

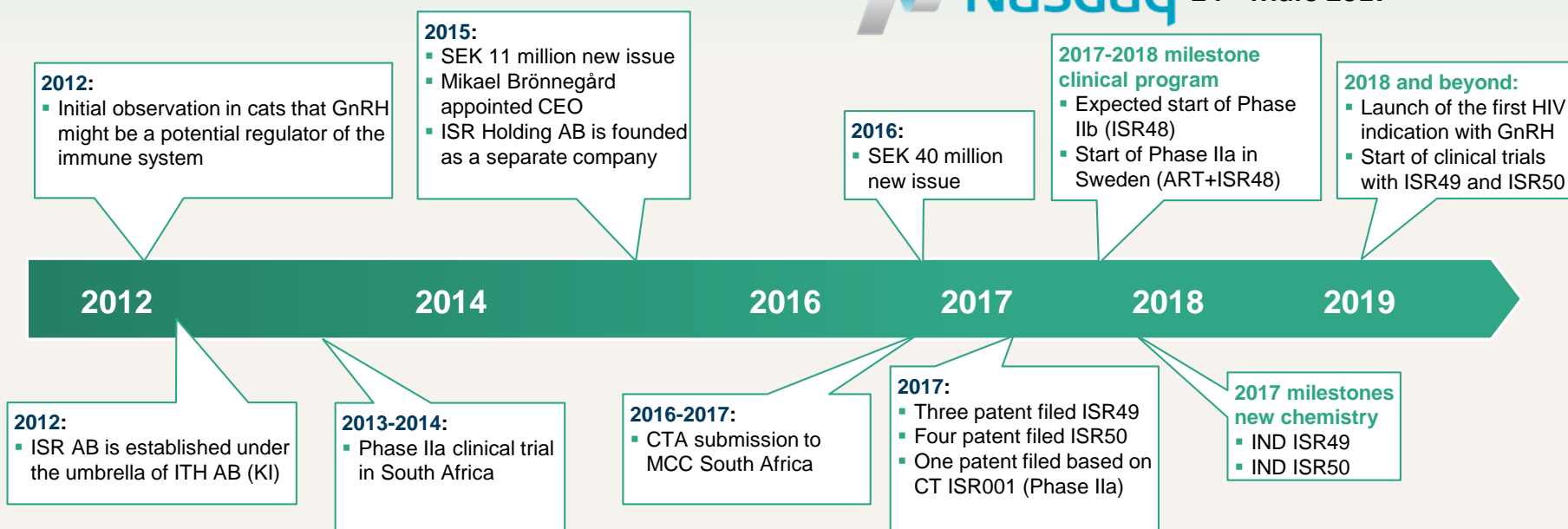
# Immune System Regulation Holding AB

[www.israb.se](http://www.israb.se)



# ISR Holding AB – At a Glance

- Headquartered in Stockholm, Sweden
- Listed on Nasdaq First North in Stockholm
- R&D facilities at Karolinska Institute, Solna, Sweden
- A broad product portfolio and a strong patent base
- PoC Phase II data and several lead drug candidates in preclinical phase
- Strong R&D engine and partnership in UK



Capital raised until Q4 2016, 51 MSEK - High level of cost effectiveness

# Clinical challenges in patients with life-threatening virus infections



# The Immune System – Target for Drug Development



THINGS YOU DO THAT HARM YOUR  
**IMMUNE SYSTEM**

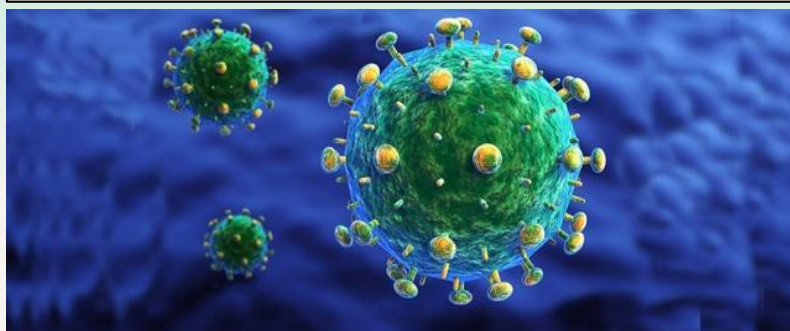
Top 10  
Home Remedies

				
BINGE DRINKING	SMOKING & EXPOSURE TO SECONDHAND SMOKE	SCRIMPING ON SLEEP	PHYSICAL INACTIVITY	CARRYING NEGATIVE EMOTIONS
				
AVOIDING SUNLIGHT	IGNORING PERSONAL HYGIENE	USING TOXIC MAKEUP & HYGIENE PRODUCTS	NEGLECTING THE IMPORTANCE OF WATER	MISUSE OF ANTIBIOTICS

