



# Medivir

*A collaborative and agile pharmaceutical company with an R&D focus on infectious diseases and a leading position in hepatitis C*

**EASL Medivir presentation 27 April**

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**Bertil Samuelsson CSA**

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# Value proposition – a platform for growth and profitability

## Innovative portfolio that will evolve over time

- World class expertise in polymerase and protease drug targets
- R&D focus on infectious diseases

## Strong position in HCV – goal is take part in eradicating hepatitis C

- Simeprevir, partnered with Janssen Pharmaceuticals
  - Regulatory files have been submitted in EU, US and Japan
  - Many interferon-free combination treatments opportunities
- In-house HCV programs will offer new combination opportunities

## Commercial presence in the Nordic region creates stability

- Solid brand names with annual sales of ~85 MUSD
- Commercial platform for the launch of simeprevir in the Nordics in 2014
- Pharmaceutical portfolio will be broadened

**BioPhausia**  
– a Medivir sales company

# 2013 - Setting the framework for becoming *The Emerging European Pharma Company*

## Structure

- Broader, risk balanced, R&D pipeline
- Continued commitment towards targets in infectious diseases
- Addressing new therapeutic areas based on core competence

Therapeutic area	Product/Target	Partner	Preclinical phase				Clinical phase				
			Research	Phase I	Phase II	Phase III	Phase I	Phase II	Phase III	Market	
<b>ANTIVIRALS</b>	<b>Leads/Target</b>	Merck/Merck, Novartis, Novartis, Novartis	█	█	█	█	█	█	█	█	█
	<b>Regeneron C</b>	Novartis, Novartis, Novartis, Novartis	█	█	█	█	█	█	█	█	█
	<b>Novartis B</b>	Novartis, Novartis, Novartis, Novartis	█	█	█	█	█	█	█	█	█
	<b>Novartis A</b>	Novartis, Novartis, Novartis, Novartis	█	█	█	█	█	█	█	█	█
<b>OTHER INDICATIONS</b>											
<b>Novartis A</b>	Novartis, Novartis, Novartis, Novartis	Novartis	█	█	█	█	█	█	█	█	█
<b>Novartis B</b>	Novartis, Novartis, Novartis, Novartis	Novartis	█	█	█	█	█	█	█	█	█
<b>Novartis C</b>	Novartis, Novartis, Novartis, Novartis	Novartis	█	█	█	█	█	█	█	█	█
<b>Novartis D</b>	Novartis, Novartis, Novartis, Novartis	Novartis	█	█	█	█	█	█	█	█	█

- Partner of choice for both pharmaceuticals and development programs
- Expansion of product portfolio, including simeprevir and other in-house developed pharmaceuticals



## External perspective

- Top ranked as a listed company
- Profitable and fast growing Nordic based pharmaceutical company

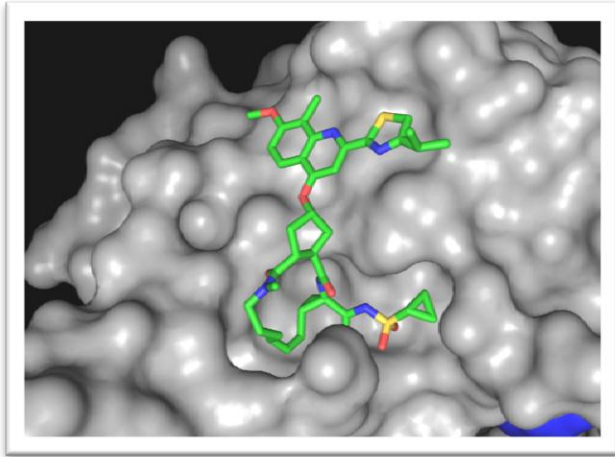




# **Simeprevir – An update**

**Charlotte Edenius**

# Simeprevir



One-pill, once-daily, investigational, oral HCV NS3/4A protease inhibitor

- Antiviral activity against HCV GT 1, 2, 4, 5, and 6
- Safe and well tolerated in clinical trials, with high SVR rates
- Three large pivotal phase III studies of SMV 150 mg QD plus PegIFN/RBV completed (QUEST-1 and QUEST-2 in treatment-naïve and PROMISE in prior relapsers)
- Simeprevir is currently being studied in a number of IFN-free regimens, including the COSMOS study

