



# Medivir

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

**Q4-2012 Conference Call - Presenting team**

**Maris Hartmanis, CEO  
Charlotte Edenius, EVP R&D  
Rein Piir, EVP Corporate Affairs & IR**



## **Reflections on 2012**

**Maris Hartmanis, CEO**

# 2012 – we set the foundation for becoming THE emerging European pharma

## R&D operations

- Progress in our R&D pipeline, both internally driven and partnered projects
- Reported simeprevir (TMC435) phase III data showed strong and consistent results, followed by filing in Japan, as announced this morning
- Broadening of our research platform and know-how through new collaborations and an acquisition

## Pharmaceuticals

- Consistent product portfolio performance – earnings in line with expectations at the acquisition in 2011, with EBITDA contribution of approximately SEK 100m
- GSK started the OTC launch in Europe and obtained OTC approval in Russia with the Medivir developed cold sore pharmaceutical branded as Zoviduo/Zovirax Duo.
- Preparations and awareness building around simeprevir in the Nordics made strong progress

## Finance

- Solid financial position at year end with approximately SEK 300m in cash
- Stable cost base with a net burn rate of approximately SEK 200m

# Value proposition



## **Collaborative and innovative pharmaceutical company**

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



## **Strong position in HCV – both partnered and internal programs**

- Simeprevir (TMC435), considered “best in class HCV protease inhibitor”
  - Partnered with Janssen Pharmaceuticals with retained Nordic rights
  - Regulatory filing began already in Q1, 2013 as a triple combination treatment with PegIFN and ribavirin
  - Optimal profile for future interferon-free combination treatments
- In-house HCV programs will offer combination opportunities

## **Commercial presence in the Nordic region**

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

**BioPhausia**<sup>®</sup>  
– a Medivir sales company

## Consolidated profit performance

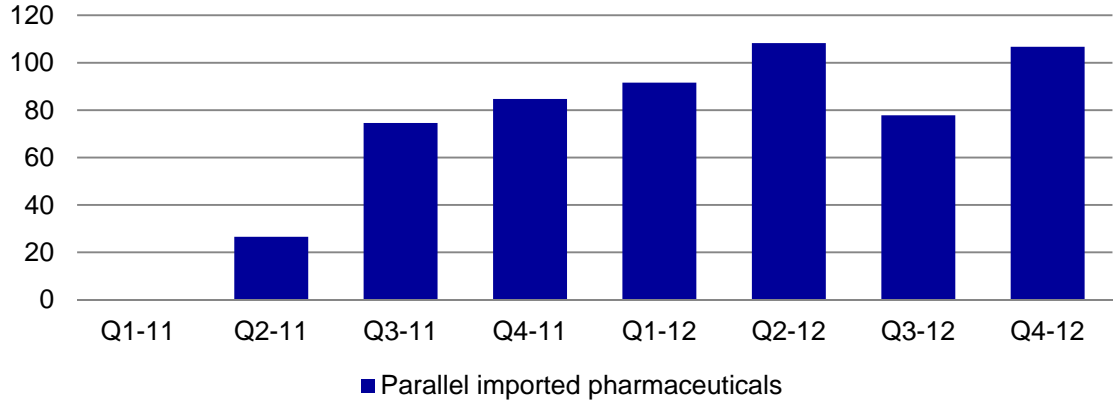
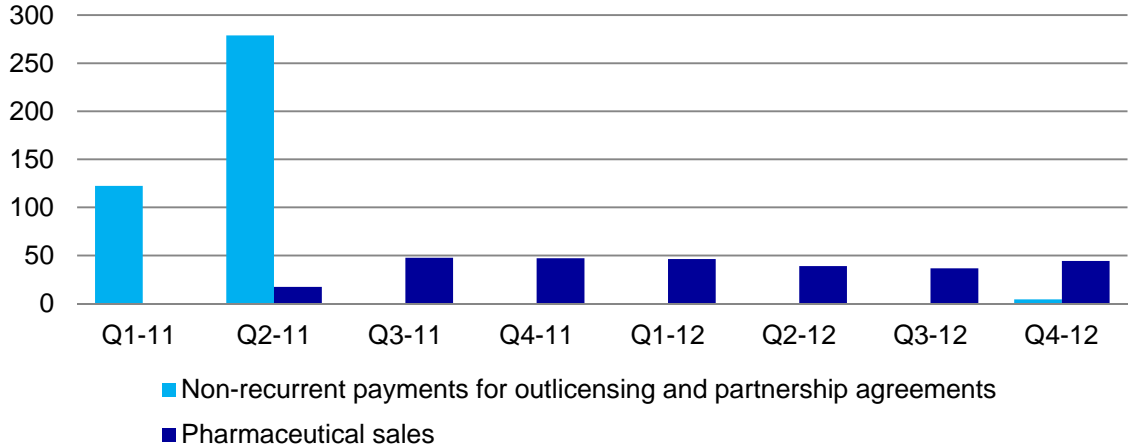
(MSEK)	2012 Oct-Dec	2011 Oct-Dec	2012 Jan-dec	2011 Jan-Dec
Net turnover	155.5	131.8	555.0	698.6
Gross profit	45.6	35.1	152.3	458.0
EBITDA	-39.9	-35.7	-150.9	135.3
EBIT	-48.5	-44.1	-185.8	111.9
Profit/loss before tax	-50.0	-47.5	-193.0	111.2
Profit/loss after tax	-65.3	-53.1	-219.1	113.8

