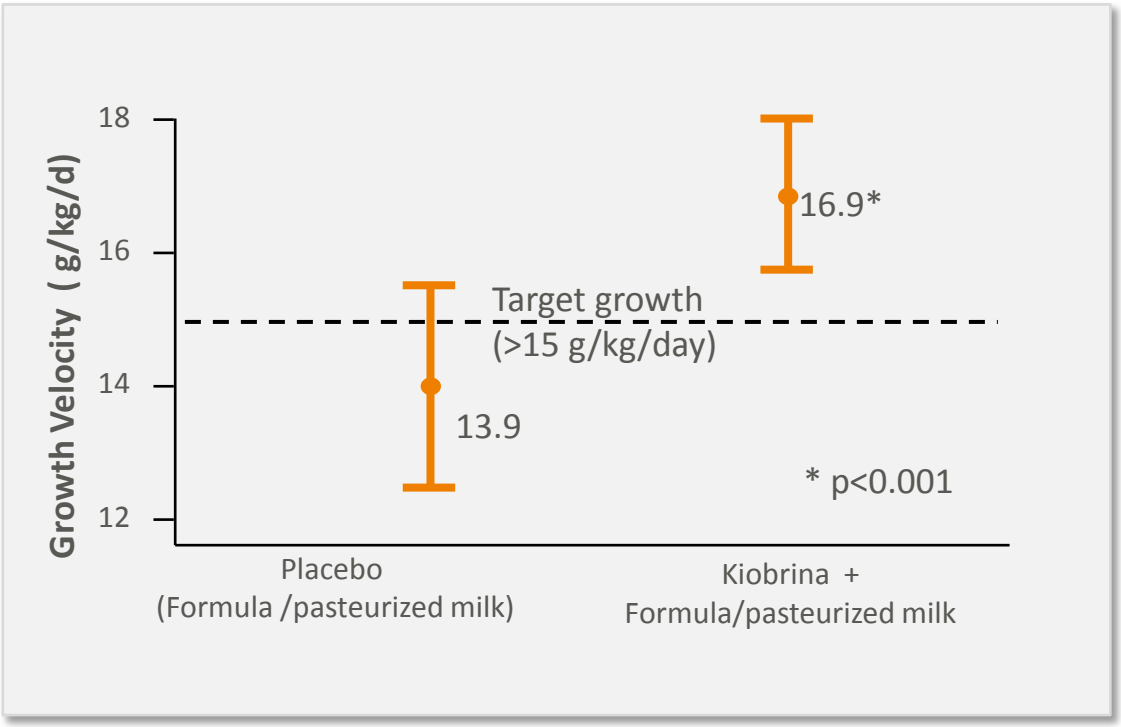
- Same amino acid sequence and properties as native BSSL
- Enzyme therapy in preterm infants unable to receive fresh breast milk
- Restores the natural lipase activity

The research aims to demonstrate improved growth which may:

- Reduce morbidity
- Reduce length of stay in NICU
- Improve neurodevelopment

Phase II Double-blind Placebo Controlled Crossover Study - Growth Improved after 1 Week Treatment

- Two parallel prospective randomized double-blind crossover studies (n=63)
- Kiobrina or placebo, was administered in pasteurized milk, or preterm infant formula
- One week of treatment
- All infants were born before week 32 of gestational age



References:

- *Casper C, Carnielli VP et al Submitted*
- *Carnielli VP et al Abstract PAS 2011 ,*
- *Maggio L et al Abstract PAS 2011*
- *Montjaux et al Abstract PAS 2011*

Pivotal Trial to Read Out 1Q 2014

Double Blind, Placebo Controlled, Randomized

Population

- > 400 Preterm Infants born < 32 weeks GA

Feeding

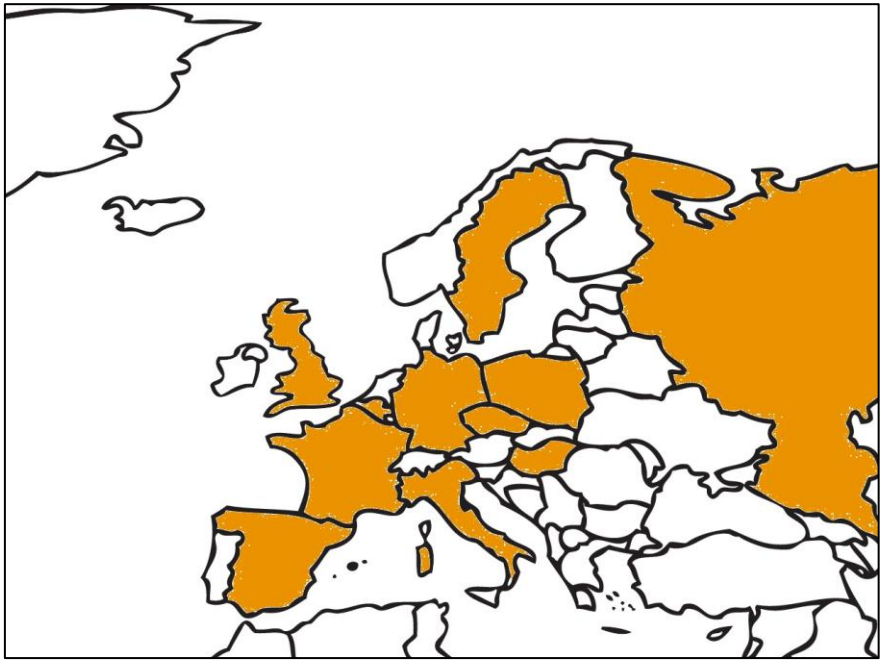
- Formula or pasteurized breast-milk

Primary endpoint

- Improve growth velocity

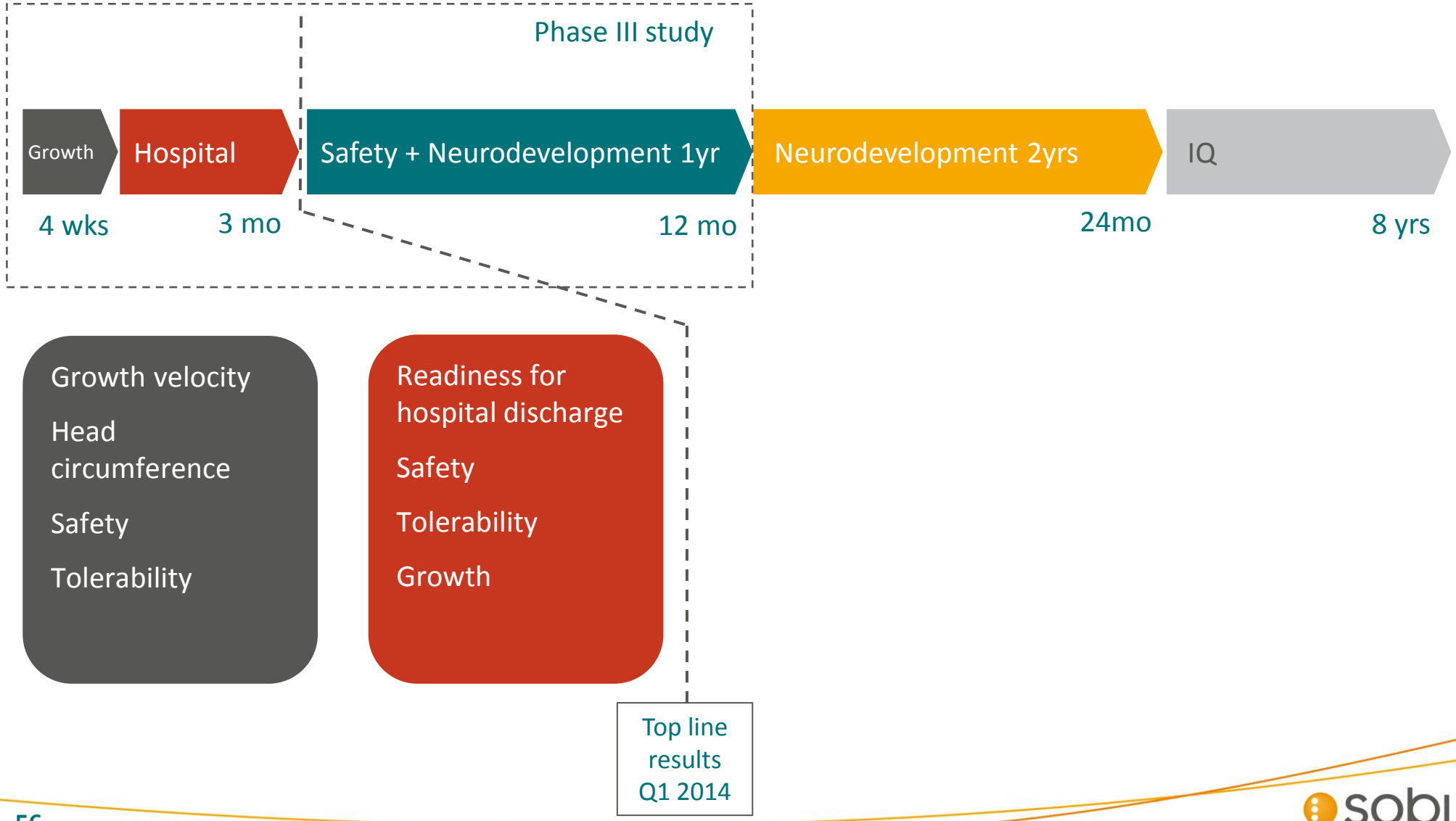
Secondary endpoints

- Head circumference, time to hospital discharge, tolerability and safety , neurodevelopment etc.