# Simeprevir - clinical development programs in HCV G1 & 4 infected patients

## Pivotal phase III studies:

- **QUEST 1** treatment-naïve
- **QUEST 2** treatment-naïve
- **PROMISE** prior relapsers
- **Japan** naïve & experienced (four studies)

Regulatory files submitted in US (March-13)  
and in EU (April-13)

Regulatory file submitted February 2013

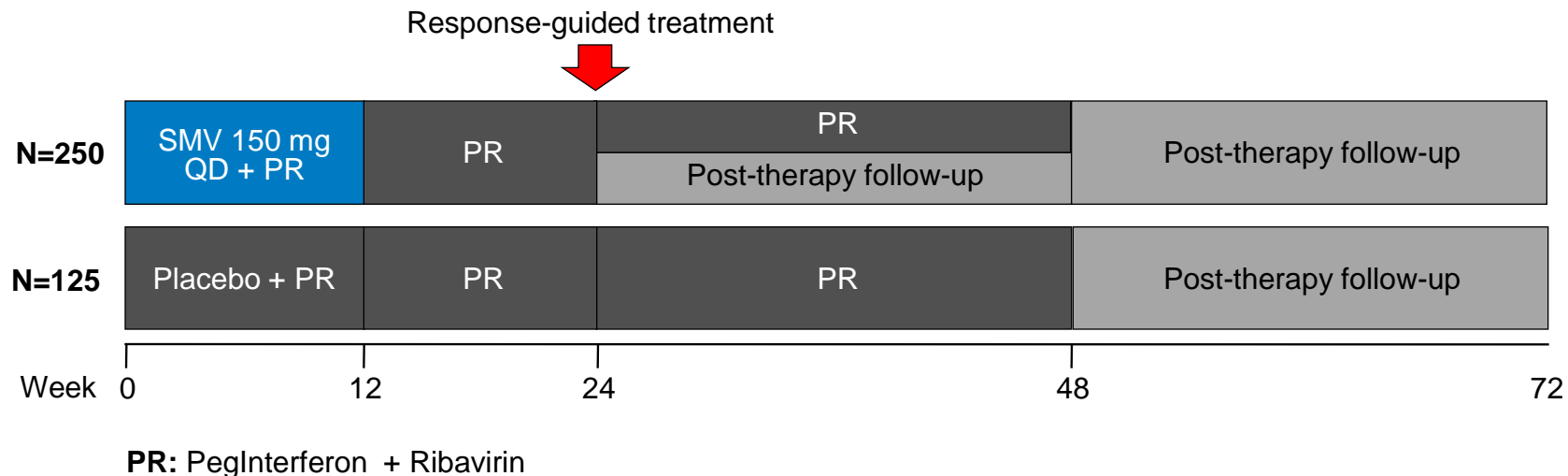
## Other ongoing phase III studies:

- **China:** Efficacy, PK, safety and tolerability in naïve patients
- **ATTAIN:** Simeprevir vs telaprevir in prior null or partial responders
- **RESTORE:** HCV genotype 4 infected naïve or treatment experienced patients
- **C212:** HIV-HCV co-infected treatment naïve and treatment experienced patients

Regulatory filings for simeprevir triple combination submitted in US, EU & Japan

# Simeprevir - Phase III Study designs in HCV GT1 infected patients (QUEST-1, QUEST-2 and PROMISE)

- Randomized, double-blind, placebo controlled design
- Patients were stratified by HCV subtype and IL28B genotype



## Studies:

- QUEST-1: n=394, naive (METAVIR score F3-F4: 30%)
- QUEST-2: n=391, naive, (METAVIR score F3-F4: 22%)
- PROMISE: n=393, prior relapsers, (METAVIR score F3-F4: 31%)