## Net sales split Q/Q

<b>Net turnover breakdown* (MSEK)</b>	<b>2012 Oct-Dec</b>	<b>2011 Oct-Dec</b>	<b>2012 Jan-Dec</b>	<b>2011 Jan-Dec</b>
Outlicensing and partnership agreements/Non-recurrent payments	4.4	-	4.4	401.2
Pharmaceutical sales	44.3	47.5	164.9	111.2
Parallel imports	106.6	84.7	384.4	185.9
Other services	0.3	-0.4	1.3	0.3
<b>Total</b>	<b>155.5</b>	<b>131.8</b>	<b>555.0</b>	<b>698.6</b>

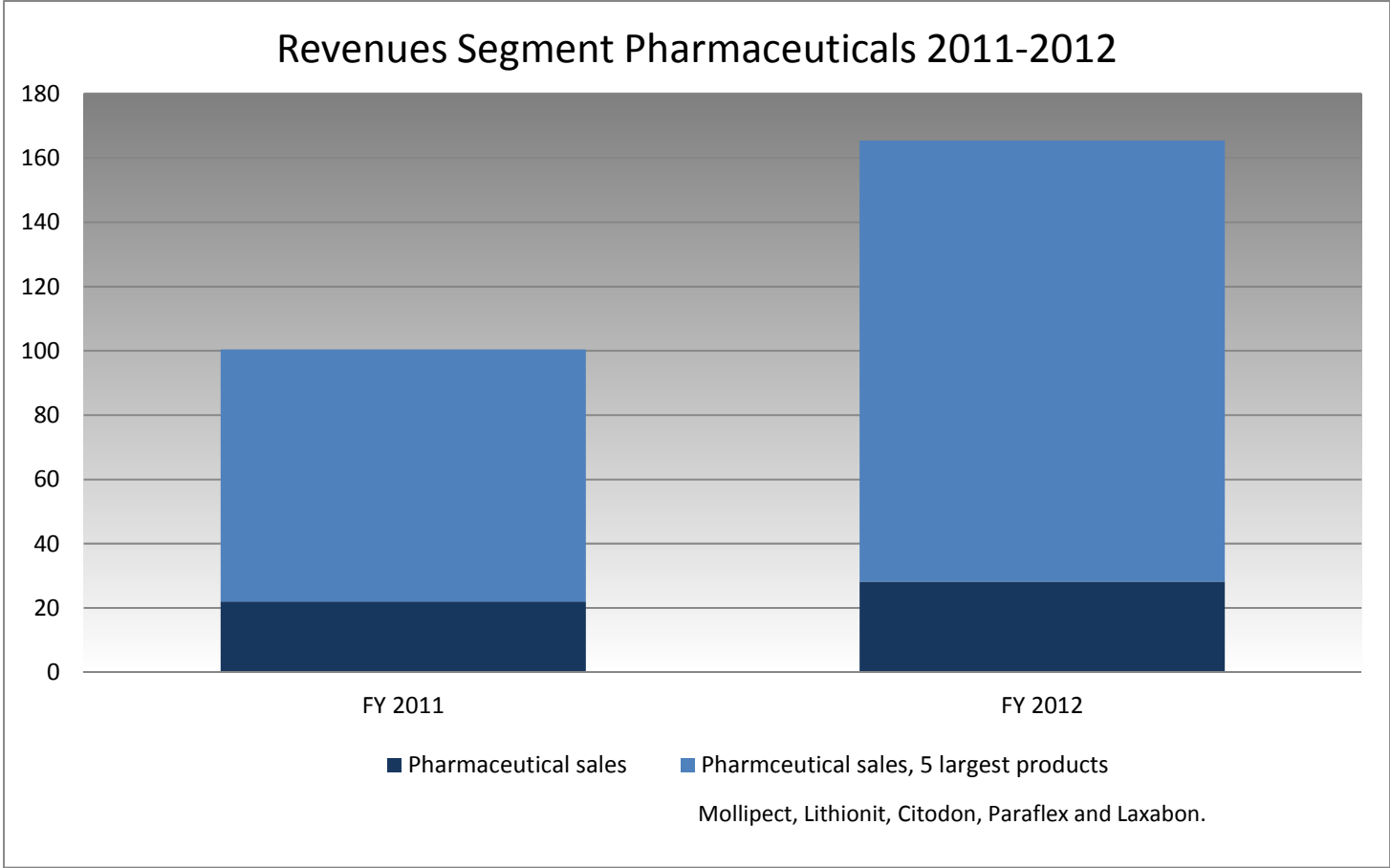
\*The BioPhausia group is included from 31 May 2011.

# Quarterly sales trend in pharmaceuticals and parallel imports, SEK m\*



\*The BioPhausia group is included from 31 May 2011.

# Pharmaceutical sales





# 2013 marks the beginning of an exciting journey

## We will continue to build the foundation by:

- Supporting the development and positioning of simeprevir both in the triple and interferon free HCV landscapes, thereby maximizing the patient benefit
- Entering into new partnerships for our internally R&D driven projects, cathepsin K and S, when the timing is right and continuing the evaluation of our internal HCV projects
- Evaluating new therapeutic and product opportunities as they emerge
- Continuing the development of our pharmaceutical and business opportunities in the Nordics

## THE emerging European pharma company

### *Structure*

- Partner of choice for both pharmaceuticals and development programs
- Continued commitment towards targets in infectious diseases
- Addressing of new therapeutic areas based on core competence
- Aggressive expansion of product portfolio, including simeprevir and other in-house developed pharmaceuticals
- Broader, risk balanced, R&D pipeline