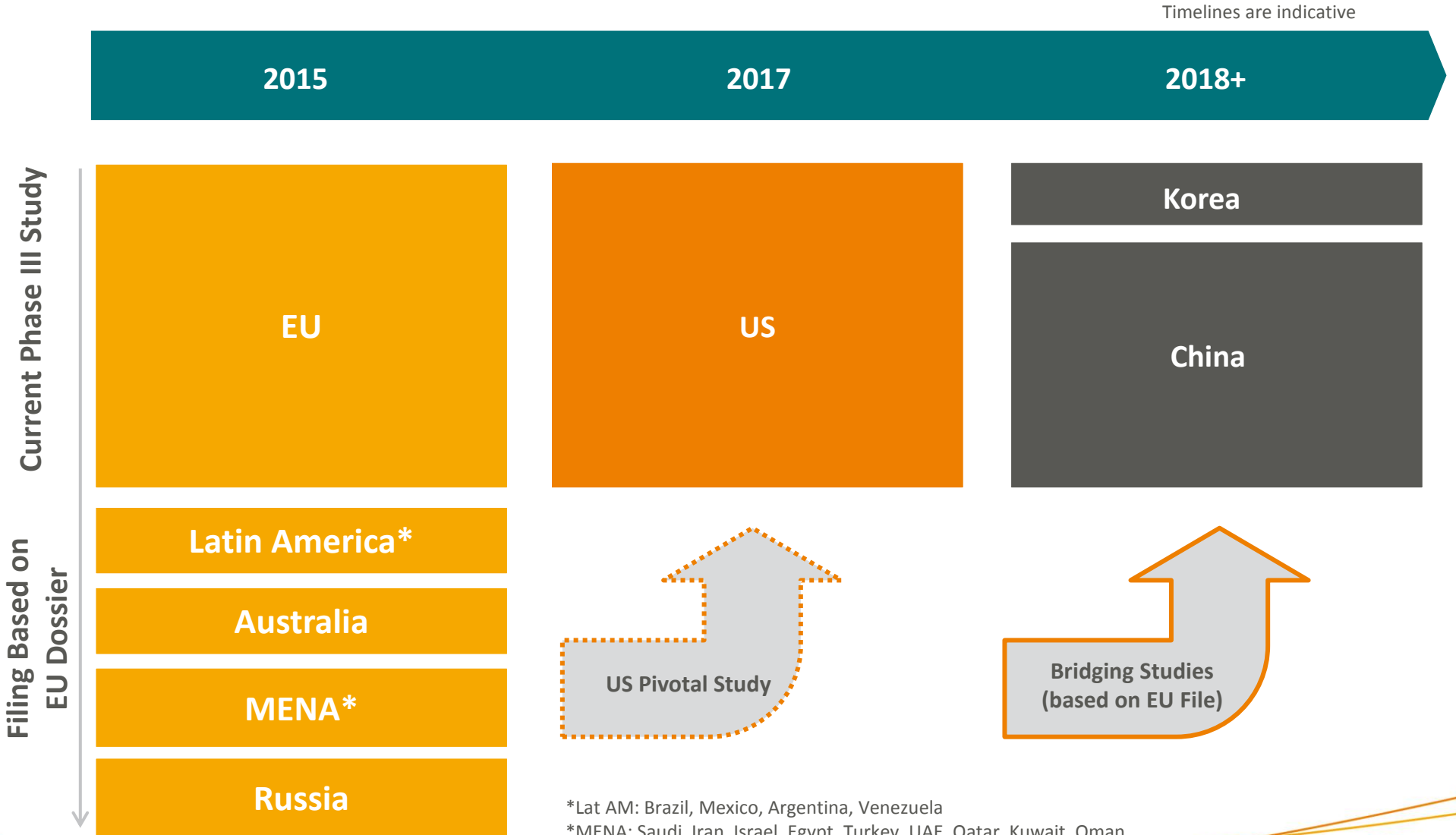


→ Top line results: Q1 2014

Top Line Results to Include Growth, Safety and Hospital Outcomes



EMA Approval Basis for Initial Expansion



*Lat AM: Brazil, Mexico, Argentina, Venezuela
*MENA: Saudi, Iran, Israel, Egypt, Turkey, UAE, Qatar, Kuwait, Oman

Early R&D Portfolio

Stephen James, Ph.D.
Vice President, Head of Drug Design and Development

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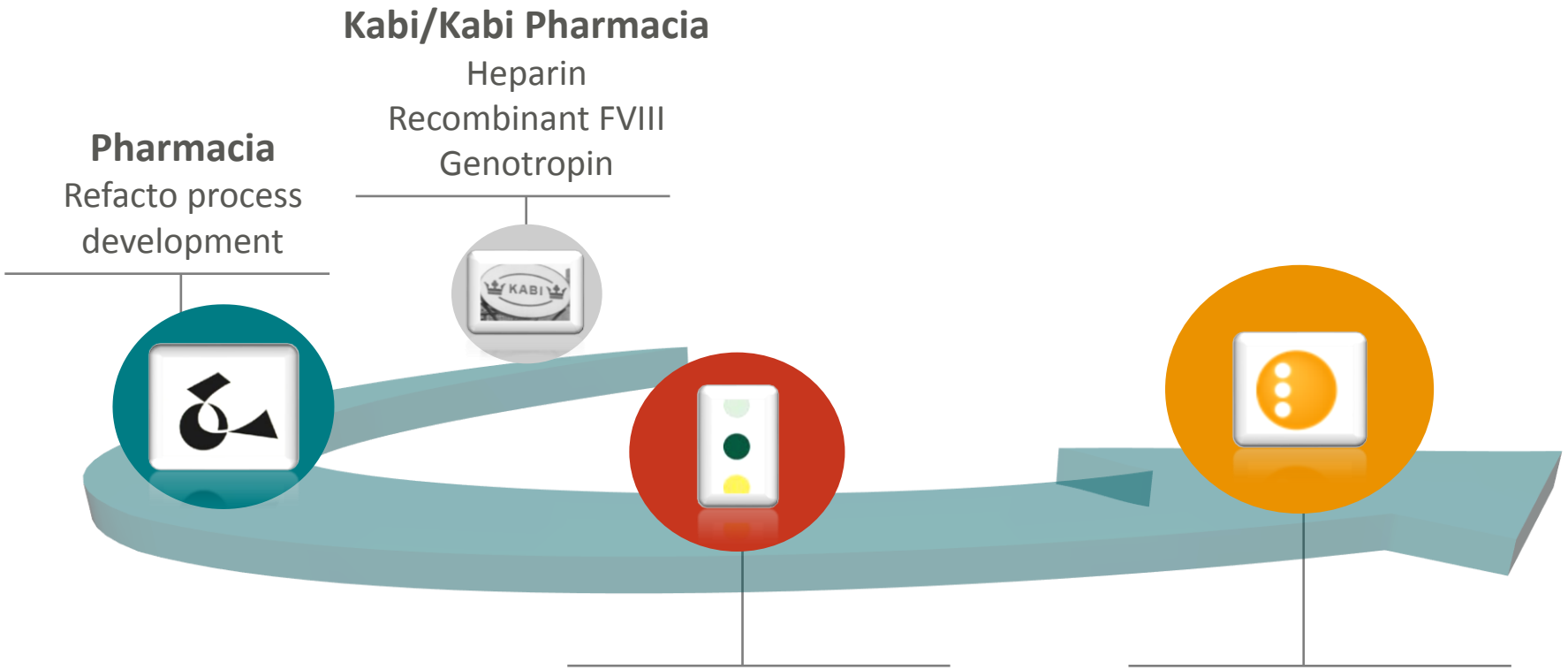
Pioneer in Rare Diseases

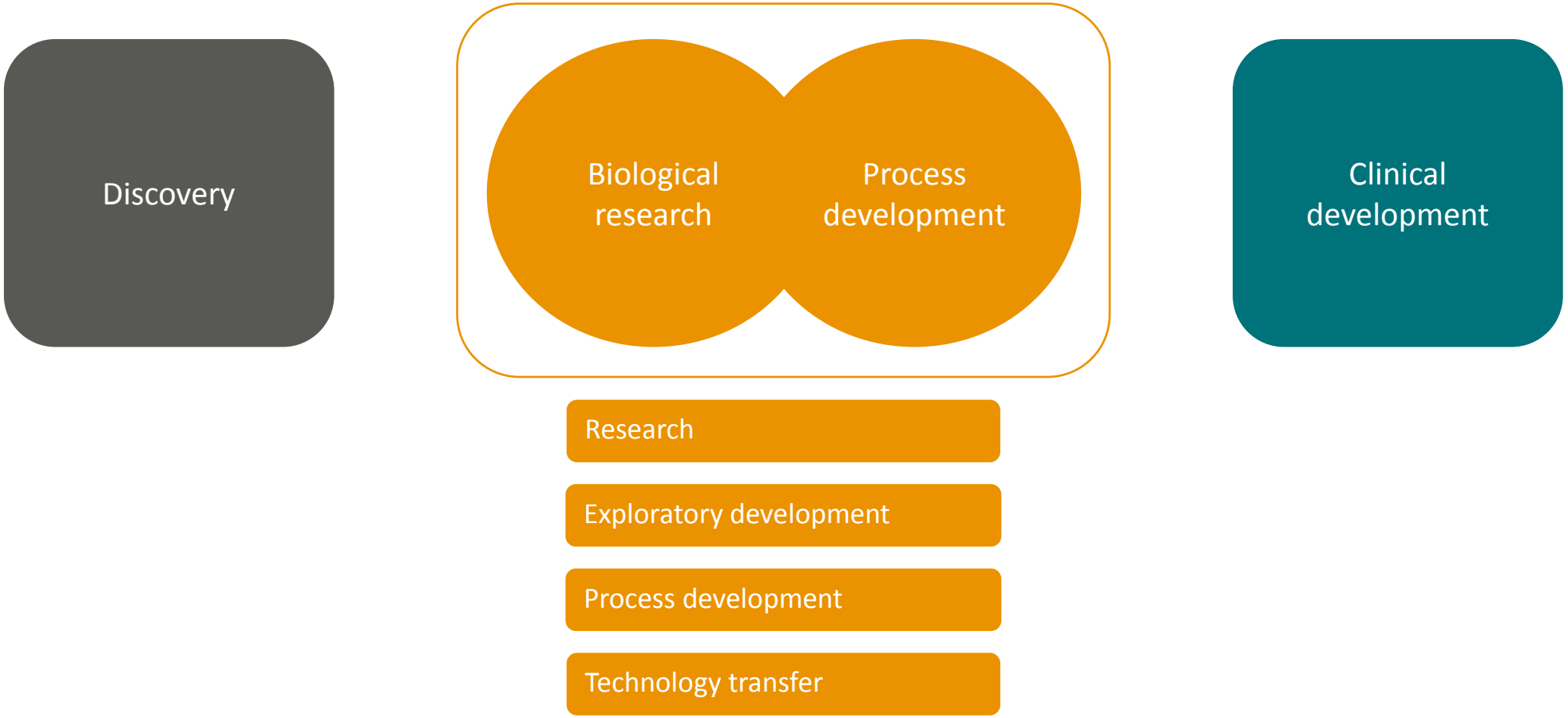
Stephen James, Ph.D.

- 2011- VP, Head of Drug Design & Development, **Sobi**
- 2008- Head of Research, **Biovitrum** and **Sobi**
- 1997-2008 Various project and department director positions, **PnU**, **Pharmacia Corp** and **Biovitrum**
- 1991-1997 Group Leader **Inositol Lab** and **University Research Fellow**, Dundee, Scotland
- BSc (Hons) (St. Andrews, 1988); PhD (Leeds, 1991) in Biochemistry

Where Do We Come From?



The Sobi Drug Design & Development Model



Our Focus: Biologics Development and CMC

Research

- Protein engineering and optimization

Exploratory Development

- Pharmacology, toxicology, DMPK, bio analysis method devt.

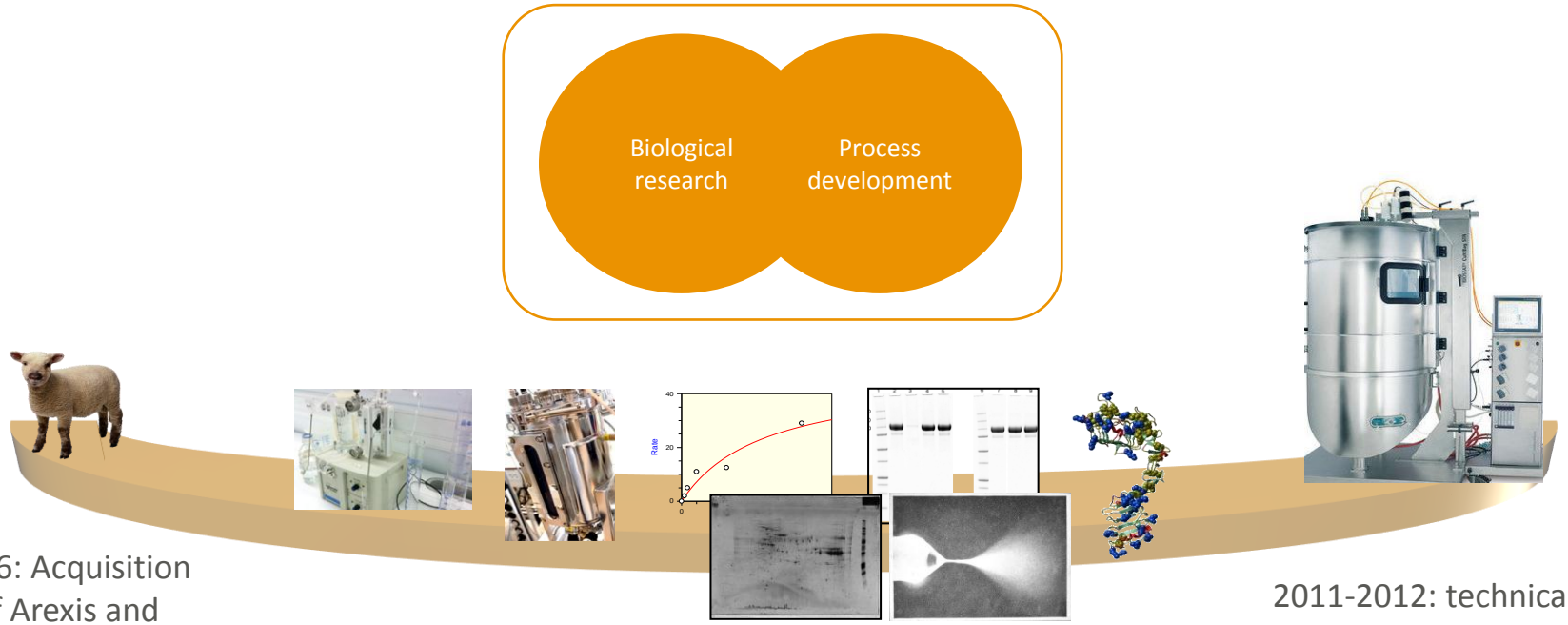
Process Development

- Upstream, midstream and downstream processes, protein analysis & characterization, formulation