To explore more, visit [www.Top10HomeRemedies.com](http://www.Top10HomeRemedies.com)

# A new era in medicine - *Immunotherapy*

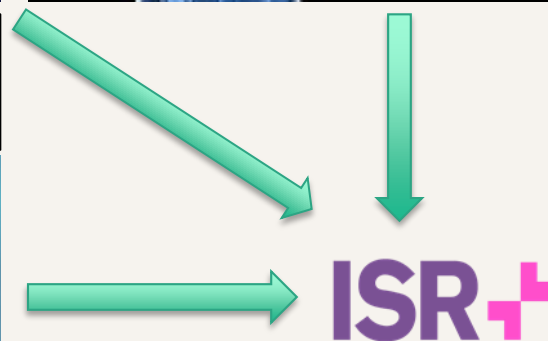
Immunotherapy and viral disease  
New and more aggressive viruses



Immunotherapy and cancer  
Growing elderly population



Immunotherapy and bacterial disease  
Resistance to antibiotics

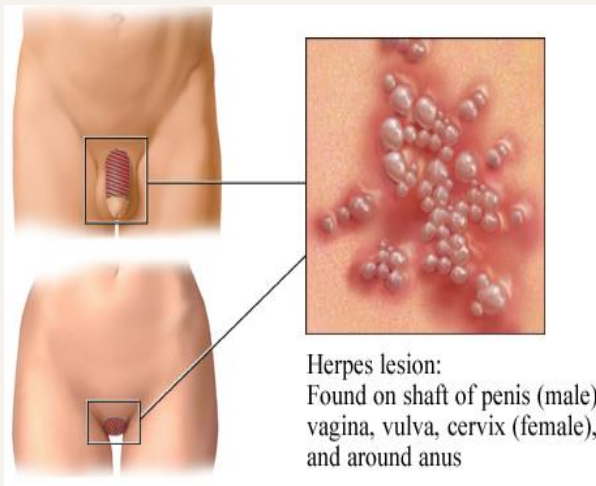


**ISR+**  
Offers solutions to life threatening diseases



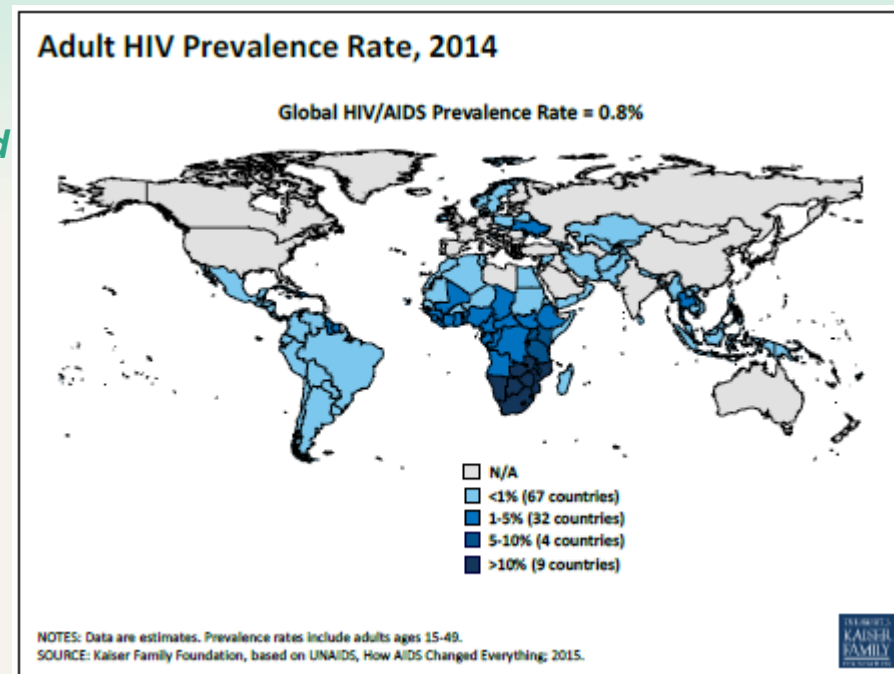


## Primary Diseases for ISR's Products



# Market Review and Competitive Analysis

- *HIV continues to be a major global public health issue with a significant burden of disease*
- *There is no cure for HIV infection*
- *New and more effective therapies are still needed*
- *No alternative treatment to ART in cases of ART resistance and ART intolerance – 10-20% = Business opportunity \$200-300 MUSD*
- *No current competition in terms of new drugs*
- *Several of the HIV leaders will begin losing market protection in 2017*
- *In 2016, four of the top 10 selling branded HIV drugs will still expand sales*
- *New international guidelines – early treatment*