### *External perspective*

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



## **Key R&D highlights from Q4 2012**

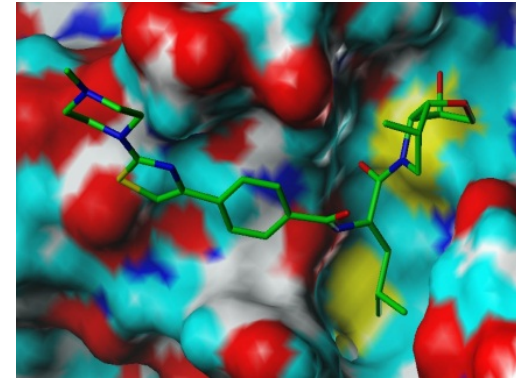
**Charlotte Edenius, EVP R&D**

# Cathepsin K inhibitor

## - a phase I clinical program

### Disease

Osteoarthritis, osteoporosis, and metastatic bone disease



### MIV-711: Phase I clinical trial ongoing

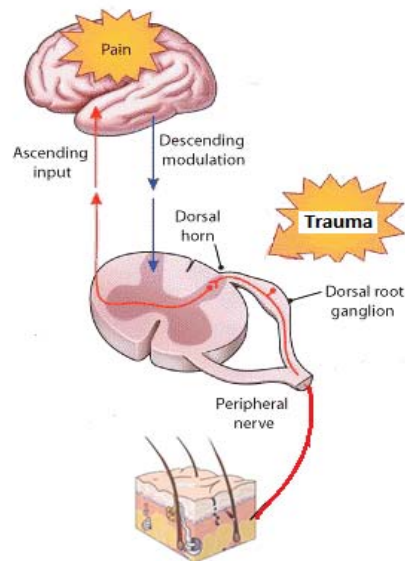
- Adaptive, placebo controlled, double-blind study in healthy volunteers incl. post menopause women
- Ascending single and multiple (7 - 28 days) once daily dosing
- Biomarkers for bone and cartilage turnover
  
- Phase I completed and data available H1-2013

**MIV-711 - a phase I clinical candidate efficacious on bone and cartilage biomarkers in osteoarthritis and osteoporosis models**

# Cathepsin S inhibitor – neuropathic pain and rheumatoid arthritis

## Principle for neuropathic pain (NP)

- Associated with a lesion or disease affecting the somatosensory system
- Includes e.g. diabetic neuropathic pain, post-herpetic neuralgia & neuropathic lower back pain



## Medical need and market

- Current treatments incl. anticonvulsants and antidepressants
  - Pain persists in 75% patients with at best a 50% reduction in overall pain
  - Significant side effects e.g. dizziness, somnolence

## Mechanism of action:

- Inhibition of Cathepsin S prevents inflammatory damage to the sensory system by blocking fractalkine activation