Technology Transfer

- Scale-up, Manufacturing

Our Model in Action: Kiobrina

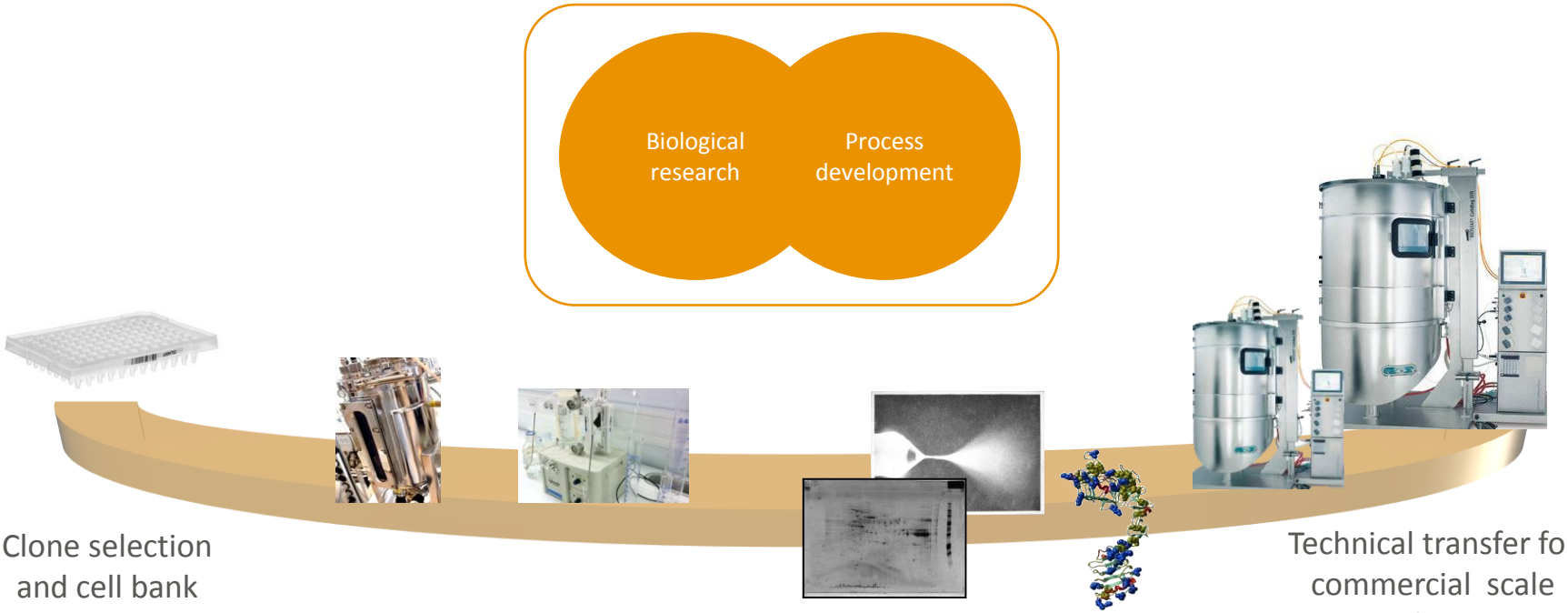


2006: Acquisition of Arexis and Kiobrina project BSSL produced in ovine bioreactor

2006-2011: CMC process development in CHO cells, full enzyme characterization and preclinical development package

2011-2012: technical transfer to commercial manufacturer

Our Model in Action: FIXFc



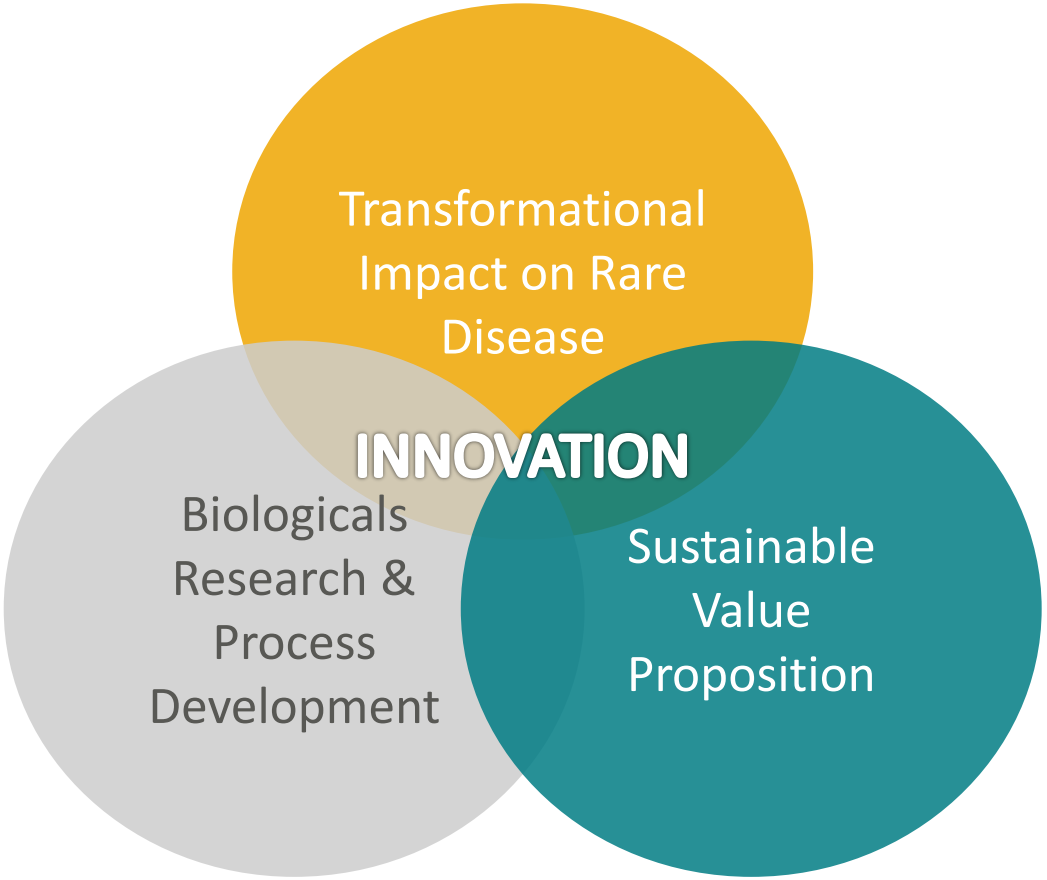
Clone selection and cell bank characterization

Upstream & downstream process development

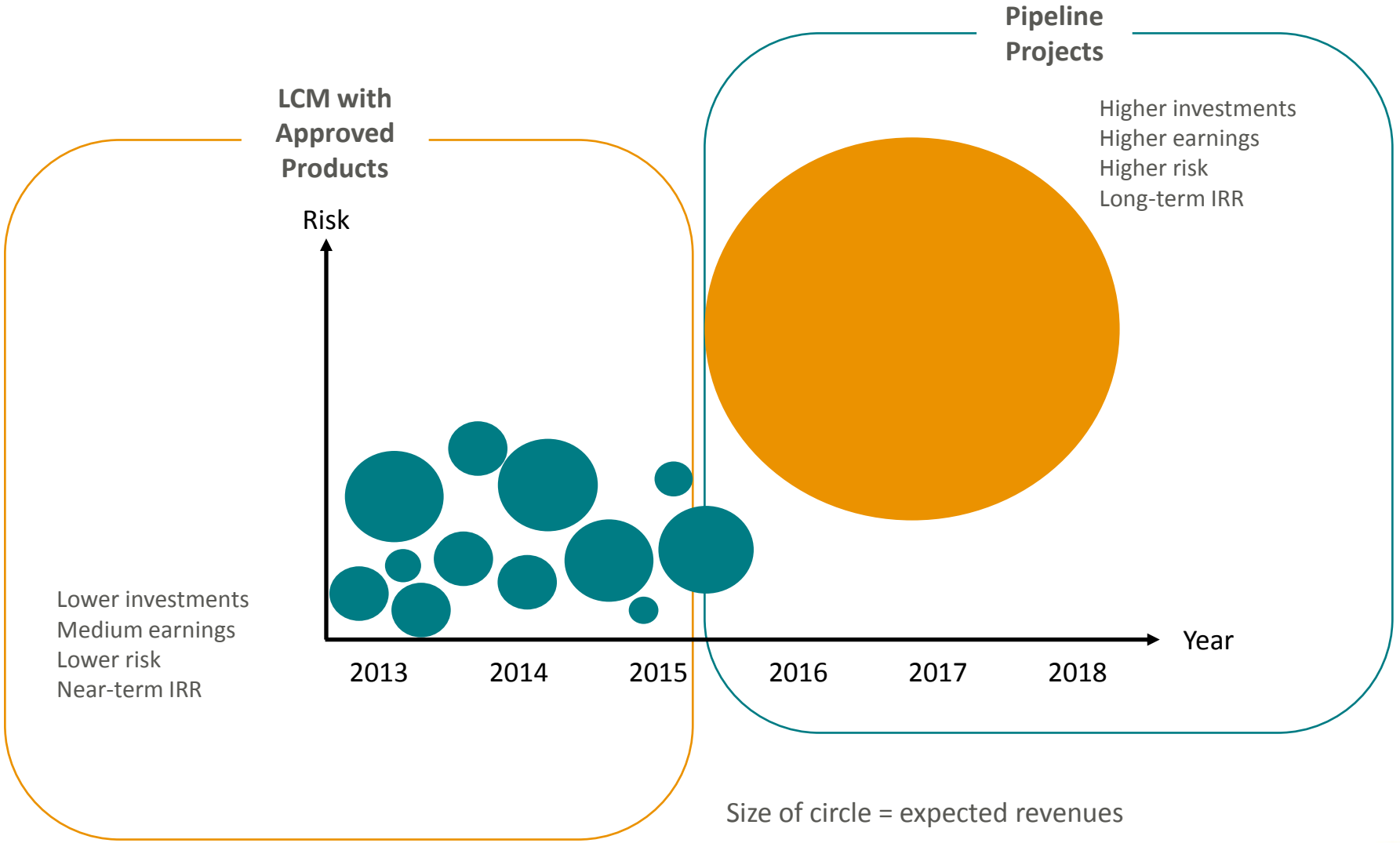
Analytical method development for release, virus validation, drug substance and drug product formulation

Technical transfer for commercial scale production

How Do We Think About Innovation?