# Immune System Regulation Holding AB

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## Business Model

### Reposition of Old Drugs for New Indications

- Cost- and Time Effective Route to Market
- Out-licensing of indications beyond HIV and virus infections

## Scientific Model

### To Increase Cure Rates Through Stimulation of the Immune System

- Elimination of Virus Infected Cells - Eradication





# Old Drugs Are New Again

## Business Opportunity – Life Cycle Management

### Drug repositioning vs typical drug development

	Typical drug development	Drug repositioning
Avarage cost to bring new drugs to market	USD 1.24 billion	Significantly lower costs 5 – 10 MUSD
Time required	10 – 17 years	3 – 12 years
Failure rates in later stages	High	Low
Increasing focus on	Drugs to treat chronic and complex diseases	Drugs for rapidly emerging and re-emerging infectious diseases
	Key messages;	Key messages;
	<ul style="list-style-type: none"> <li>▪ Expensive</li> <li>▪ Time consuming</li> <li>▪ Risky</li> </ul>	<ul style="list-style-type: none"> <li>▪ To accelerate drug development</li> <li>▪ Reduced risk of failure</li> <li>▪ Lower costs</li> </ul>

## Old Drugs Are New Again

### Business Opportunity – Life Cycle Management

# Repositioning of GnRH – ISR's first drug ISR48

Drug repositioning:

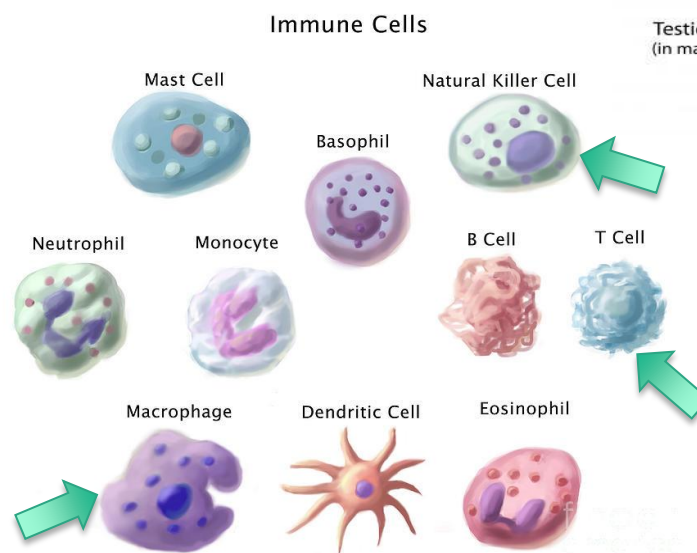
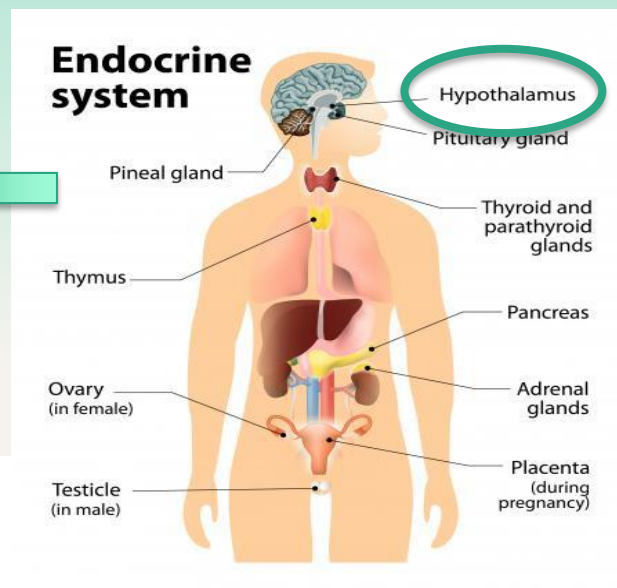
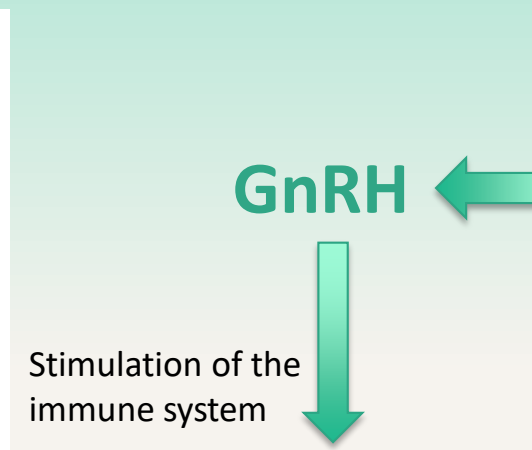
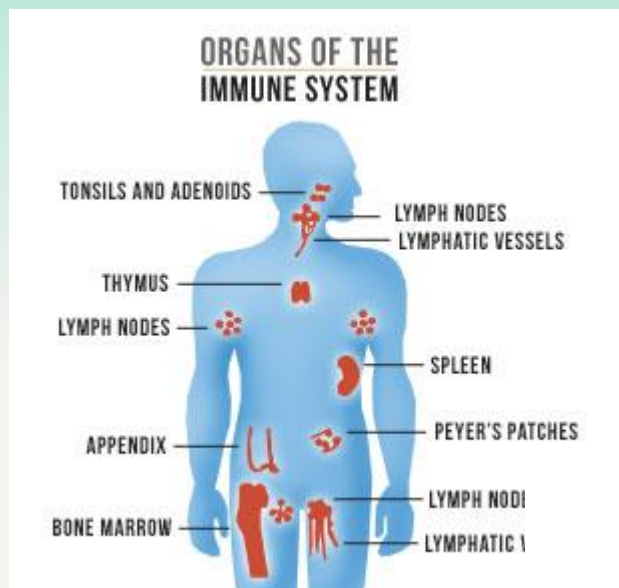
Re-investigating existing drugs for new therapeutic indications