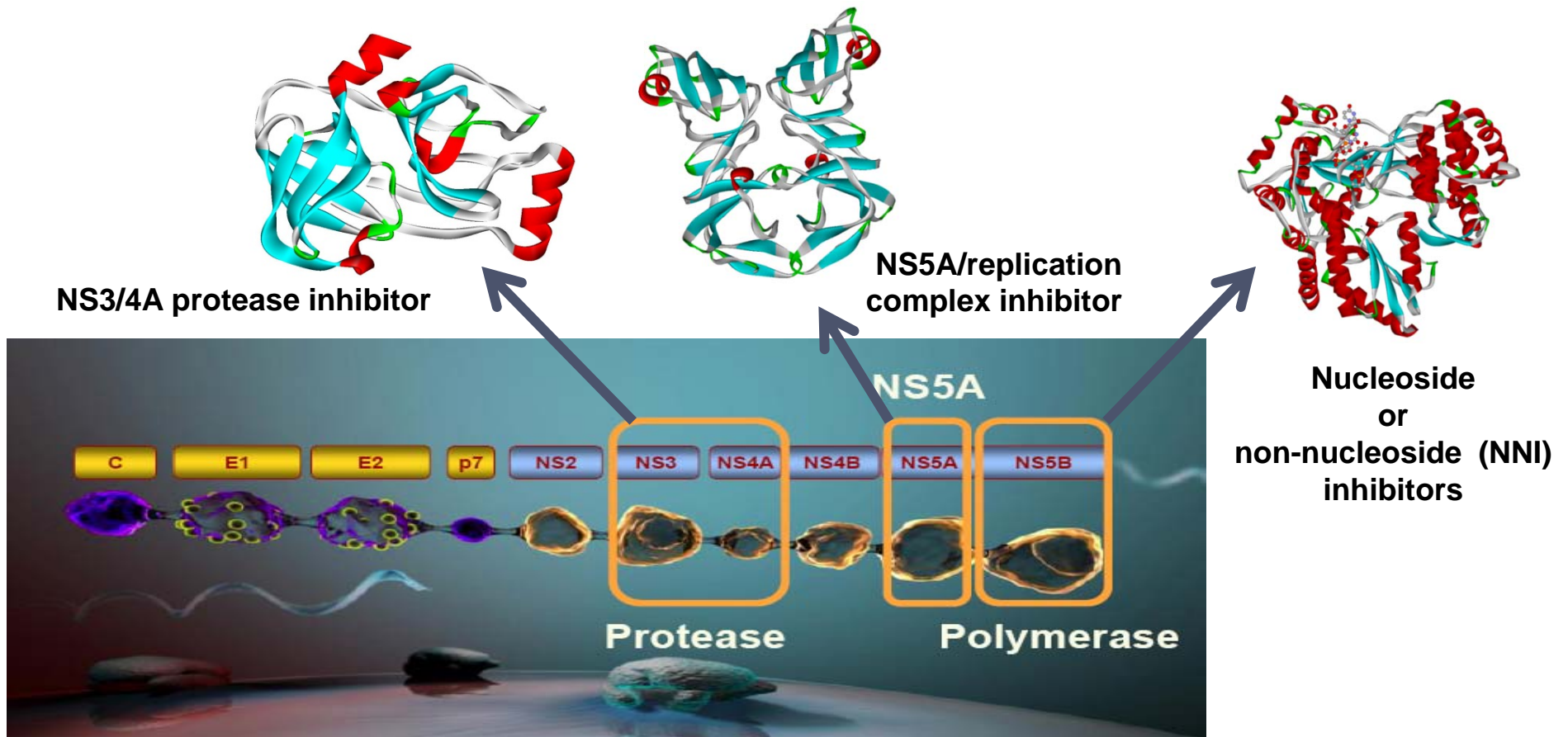
## Cathepsin S inhibitor program

- Potent, selective and orally bioavailable inhibitors available
- Aiming for candidate drug selection in H1 2013

**Cathepsin S inhibition is efficacious as monotherapy and is synergistic with gabapentin in a neuropathic pain model**

# Our commitment in hepatitis C

– on-going programs versus the three major targets



**Simeprevir – An efficacious, safe and tolerable protease inhibitor\***



\*as demonstrated in 3 pivotal phase III studies in GT1 HCV infected naive and relapser patients