Balancing Risk + Allocation of Capital



R&D Pipeline 2013

Indication	Project	Partner	Pre-Clin.	Phase I	Phase II	Phase III	Launch
CAPS	Kineret	sobi					
Hemophilia A	rFVIIIFc	biogen idec					
Hemophilia B	rFIXFc	biogen idec					
Improve growth in preterm infants	Kiobrina	sobi					
Oral Mucositis in Head & Neck Cancer	Kepivance	sobi					
Hereditary Tyrosinemia Type 1	Orfadin Liquid	sobi					
Hereditary Tyrosinemia type 1	Orfadin 20mg capsule	sobi					
Alkaptonuria	Orfadin	AKU alkaptonuria society					
Complement –mediated disease	SOBI002	AFFIBODY					
ERT	SOBI003	sobi					
IL-1-driven disease	IL-1 Affibody	AFFIBODY					

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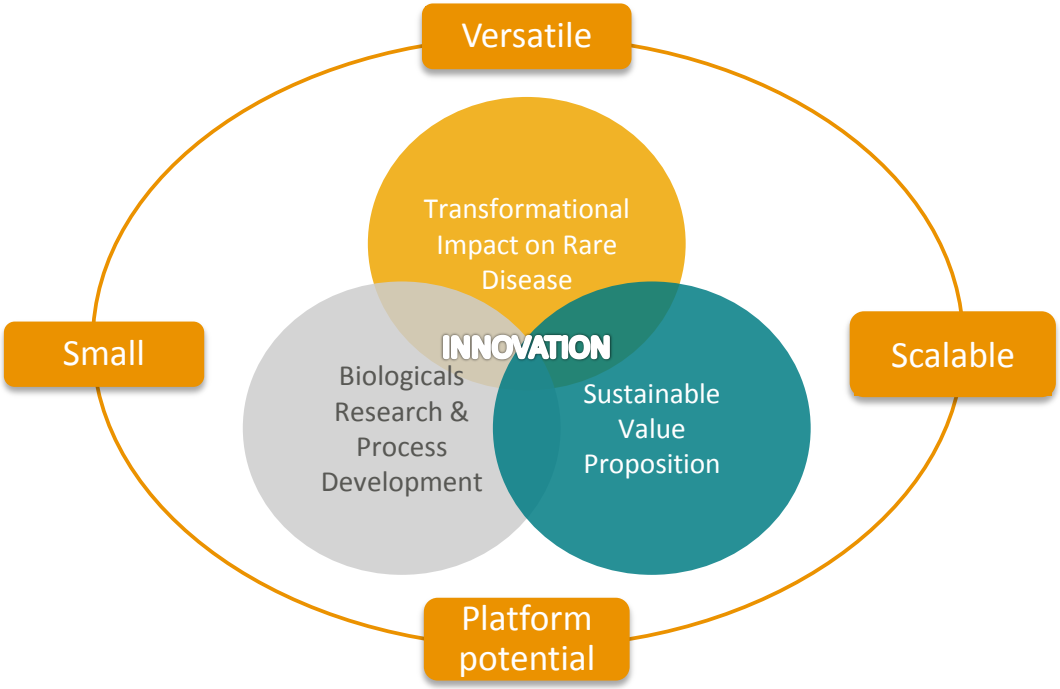
Affibody Platform for c5 Inhibition

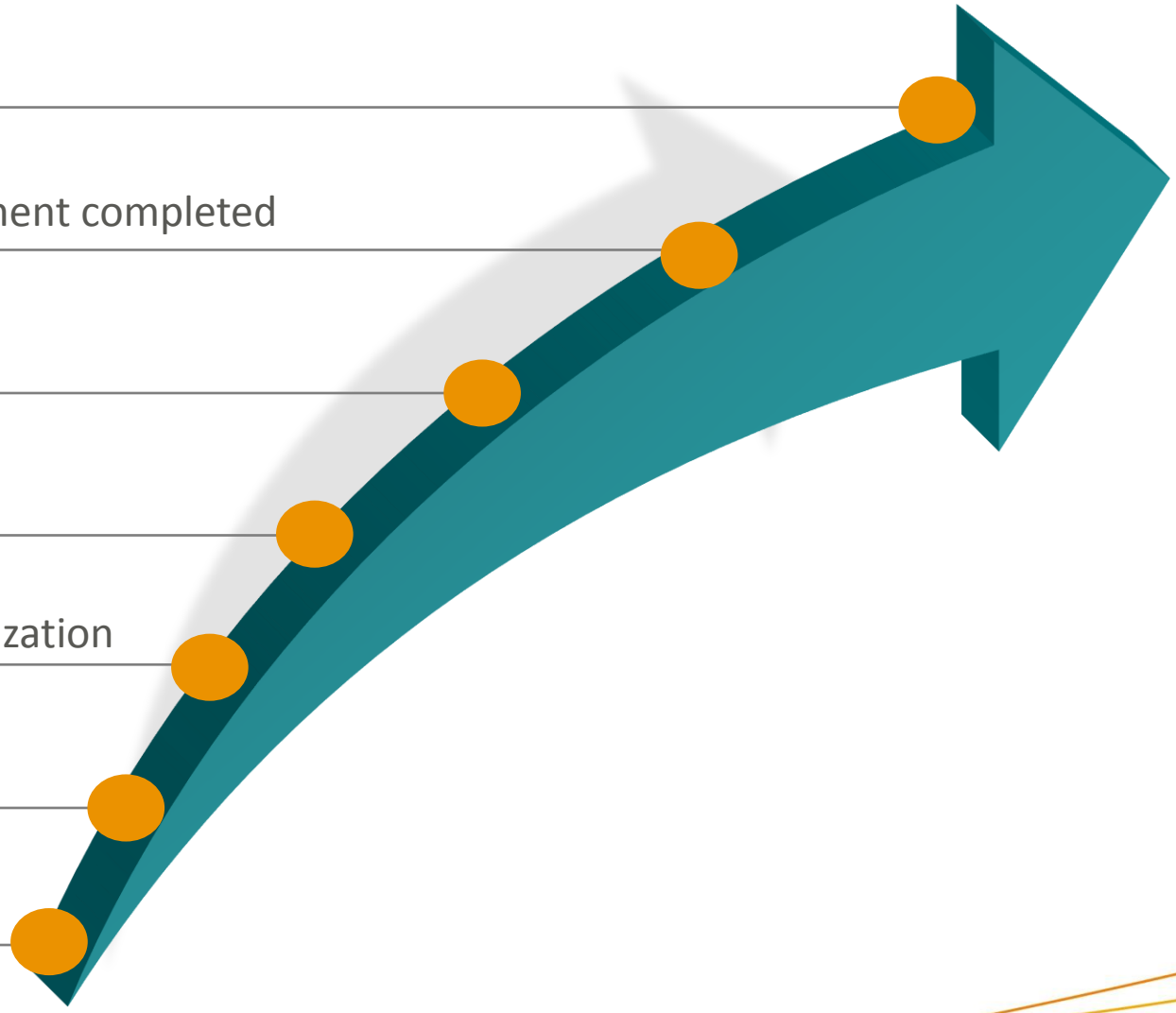
Affibody

- **Biotech company** focused on developing biopharmaceuticals based on **Affibody®** molecules and **Albumod™**
- **Commercial relationships** with a numerous companies
- Founded in **1998** in Stockholm, Sweden.



Generation of Affibody C5 Inhibitors

- 2014: Phase I
- 2013: Pre-clinical development completed
- 2011: Lead optimization
- 2010: Affinity maturation
- 2010: Functional characterization
- 2009: Affibody screening
- 2009: Affibody selection



Introducing SOBI002 – A Novel Biologic inhibitor of C5

Patrik Strömberg Ph.D.
Principal Scientist, Nonclinical Safety and Pharmacology

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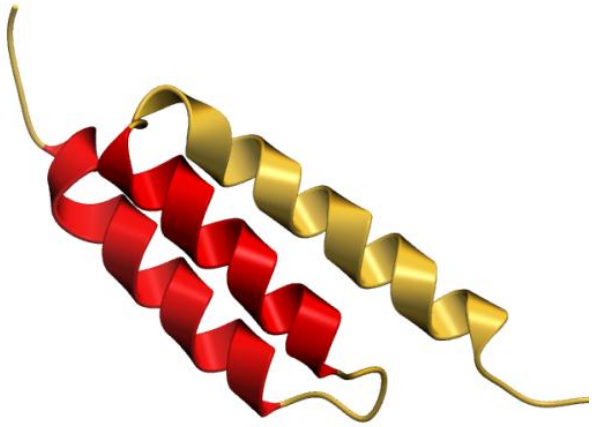
Pioneer in Rare Diseases

Patrik Strömberg, Ph.D.

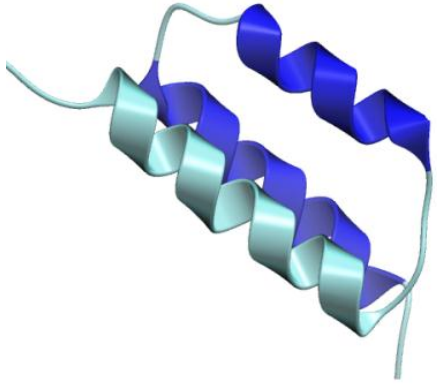
- 2011- Principal Scientist, Nonclinical Safety and Pharmacology, **Sobi**
- 2009 Project Leader R&D, **Biovitrum** and **Sobi**
- 2007-2009 Senior Scientist, Preclinical Development, **Biovitrum**
- 2002-2007 Senior Scientist, **AstraZeneca Biotech Laboratory**
- 1995- 2002 **MSc** Biomedicine, **PhD** Medical Biochemistry, Karolinska Institutet

The Affibody Technology Platform Consists of Two Innovative Protein Domains

The Affibody Ligand

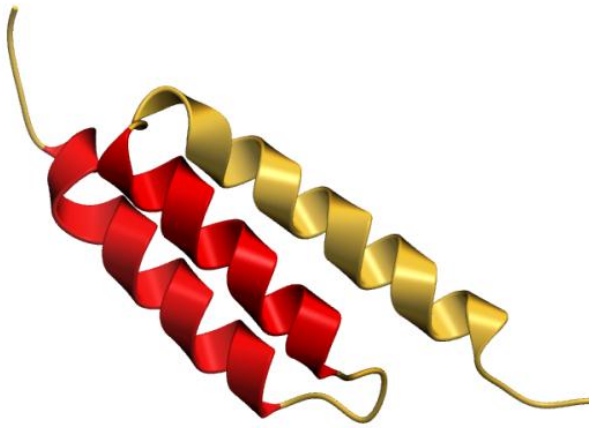


The Albumin Binding Domain (ABD)



The Affibody Technology Platform Consists of Two Innovative Protein Domains

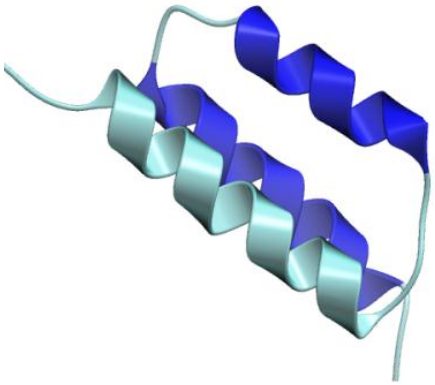
The Affibody Ligand

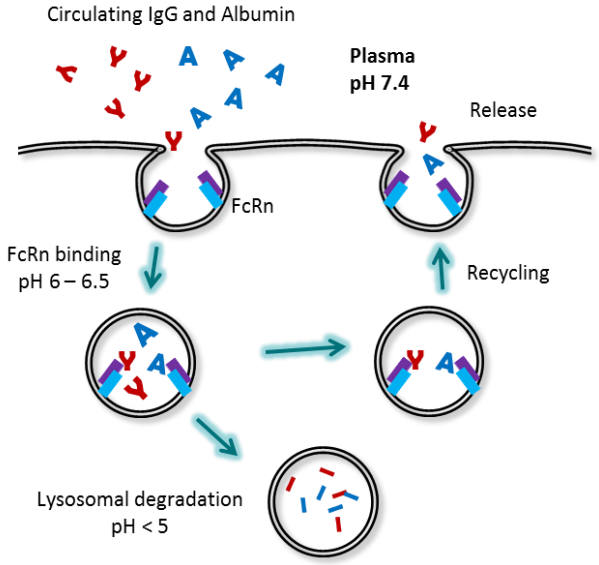


- Small and robust non-Ig scaffold for protein targeting
- Specific targeting by randomization of surface exposed residues followed by selection by phage display
- Efficiently produced in *E.coli*
- Rapid clearance due to the small size