GnRH i.e. Decapeptyl Depot®;

- Approved indications are prostate cancer, endometriosis, pubertas preacox in children
- New indications; HIV, viral infections, cancer



# Communication between The Immune and Endocrine Systems



## Approved indications for GnRH agonist treatment;

- Prostate cancer
- Endometriosis
- Pubertas precoc

# ISR's Lead Product a GnRH-agonist

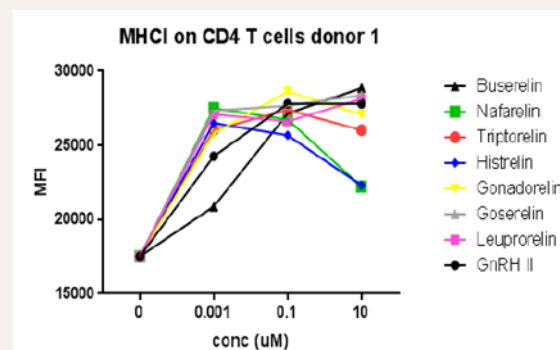
## GnRH agonists as antiviral therapeutics



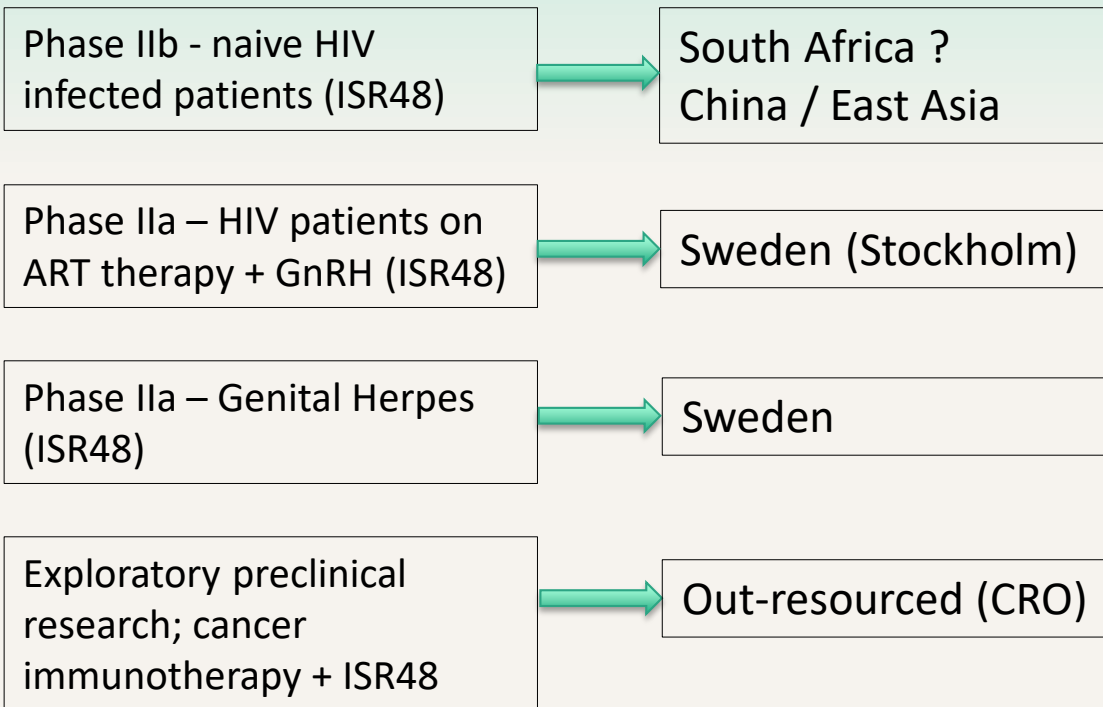
Feline Immunodeficiency  
Virus = Cat AIDS

### In vitro/ex vivo preclinical data

- T cells express GnRH receptors (subtype?)
- GnRH activates T-cells
- GnRH upregulates class I (CD69, CD25, CD27) on human T-cells
- Lymphocytes from HIV patients upregulate class I after GnRH stimulation
- Lymphocytes from healthy donors upregulate class I after GnRH stimulation
- Lymphocytes from monkeys upregulate class I after GnRH stimulation



# Accelerate time to market of ISR48 through a parallel Phase IIa strategy



## Objectives;

- Confirmation of Phase IIa results