## **Simeprevir (TMC435)**

**- 1<sup>st</sup> regulatory file submitted (Japan)**

# Simeprevir (TMC435), clinical development programs in HCV G1 & 4 infected patients

## Pivotal phase III studies:

- **QUEST 1** treatment-naïve
  - **Quest 2** treatment-naïve
  - **PROMISE** prior relapsed
  - **Japan** naïve & experienced (four studies)
- Top-line data available
- Regulatory file submitted 22 Feb 2013

## Other ongoing phase III studies:

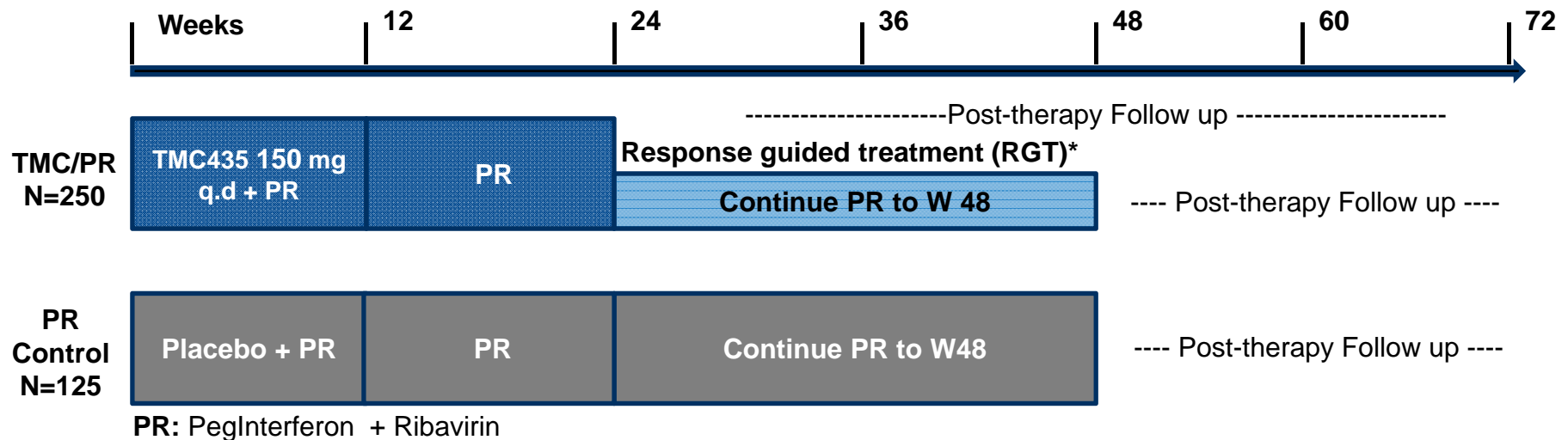
- **China:** Efficacy, PK, safety and tolerability in naïve patients
- **ATTAIN:** Simeprevir vs telaprevir in prior null or partial responders
- **HCV genotype 4 infected** naïve or treatment experienced patients
- **HIV** co-infected patients