The Affibody Technology Platform Consists of Two Innovative Protein Domains

The Albumin Binding Domain (ABD)

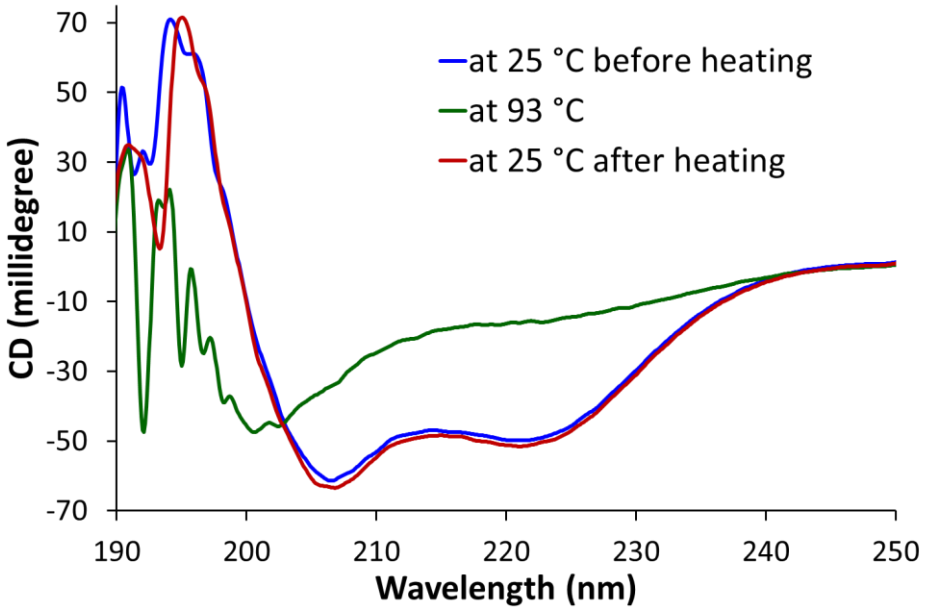




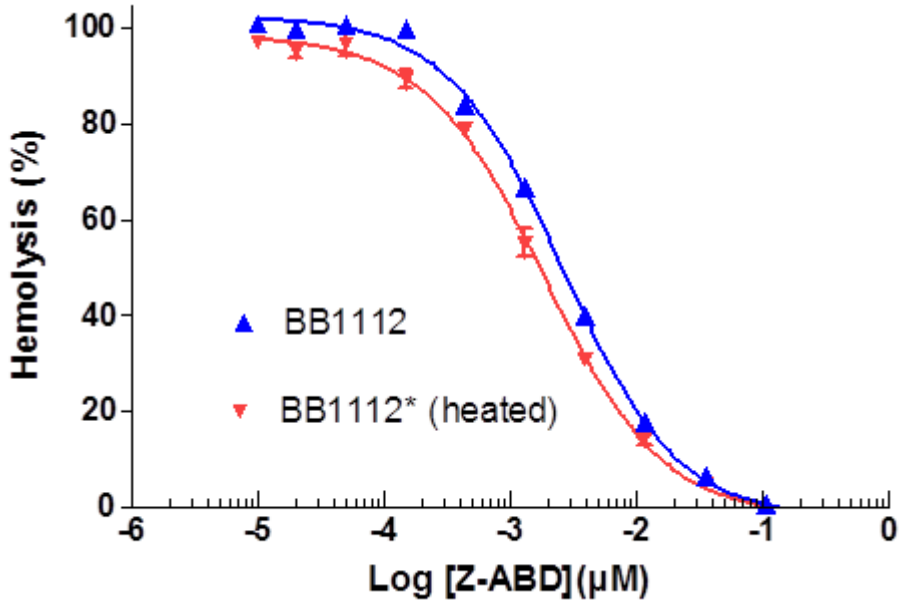
- Small protein that binds to serum albumin from many species
- Engineered for reduced immunogenicity and sub-picomolar affinity
- Similar molecular properties as Affibody ligands
- Extends the plasma half-life for fusion partners by piggybacking on albumin

Affibody Molecules Refold Rapidly after Heat-induced Unfolding

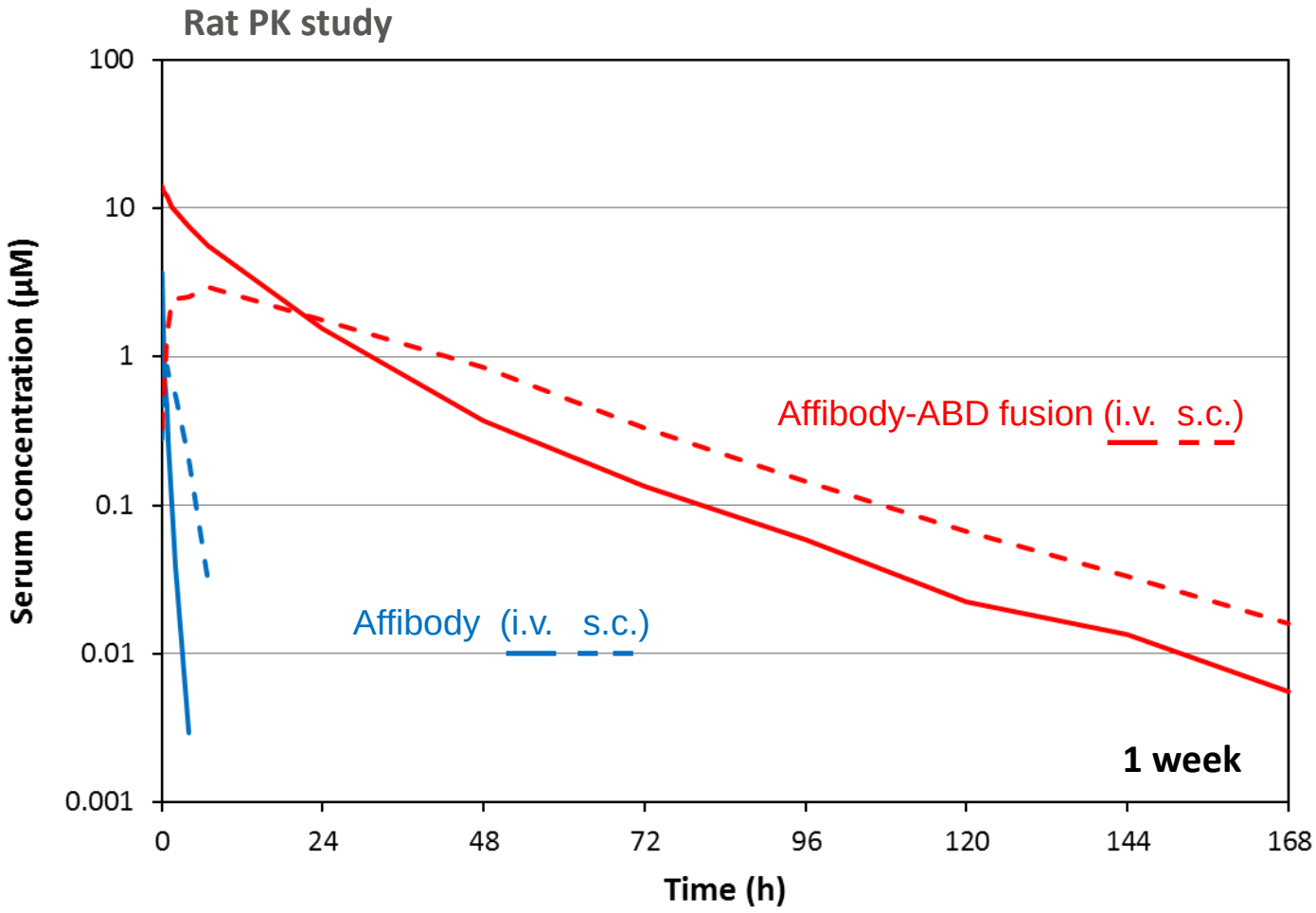
Circular Dichroism Spectra



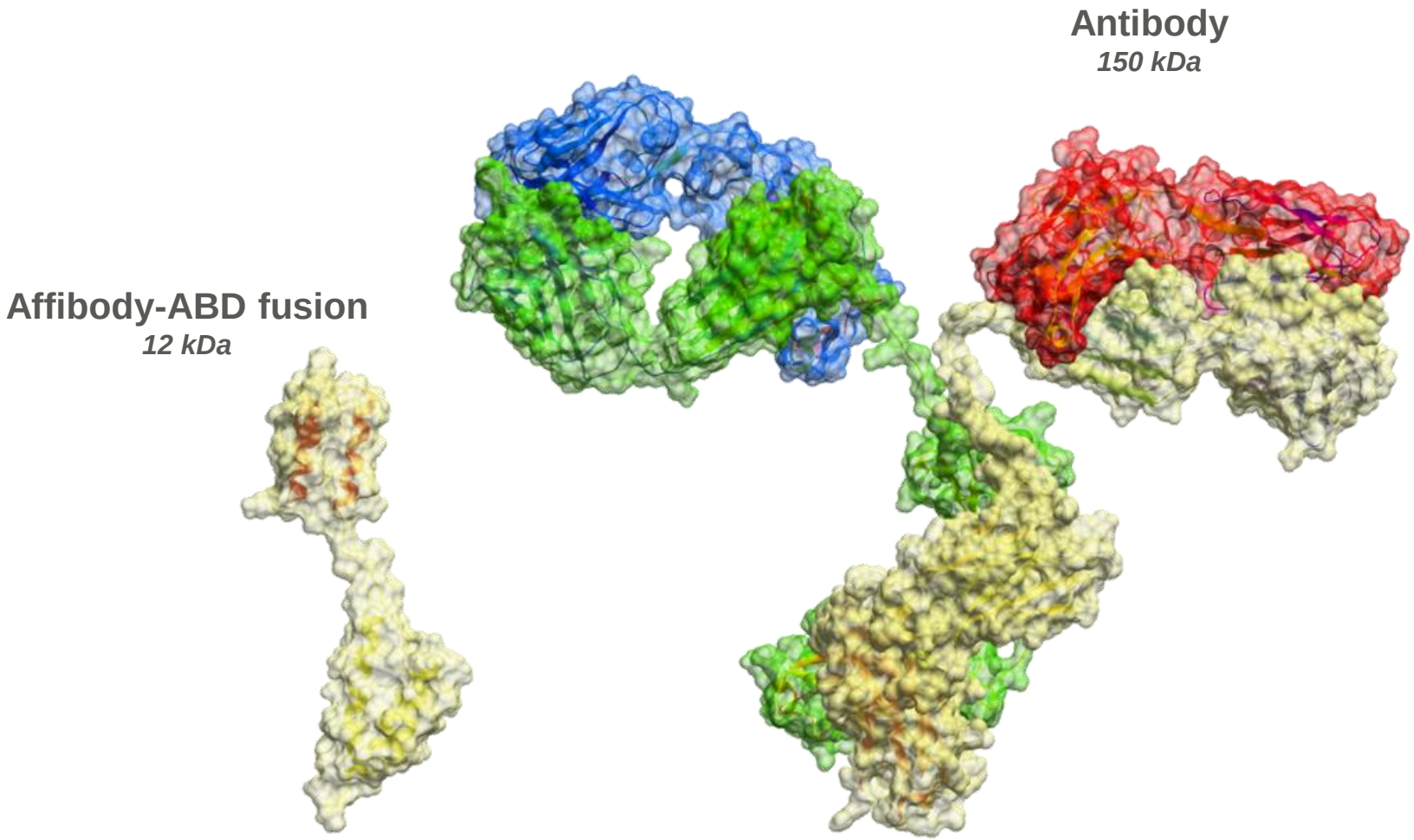
Functional activity



The Albumin Binding Domain Extends *In Vivo* Stability and Plasma Persistence

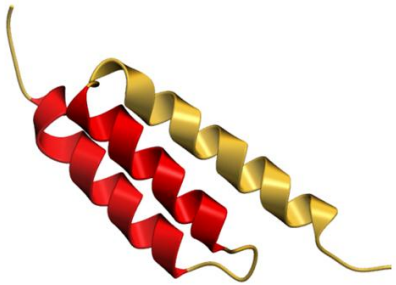


The Size of an Affibody-ABD Fusion Protein Is Less Than 10 per cent of an Antibody