- Eradication of HIV virus reservoirs
- Treatments of virus infections beyond HIV
- Effects on the immune system of ISR48 and products in pipeline



# ISR's Clinical Focus

ISR is in the forefront of immunotherapy and virus infections by having taken GnRH as an immune regulatory drug through Phase IIa

## Clinical problems

- ART medication in HIV patients does not eliminate the HIV virus from cellular reservoirs
- There are no alternative drugs in patients with ART resistance or ART intolerance



## Clinical solutions

- Drugs that regulate the immune system in such a way that the HIV virus is recognized and eliminated from cellular reservoirs - eradication drugs
- A product portfolio with specific efficacy and low risk of adverse events
- ISR's focus is on products with known mechanisms of action for severe virus diseases



## Focusing on four segments

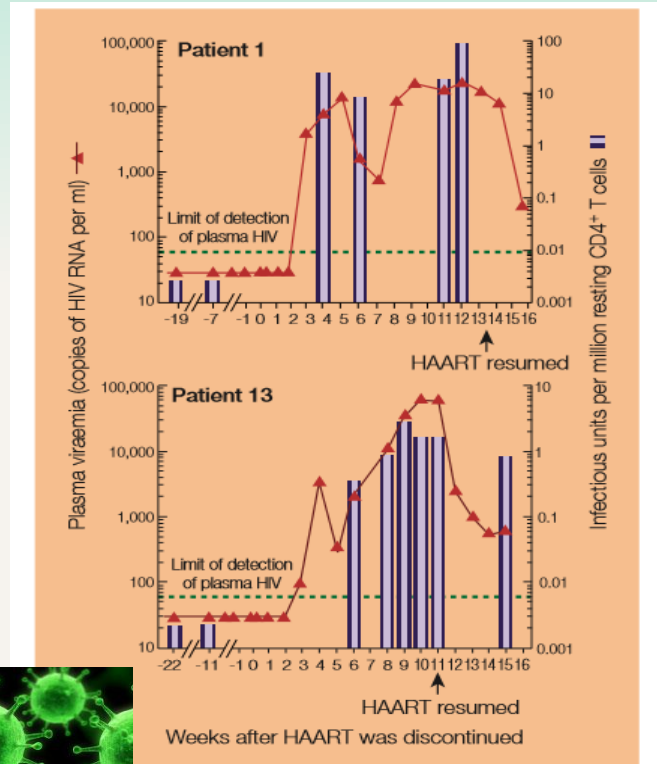
- Naive HIV infection
- ART resistance and ART intolerance in HIV patients
- ART + GnRH agonist to empty HIV reservoirs
- Genital Herpes infection