Top line data  
Dec-12

Reported at EASL 2013

## Summary: SVR12 data from QUEST-1 and QUEST-2

Patients with SVR12 %	QUEST-1		QUEST-2	
	SMV + PR	Placebo + PR	SMV + PR	Placebo + PR
All patients	<b>80</b>	50	<b>81</b>	50
SVR12 with 24 wks treatment (% pat meeting RGT criteria)	<b>91 (85)</b>	N/A	<b>86 (91)</b>	N/A
CC / CT / TT	<b>94 / 76 / 65</b>	78 / 42 / 24	<b>96 / 80 / 58</b>	81 / 41 / 19
GT1a & other / GT1b	<b>71 / 90</b>	49 / 52	<b>80 / 82</b>	46 / 53
F0-F2	<b>83</b>	60	<b>85</b>	51
F3-F4	<b>70</b>	28	<b>66</b>	47

**Robust data from two large placebo-controlled studies including a large proportion of patients with advanced liver fibrosis (F3-F4)**



# Summary: adverse events QUEST-1 and QUEST-2 across all treatment phases

Patients, %	QUEST-1		QUEST-2	
	SMV/PR (N=257)	PBO/PR (N=134)	SMV/PR (N=257)	PBO/PR (N=134)
<b>Most common AEs (<math>\geq 25\%</math> in SMV arm)</b>				
Fatigue	42	41	37	42
Pruritus	26	16	25	25
Headache	33	39	39	37
Pyrexia			31	40
Influenza-like illness			26	26
<b>Other AEs of interest</b>				
Rash (any type)	34	32	27	20
Anemia	20	28	21	28
Photosensitivity*	3	1	4	1

\* Over the first 12 weeks treatment

**Overall incidence of adverse events was similar to placebo control**

# Simeprevir - Phase III triple therapy

## Summary

### **Robust efficacy with high cure rates (SVR12):**

- Naive and relapser patients in three large global studies: 79-81%<sup>1</sup>
- Confirmed in Japan program, where high cure rates were demonstrated<sup>2</sup>
  - ✓ Broad filing on treatment naive and non-responders

### **High cure rates with 24 weeks treatment duration**

- 85-93% stopped all treatment at 24 weeks (QUEST-1 & -2 and PROMISE)
- High SVR12 rates 86-91% (QUEST-1 and -2, PROMISE data to be presented)

### **Excellent safety and tolerability**

- Overall incidence of adverse events similar to placebo, including rash and anemia
- Confirmed in Japanese studies

**Regulatory filings for simeprevir triple combination submitted in US, EU & Japan**

# Simeprevir - clinical development programs in HCV G1 & 4 infected patients

## Pivotal phase III studies:

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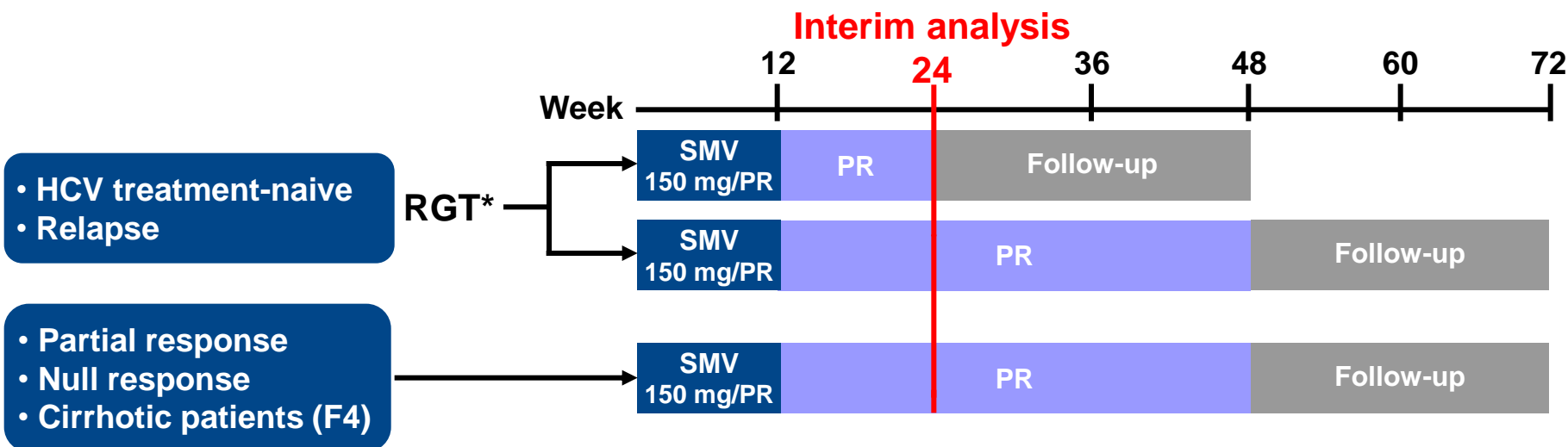
## Other ongoing phase III studies:

- **China:** Efficacy, PK, safety and tolerability in naïve patients
- **ATTAIN:** Simeprevir vs telaprevir in prior null or partial responders
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# C212 HCV-HIV Co-infected

## Study design



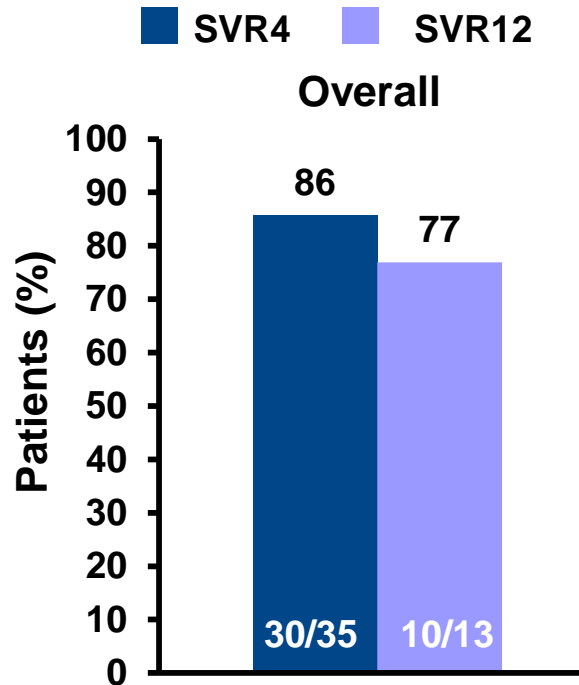
### Interim analysis:

➤ All patients included in the analysis had completed 24 weeks of treatment or had discontinued prior to that point

➤ No. of patients: Week 24: N=100  
Week 28: N=71  
Week 36: N=27

# C212: HCV-HIV Co-infected

Preliminary SVR4 and SVR12 rates in patients treated with SMV/PR



- 82% GT1a,
- 21% (METAVIR F3/4)
- 93 out of 106 patients on ARV therapy
- 88% met RGT criteria and stopped all treatment at W24
- Simeprevir was safe and well tolerated
- No HIV breakthroughs