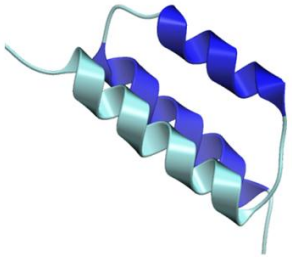


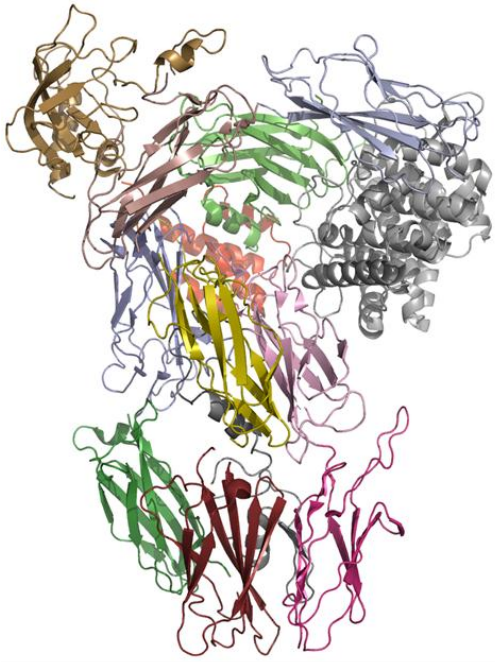
Can We Apply Affibody Technology to Rare Diseases?

The Affibody Ligand



The Albumin Binding Domain (ABD)





Human C5 structure (3CU7)
(Fredslund, *Nature Immunol,* 2008)

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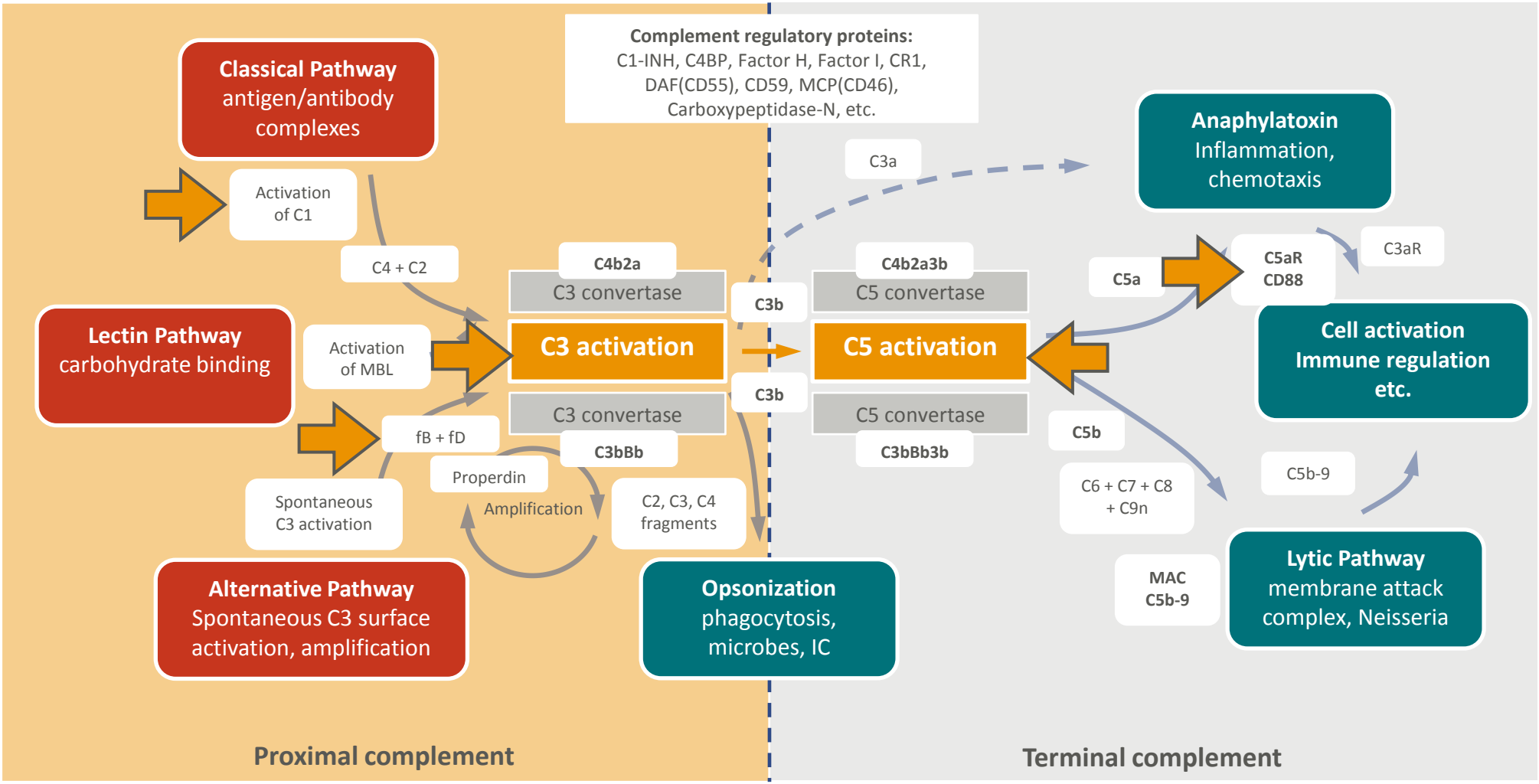
The Complement System



C5 Inhibition - Rationale

- C5 is a highly tractable target:
  - Common to all complement pathways
  - Proximal complement intact
  - Clear disease mechanism and validated therapeutic rationale for PNH and aHUS
- Feasible to neutralize C5 activity with Affibody technology
- Many possible opportunities, both validated and exploratory

Table 2
Diseases for which therapeutic complement inhibitors are approved or which might potentially benefit from complement inhibition.

Hereditary angioedema (HAE)
Paroxysmal nocturnal hemoglobinuria (PNH)
Cold agglutinin disease (CAD)
Hemolytic transfusion reaction after major-incompatible RBC transfusion
(Atypical) hemolytic uremic syndrome
Arthritis
Vasculitis
System lupus erythemaodes
Catastrophic antiphospholipid syndrome
Dermatomyositis
Psoriasis
Crohn's disease
Membranoproliferative glomerulonephritis
Dense deposit disease; C3 nephropathy
Allergic asthma
Age-related macular degeneration (AMD)
Multifocal motor neuropathy
Sepsis, system inflammatory response syndrome
Tissue damage; ischemia/reperfusion injury
Transplant rejection

Schrezenmeier and Höchsmann, *Transf Apheres Sci,* 2011

Generation of Affibody C5 Inhibitors

2011: Lead optimization

PK/PD, process feasibility, preclinical immunogenicity assessment

2010: Affinity maturation

Library design, phage display selection and screening

2010: Functional characterization

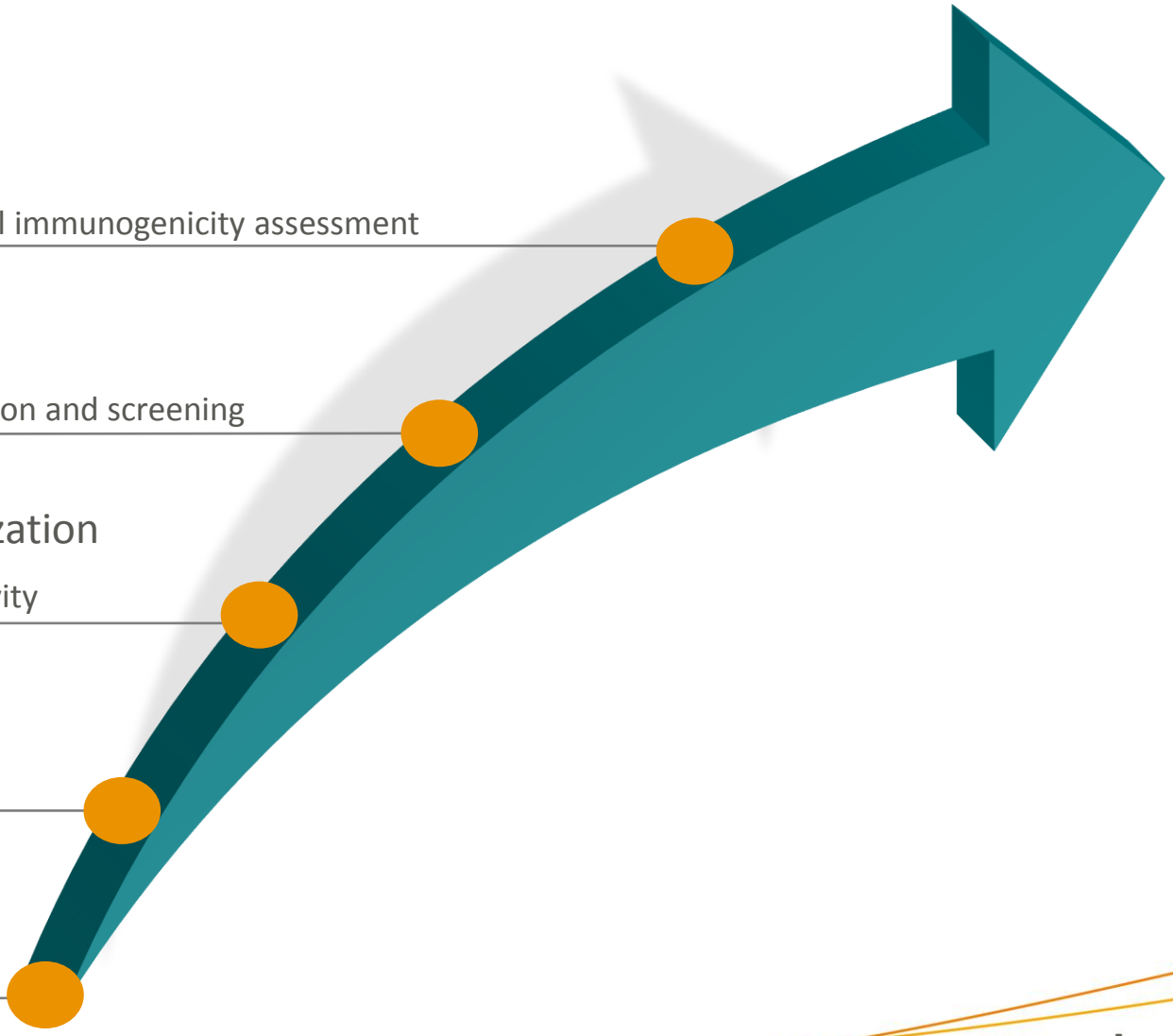
In vitro, *in vivo*, species cross reactivity