# The problem with ART treatment and ISR's solution

The ART medication target the virus and its replication machinery only – No eradication

Clinical problems with stopping ART treatment

- ART medication in HIV patients does not eliminate the HIV virus from cellular reservoirs and when ART treatment stops.....
- .....viral load increases within 1-2 weeks leading to AIDS



Ref; Chun et al  
Nature 1999

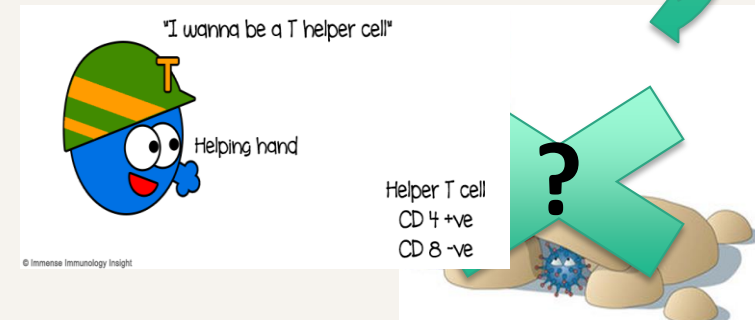
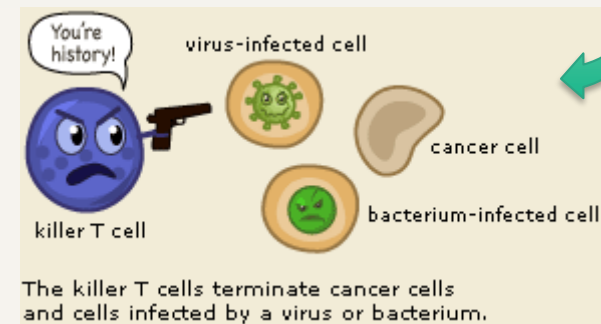
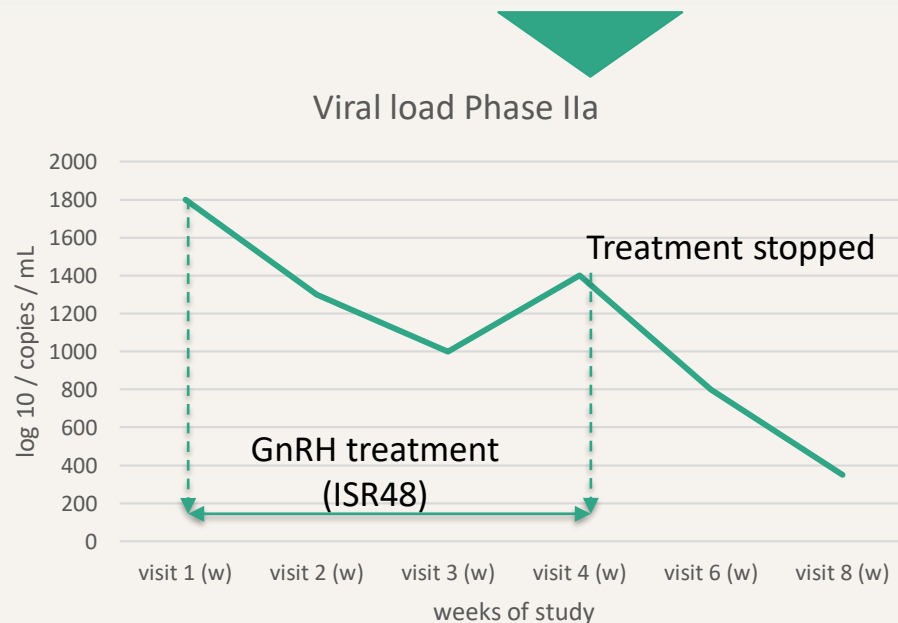
# The problem with ART treatment and ISR's solution