**In the US 25 % of HIV patients are coinfectd with HCV**



## **Simeprevir**

**- All oral interferon free combination update**

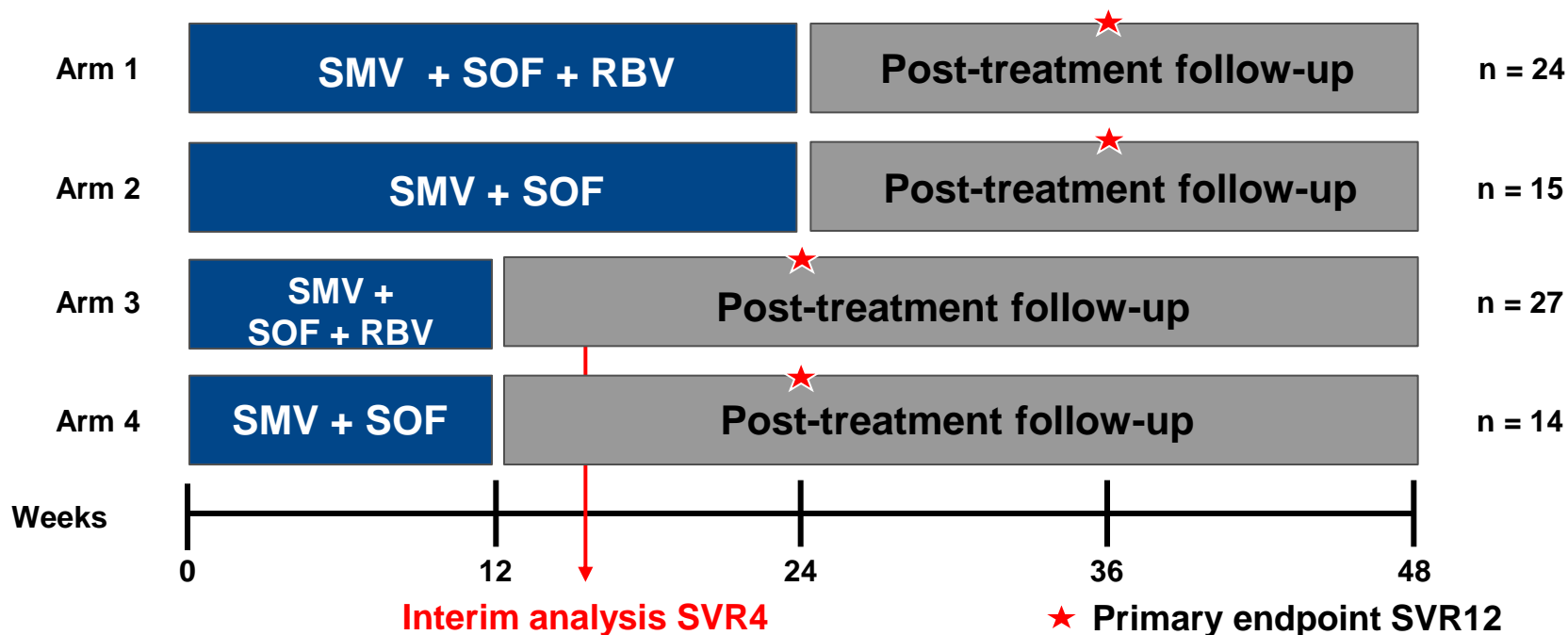


# **COSMOS Study**

(interim analysis)

**Once-daily regimen of simeprevir plus sofosbuvir with or without ribavirin in HCV genotype 1 null responders\***

# COSMOS study - Design



- Cohort 1: n=80, nulls, F0-F2
- Cohort 2: n=87, naives and nulls, F3-F4
- SMV 150 mg QD + SOF 400 mg QD with/without RBV
- Interim analysis of Cohort 1 conducted when all patients in 12 week treatment arms reached SVR4 time point or discontinued early



# COSMOS study - Baseline patient demographics and HCV disease characteristics

Patients		Total (n=80)
<b>Patient demographics</b>		
Male		61%
Race	Caucasian	71%
	African American	29%
Ethnicity	Hispanic/Latino	25%
Age, years, median		56.0
BMI, kg/m <sup>2</sup> , median		27.5
<i>IL28B</i>	nonCC	94%
<b>Baseline characteristics</b>		
HCV subtype	1a	78%
HCV RNA, median, log <sub>10</sub> IU/mL		6.8
METAVIR score	F0-F1	41%
	F2	59%

# COSMOS study – Efficacy results (interim analysis)

Patients	24 weeks		12 weeks	
	SMV + SOF +RBV (n=24)	SMV + SOF (n=15)	SMV + SOF+ RBV (n=27)	SMV + SOF (n=14)
RVR <sup>1</sup> , n/N (%)	18/22 (81.8)	10/15 (66.7)	23/27 (85.2)	8/14 (57.1)
Undetectable end of treatment, n/N (%)	10/12 (83.3)	8/9 (88.9)	27/27 (100)	14/14 (100)
Relapse, n	0	0	1	1
SVR <sub>4</sub> , n/N (%)	4/6 (66.7)	5/5 (100)	26/27 (96.3)	13/14 (92.9)
<b>SVR<sub>8</sub>, n/N (%)</b>	<b>4/6 (66.7)</b>	<b>5/5 (100)</b>	<b>26/27 (96.3)</b>	<b>13/14 (92.9)</b>