2009: Affibody screening

ELISA, functional assays

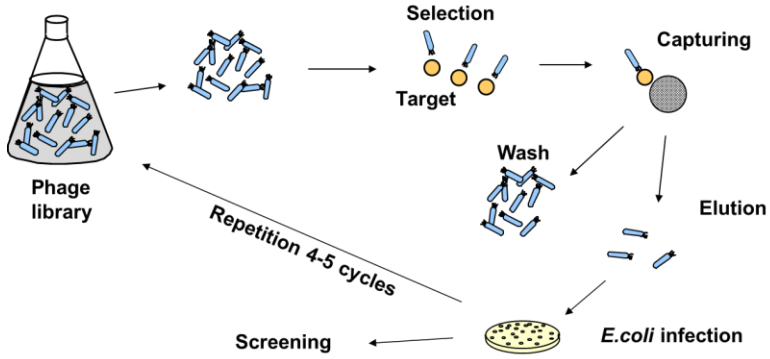
2009: Affibody selection

Phage display

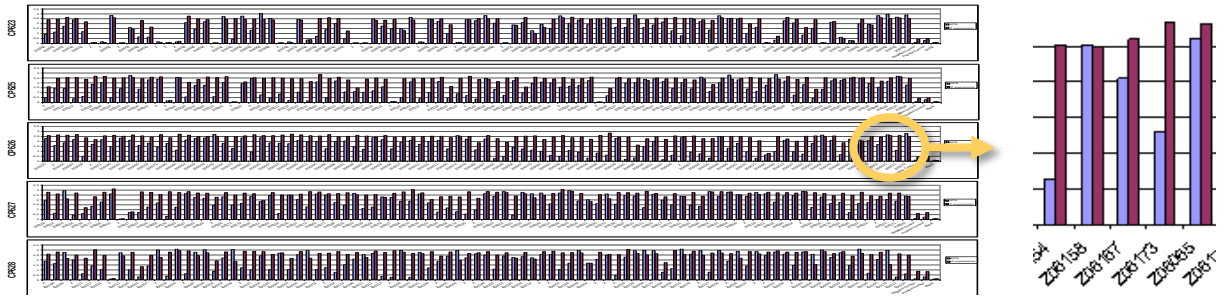


Generation of Affibody C5 Inhibitors

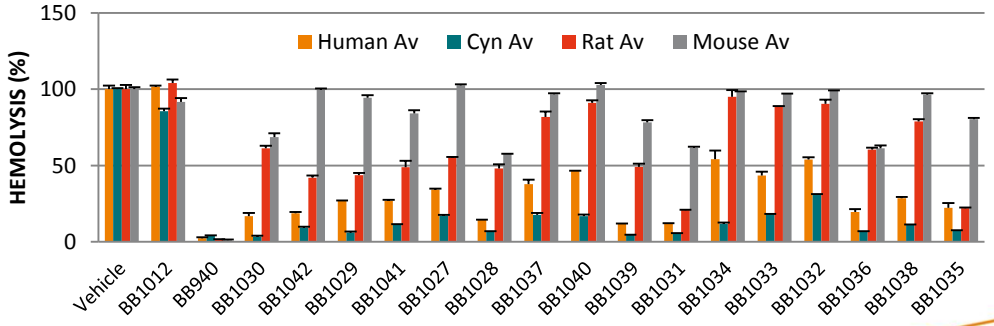
i. Selection by phage display
- Human C5 as target protein



ii. Screening for target binding
- ELISAs, competition assay etc.



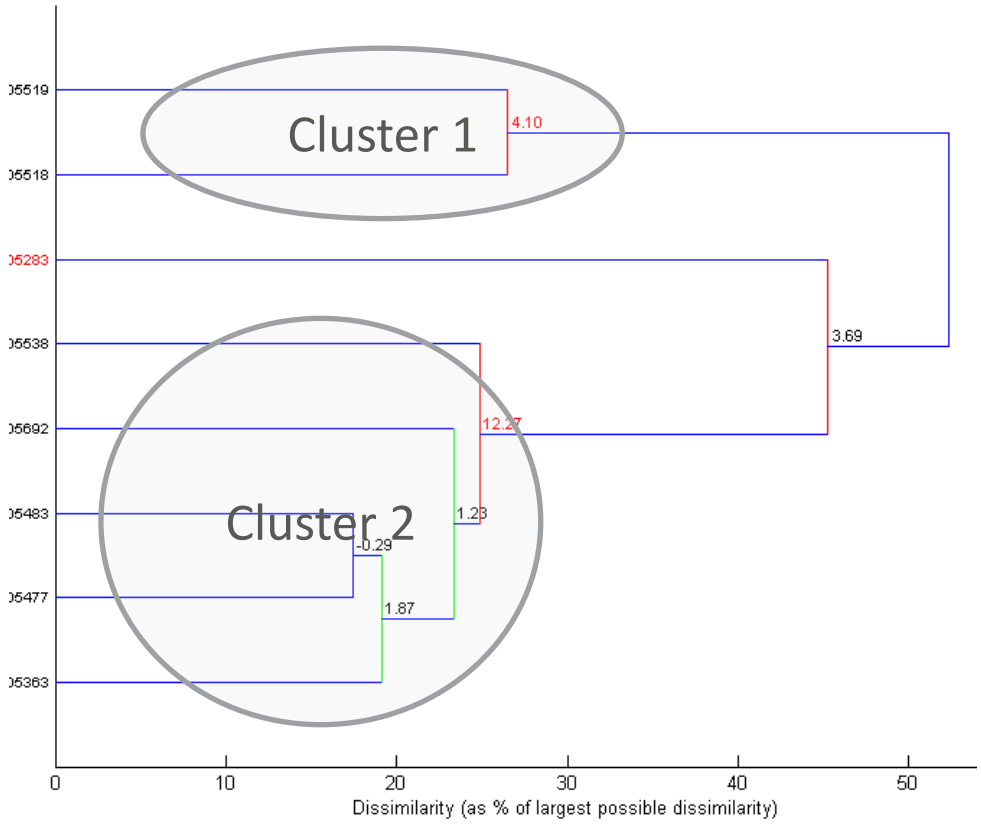
iii. Functional screening
- Hemolysis assays
- Cross-species activity



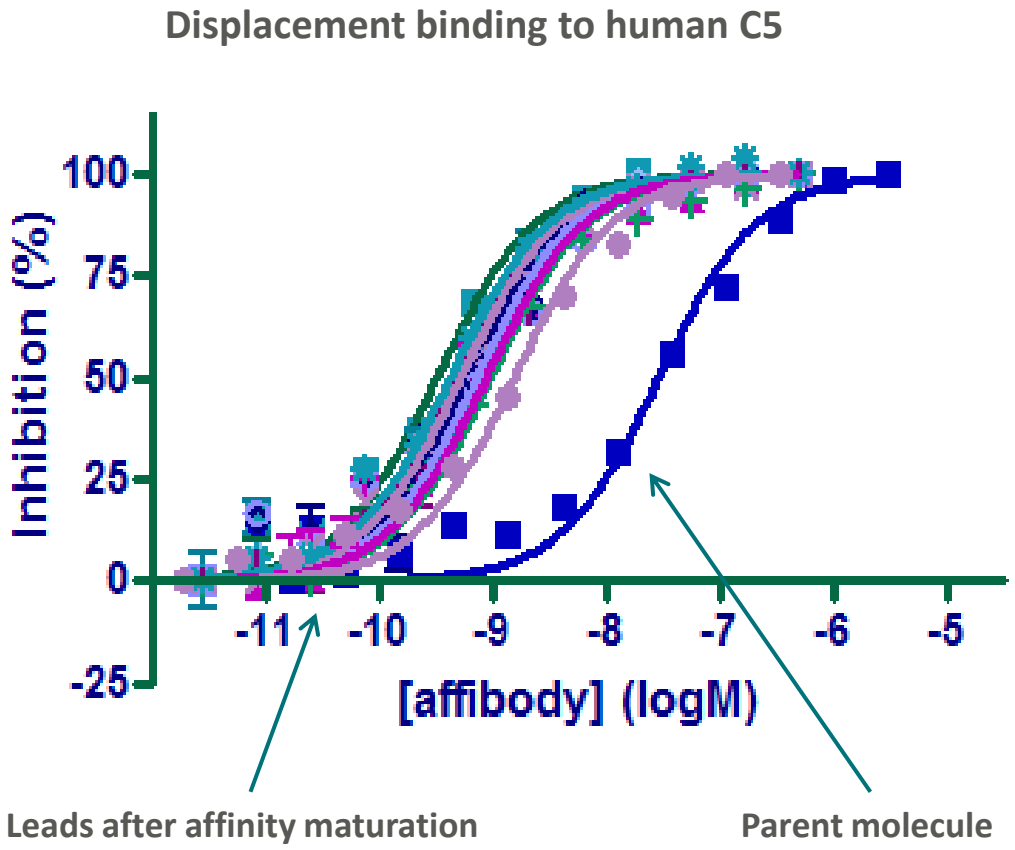
Identifying Clusters of Leads Combining Sequence Information and Screening Assay Data

Functional activity (hemolysis)

Affibody ligand	Human	Cyno	Mouse	Rat
Z05519	+	++	-	(+)
Z05518	+	+	-	-
Z05283	+++	-	-	-
Z05538	+	++	++	++
05692	++	+++	-	++
Z05692	++	++	(+)	(+)
Z05477	++++	++++	++++	++++
Z05363	(+)	(+)	-	(+)

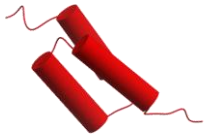


Affinity Maturation Increased Affinity 100-fold

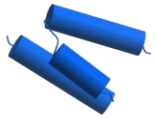


Lead Optimization - Designing the Fusion Protein

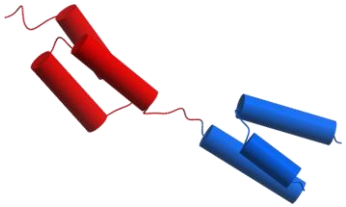
- Order of domains
- Multiple C5-binding domains
- Different linkers
- Without ABD



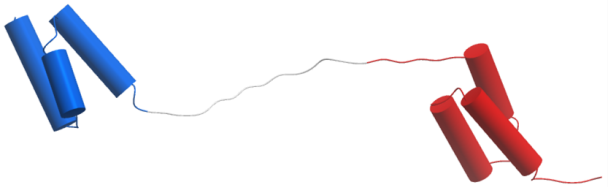
Anti C5
Affibody ligand



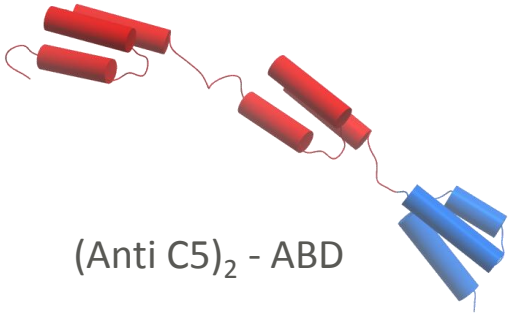
Albumin binding
domain (ABD)