ISR's immunostimulatory medications target the immune system

Eradication strategy

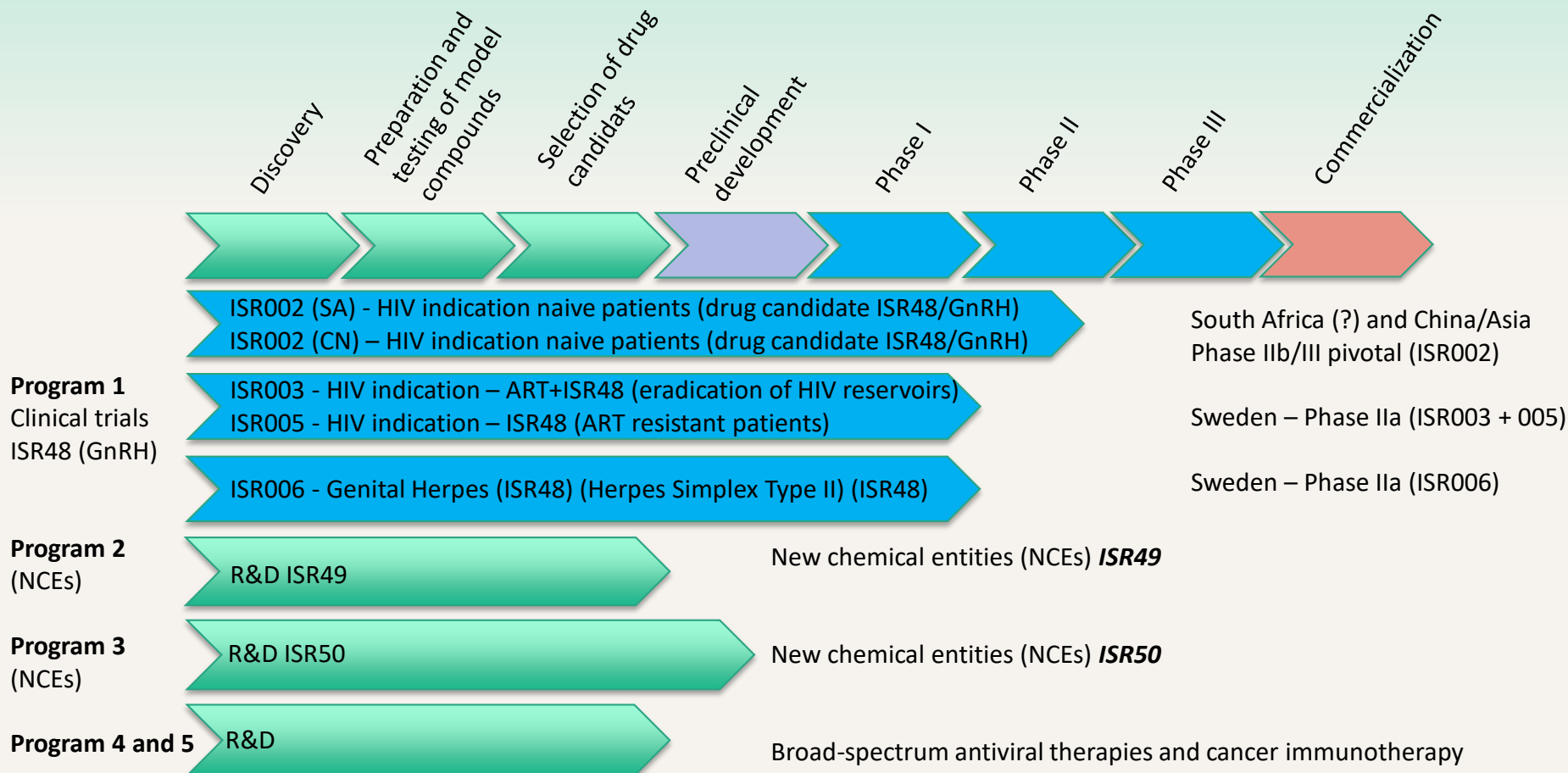
Clinical solution with ISR's first product GnRH (ISR48)

- When GnRH treatment stops.....the immune system is activated.....
- .....viral load stays low and potentially the HIV virus is eliminated



# Product and Program Pipeline – Base Case

- Three independent projects in clinical development phases
- Potential to address a pressing medicinal need in HIV and other virus infections
- No pharmaceuticals registered at present for immune regulation in HIV and virus infections
- Strong project and patent portfolio with ample opportunity for partnerships or out licensing



# Immune System Regulation Holding AB

## Organization and Partners

### Advisory Board

Professor Anders Sönnernborg  
Professor Hans Wigzell



### Partners

Regulatory Affairs



Synthetic Chemistry  
& Drug Development



Intellectual Property



Contract Research Organization  
(Clinical trial program)



R&D facilities and laboratories at Karolinska Institute



# Management



## **CEO Mikeal Brönnegård**

Mikael has an MD., PhD degree from the Karolinska Institute where he still holds a position as Associate Professor. Mikael also has several years of pharmaceutical industry experience at both local market company and corporate level including global business management. He has been working at an executive level in the venture capital industry focusing on start-up and early stage investments and business development within the biotechnology and life sciences sector. Finally, Mikael has a broad experience from operative positions in the biotechnology industry including a CEO position at a Nasdaq listed company Neurovive.