Regulatory filings for simeprevir triple combination H1- 2013 in US, EU & Japan

# Simeprevir - Phase III Study designs in HCV GT1 infected patients

Response guided, double-blind, placebo controlled

2:1 randomization



## Studies:

QUEST-1: n=394, naive (METAVIR score F3-F4: 30%)

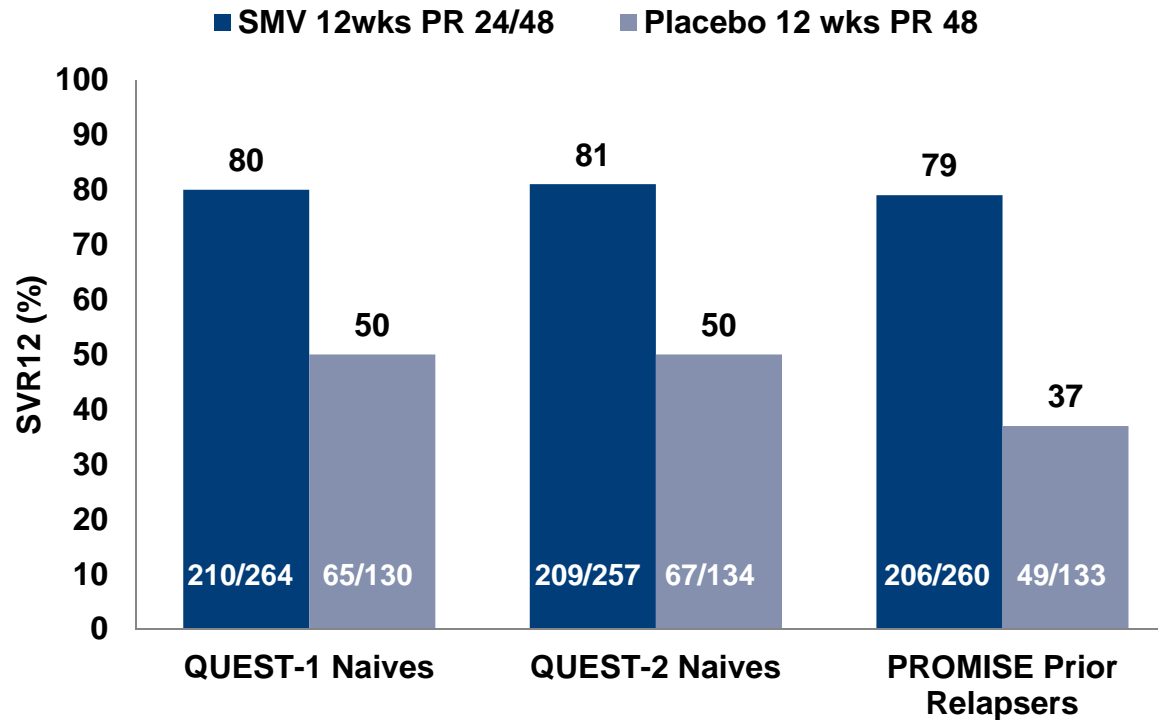
QUEST-2: n=391, naive, (METAVIR score F3-F4: 22%)