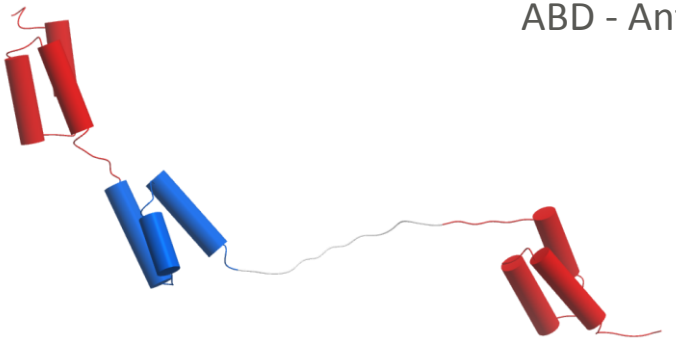
Anti C5 - ABD



ABD - Anti C5



$(Anti\ C5)_2$ - ABD



Anti C5 - ABD - Anti C5

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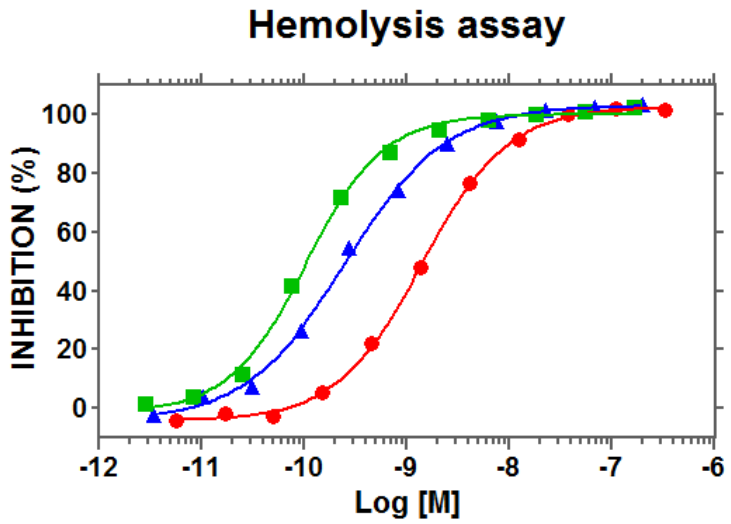
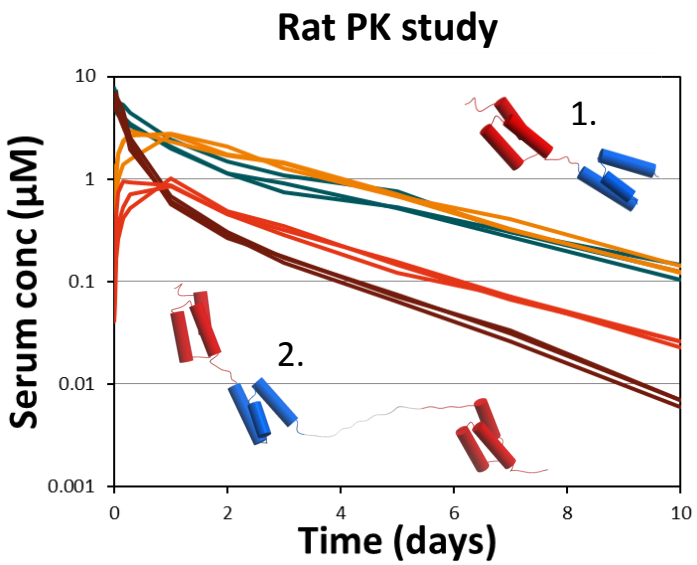
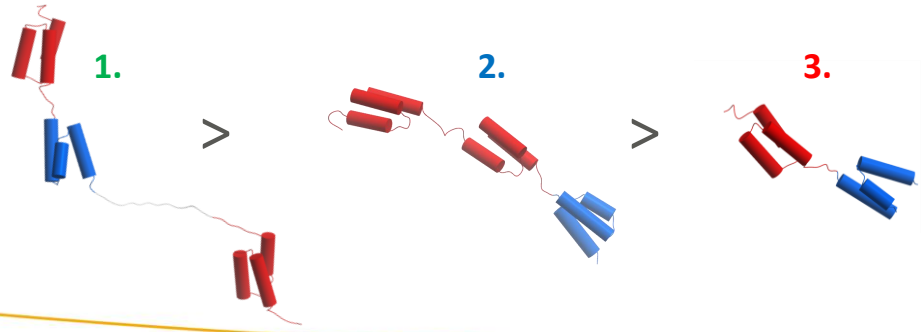
Lead Optimization - Selecting the Best Design

i. *In vitro* activity
- Hemolysis assays

ii. Pharmacokinetics in rodents
- i.v. and s.c.



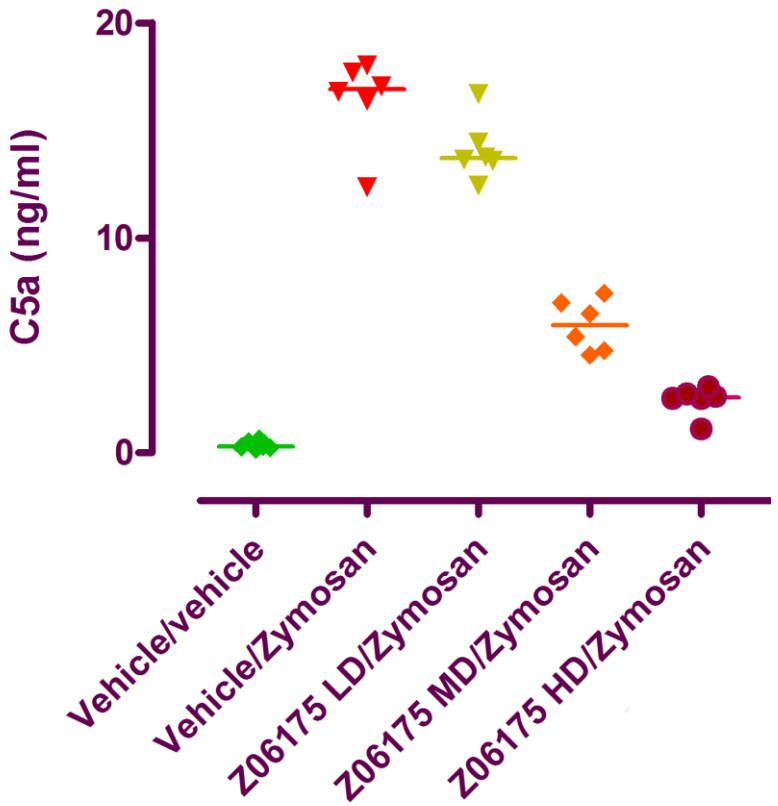


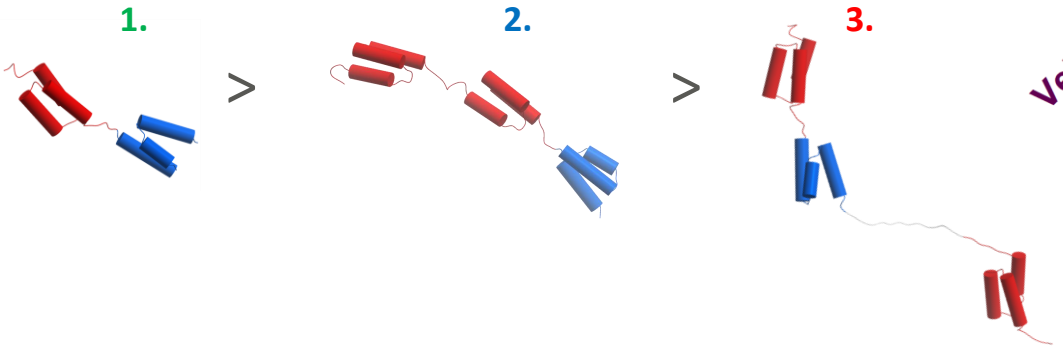


Lead Optimization - Selecting the Best Design

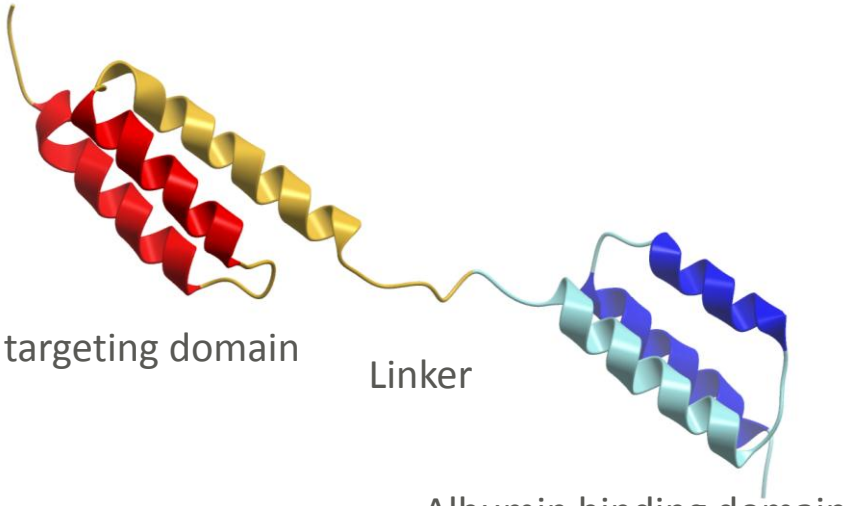
iii. *In vivo* activity

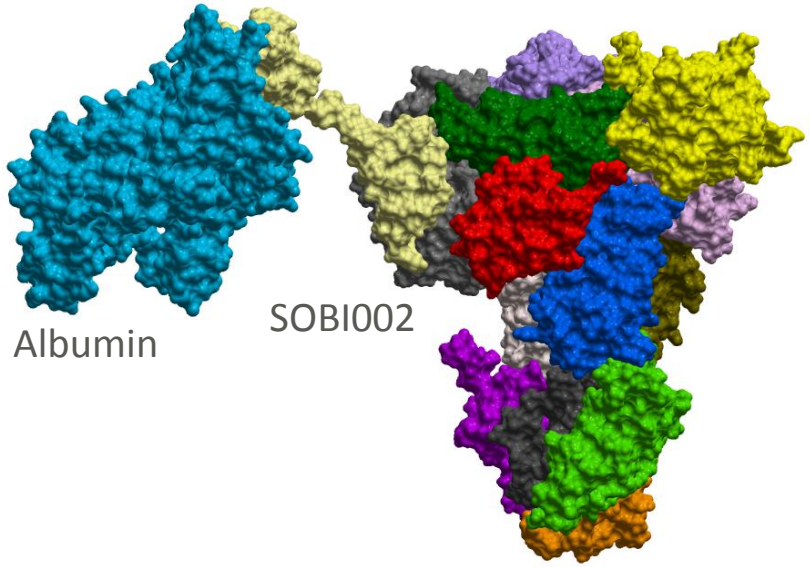
- Acute mouse inflammation model
- Zymosan induced peritonitis
- C5a in peritoneal lavage



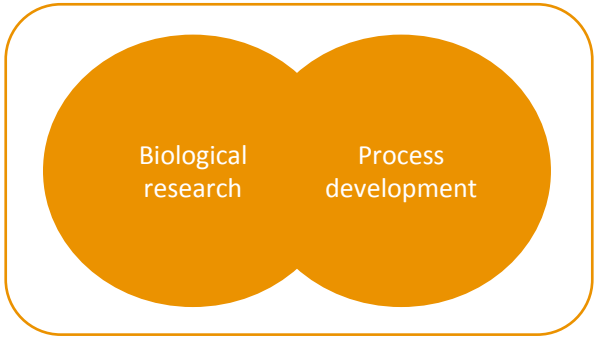


SOBI002 - A Small Designed Fusion Protein





Preclinical Development of SOBI002



CMC process development	Toxicity studies	Pharmacology	Plan for FiH study
• Upstream • Downstream • Formulation • Characterization	• Dose-range finding study in monkey • GLP study monkey • GLP study rat	• *In vitro* pharmacology • *In vivo* pharmacology • Pharmacokinetics	• Scientific advice • Advisory board • FiH protocol

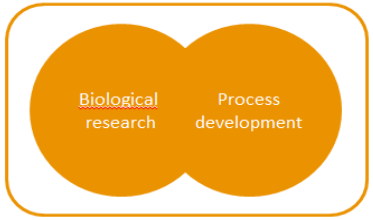
Plan for First-in-Human (FiH) Study

First-in-Human Study with seamless SAD and MAD design

Main objectives: To assess safety, tolerability, pharmacokinetics and pharmacodynamics of SOBI002 in healthy volunteers after s.c. and i.v. administration

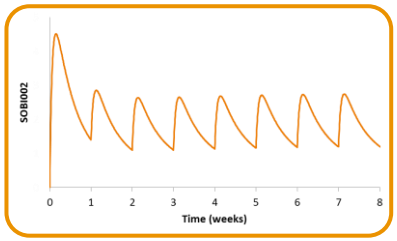
Design: Double-blind, placebo-controlled, randomized within dose cohort, sequential dose-escalation study

Conclusions



Early R&D portfolio

- First example of a candidate drug from a platform collaboration
- Validates the Sobi drug design & development model with partnered discovery research and Sobi biologics development



SOBI002 preclinical profile:

- Potent and well tolerated in animals
- Predicted PK to support weekly subcutaneous dosing in humans

If FiH is successful:

- Validation of the therapeutic potential of the Affibody platform
- Durable C5 suppression opens up many promising therapeutic utilities

End

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Pioneer in Rare Diseases