## **CSO Ola Winqvist, M.D, PhD, Professor**

Professor of Cellular Immunotherapy, Head of Translational Immunology, and Senior Consultant in Clinical Immunology at the Karolinska Institutet and Karolinska University Hospital. The Swedish Research Council and the Swedish Cancer Society have continuously supported Ola's research since 1999, and he has received various competitive grants from the European Union and Swedish Governmental Agency for Innovation Systems for the development of immunological therapeutics. Ola has an M.D and Ph.D. from Uppsala University in Sweden, and did his postdoctoral research at the Scripps Research Institute in the United States. In 2013 rewarded with the Athena Prize



## **CCO Lennart Dreyer**

Master of Business Administration from Gothenburg University and Phd. study Gothenburg University. Guest professor of Tsinghua University, Beijing 2003 and honorary Dean of Wuhan International Trade University 2006. President and Dean of IHM Business School 1993-2003. Founder of BRL in 2003 and Co-founder of Foundation Asia Pacific Ltd (FAP). Senior consultant at Deloitte and Bain. Chairman in the business magazine Chef for several years and member of the board at Vigmed AB, NeuroVive Asia Inc and Vigmed China Ltd. Participated in several start-up's, M&A and business deals in Asia.



## **Market Manager Jihua Liu**

Jihua has an M.S. in Chemical Engineering with specialization in Biology. She has worked as scientist in University of North Carolina in USA. She has served several years as management consultant for pharmaceutical industry. In early 2000 she started to work with business development focusing on Life Science companies for Asian market. Jihua is mainly working with funding and investment management of start-up and early stage biotechnology and life sciences companies at Business Research Ltd..



## **CFO Gunnar Modalen**

Gunnar has a B.A. in Finance from Lunds University and appointed Captain in the reserve in the Royal Swedish Marines. He has over twentyfive years international experience from senior positions in listed and unlisted companies active in areas such as the chemicals/manufacturing industry, shipping/offshore industry, electronic/mobile phones, gaming and international banks. Gunnar held senior positions in the Perstorp Group during 1994-2010. Since 2010 Gunnar has been an independent consultant upholding positions such as CFO for Rederi AB Transatlantic (publ) and Doro AB (publ) both listed on Nasdaq Stockholm. Gunnars latest position was Head of Investor Relations & Communication in the gaming company Cherry AB (publ) listed on AktieTorget, Stockholm.

# Board of Directors



## **Chairman of the Board, Anders Milton**

MD, PhD with a background as President and later CEO of the Swedish Medical Association, Chairman of the World Medical Association, President of the Swedish Red Cross, the Swedish Confederation of Professional Associations (SACO), etc. Member of boards of philanthropic foundations and for profit companies mostly in the life science field.



## **Member of the Board, Hans Glise**

M.D, PhD, Professor and expert in pharmaceutical product development and innovation-driven collaborative research. Prior to co-founding ITH, Hans has been Vice President and Senior Vice President at Astra Zeneca, NovoNordisk, and UCB



## **Member of the Board Gustaaf Wolvaardt**

Dr., MBChB (Pret),M.Med (Int) (Pret), FCP (SA),AMP (Manch),PGCHE (Pret) South Africa. Dr Wolvaardt is a medical specialist with post graduate qualifications in management and education. He worked as a clinician and a diplomat before founding the Foundation for Professional Development (FPD) in 1997. FPD is one of the largest health development organizations in Africa.



## **Member of the Board Gunnar Jardelöw**

MBA at Handelshögskolan at the University of Gothenburg 1972. Broad experience in international business, sales, and reconstructions of companies in distress, Sales and purchase of ships, establishing, organizing and developing international business in different areas, such as ME, Mediterranean area, former eastern European countries. Focus on growing companies from local to international business.



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