Of the patients in the **12 week arms** who achieved SVR<sub>8</sub>  
 – **24/24** who reached post-treatment Week 12 had achieved **SVR<sub>12</sub>**

# COSMOS study - Summary & Conclusions

- SMV + SOF with or without RBV for 12 weeks yielded high SVR rates in prior null responders with mild to moderate fibrosis (METAVIR F0-F2)
  - ✓ **SVR8 rate of 96% with RBV and 93% without RBV**
- SMV + SOF was safe and well tolerated
  - ✓ Anemia was seen only in RBV arms
  - ✓ Bilirubin increases only occurred in RBV containing arms

**Enrollment of Cohort 2 is complete and include prior null responders and treatment-naïve patients all with advanced fibrosis (METAVIR F3-F4)**

# Simeprevir in interferon-free combinations

Ribavirin

<b>Simeprevir</b>	<b>+</b>	<b>Sofosbuvir</b> (nucleotide)	+/-	<b>12w</b>	N=80+87 ✓ Cohort a: nulls, F0-F2 Cohort b: nulls + naives; <b>F3/4 (cirrhotics)</b>
			+/-	<b>24w</b>	
<b>Simeprevir</b>	<b>+</b>	<b>Daclatasvir</b> (NS5A inhibitor)	+/-	<b>12w</b>	N=180 Naives and nulls <b>Incl. F3/4 up to 35 %</b>
			+/-	<b>24w</b>	
<b>Simeprevir</b>	<b>+</b>	<b>TMC647055/r</b> (NNI; non-nucleoside)	+/-	<b>12w</b>	Naives/relapser and nulls Non-cirrhotics
<b>Simeprevir</b>	<b>+</b>	<b>VX-135</b> (nucleotide)	+/-	<b>12w</b>	Phase II to start H1 2013
<b>Simeprevir</b>	<b>+</b>	<b>IDX719</b> (NS5A inhibitor)	+/-	<b>12w</b>	DDI study started
		<b>+/- TMC647055/r</b>			

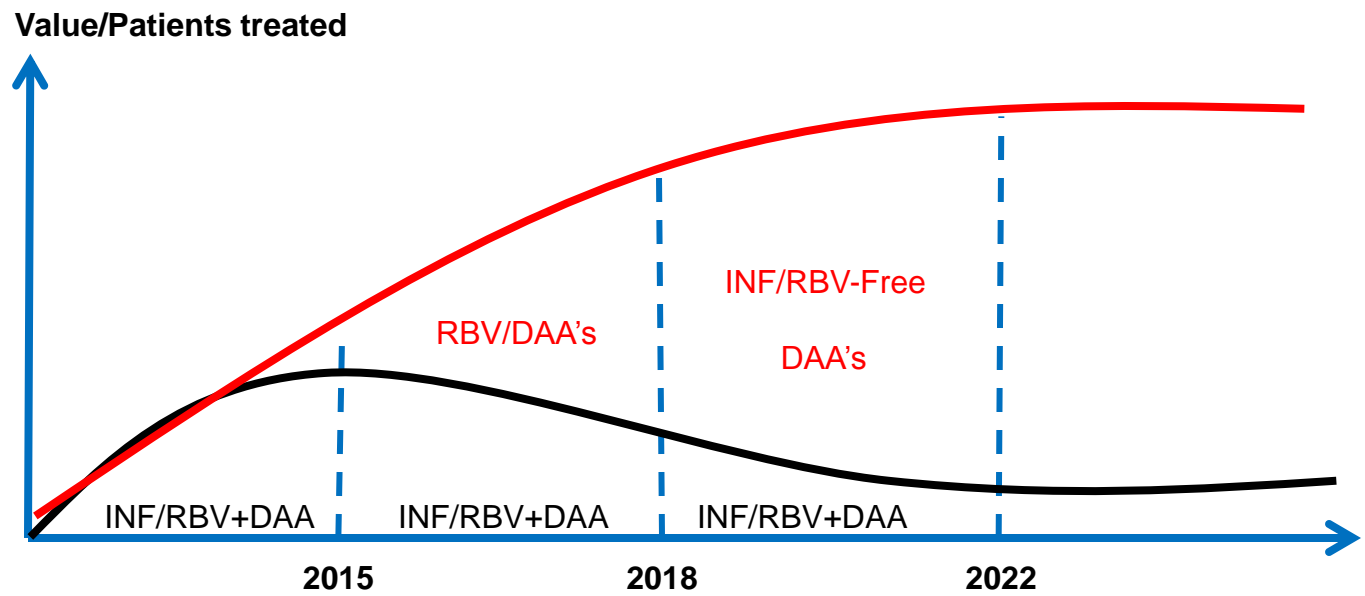
**Simeprevir is strongly positioned to become a principal component of future IFN-free therapies**



# Long term goal – eradication of hepatitis C



The evolution in treating hepatitis C will expand the market value, number of patients treated and regions over the next 10-15 years



# News flow - highlights

Therapeutic area	Product/Project	Partner	Preclinical phase		Clinical phase			Market	
			Research	Development	Phase I	Phase IIa	Phase IIb		Phase III
<b>ANTIVIRALS</b>									
Labial herpes	Xerclear® (Zovirax, Zovirax Duo)	GlaxoSmithKline (GSK)	[Progress bar]						
	Simeprevir (TMC435), NS3 protease inhibitor	Janssen Pharmaceuticals	[Progress bar]						
Hepatitis C	NS5B nucleotide polymerase inhibitor	Janssen Pharmaceuticals	[Progress bar]						
	NS5B nucleotide polymerase inhibitor	Janssen Pharmaceuticals	[Progress bar]						
Hepatitis B	NS5A replication complex inhibitor	Janssen Pharmaceuticals	[Progress bar]						
	Lagociclovir valactate (MIV-210)	Daewoong	[Progress bar]						
Dengue fever	NS3 protease inhibitor	Janssen R&D Ireland	[Progress bar]						
HIV	Protease inhibitor	Janssen Pharmaceuticals	[Progress bar]						
<b>OTHER INDICATIONS</b>									
Bone related disorders	Cathepsin K inhibitor		[Progress bar]						
Neuropathic pain	Cathepsin S inhibitor		[Progress bar]						

- ✓ Q4-12 Start of Cohort 2 with simeprevir and GS7977 phase II study
- ✓ Q4-12 Top line results from phase III trials with simeprevir (Quest 1+2 and Promise)
- ✓ Q1-13 Filing for regulatory approval in Japan
- ✓ H1-13 EoT and partial SVR data from Cohort 1 with simeprevir and sofosbuvir phase II study
- ✓ H1-13 Filing of simeprevir in Japan, the US and EU
- H1-13 Potential CD selection in Cathepsin S (neuropathic pain) program
- H1-13 Results from phase I-study with MIV-711, our cathepsin K inhibitor (bone related disorders)
- H1-13 Start of Phase II with simeprevir and VX-135
- H1-13 Step two in GSK launch strategy for Xerclear® (ZoviDuo), launch in major European OTC markets
- H2-13 Potential CD selection in our internal Nucleotide NS5B inhibitor program
- H2-13 Potential CD selection in our internal NS5A inhibitor program
- H2-13 Goal to start phase I trials with Medivir/Janssen nucleotide NS5B-inhibitor
- H2-13 Data from the phase II combination study with simeprevir and daclatasvir
- H2-13 SVR data from Cohort 2 with simeprevir and sofosbuvir phase II study

[www.medivir.com](http://www.medivir.com)

**Ticker: MVIR**  
**Exchange: OMX / NASDAQ**

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