PROMISE: n=393, prior relapsers, (METAVIR score F3-F4: 31%)



# Simeprevir - Phase III Triple therapy

## Efficacy – SVR12 (cure rate)



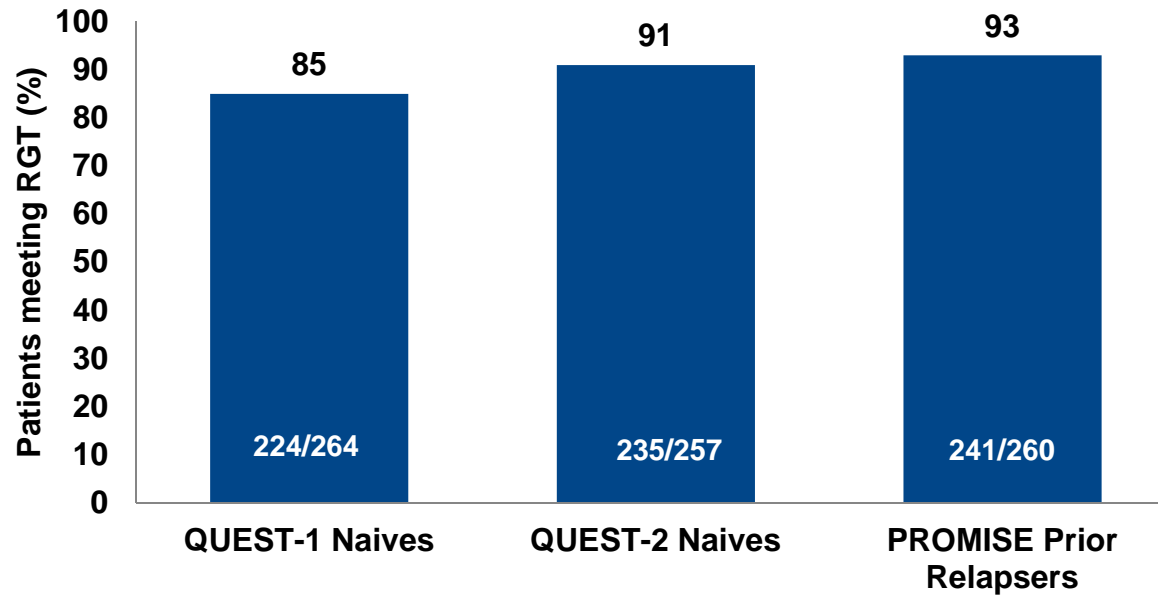
Statistically significant difference vs placebo control in all studies

**Robust efficacy in all three studies (79-81% SVR12)\* - confirming phase II studies**



\* All three trials included difficult-to-treat patients with advanced liver fibrosis/cirrhosis (METAVIR score F3-F4)

# Simeprevir - Phase III Triple therapy Efficacy – Response Guided Treatment (RGT)



**Shortened treatment durations:  
85 - 93 % of the patients were able to stop all treatment at week 24**

# Simeprevir - Phase III triple therapy

## Results – Safety and Tolerability

- Overall simeprevir was safe and well tolerated
  - ✓ Incidence of adverse events, including rash and anemia, were similar to those observed in the placebo control group
- Mild and reversible increases in bilirubin were observed in simeprevir dose groups
- Discontinuations due to AEs were consistently lower in the simeprevir treatment arms as compared to control

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

# Simeprevir - Phase III triple therapy (global and Japan)

## Summary

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

- Naive and relapser patients in 3 global studies: 79 - 81%<sup>1</sup>
- Confirmed in Japan program where high cure rates were demonstrated<sup>2</sup>

### Shorter treatment duration

- 85-93 % could stop all treatment at week 24 (naïve and relapser patients; global trials)

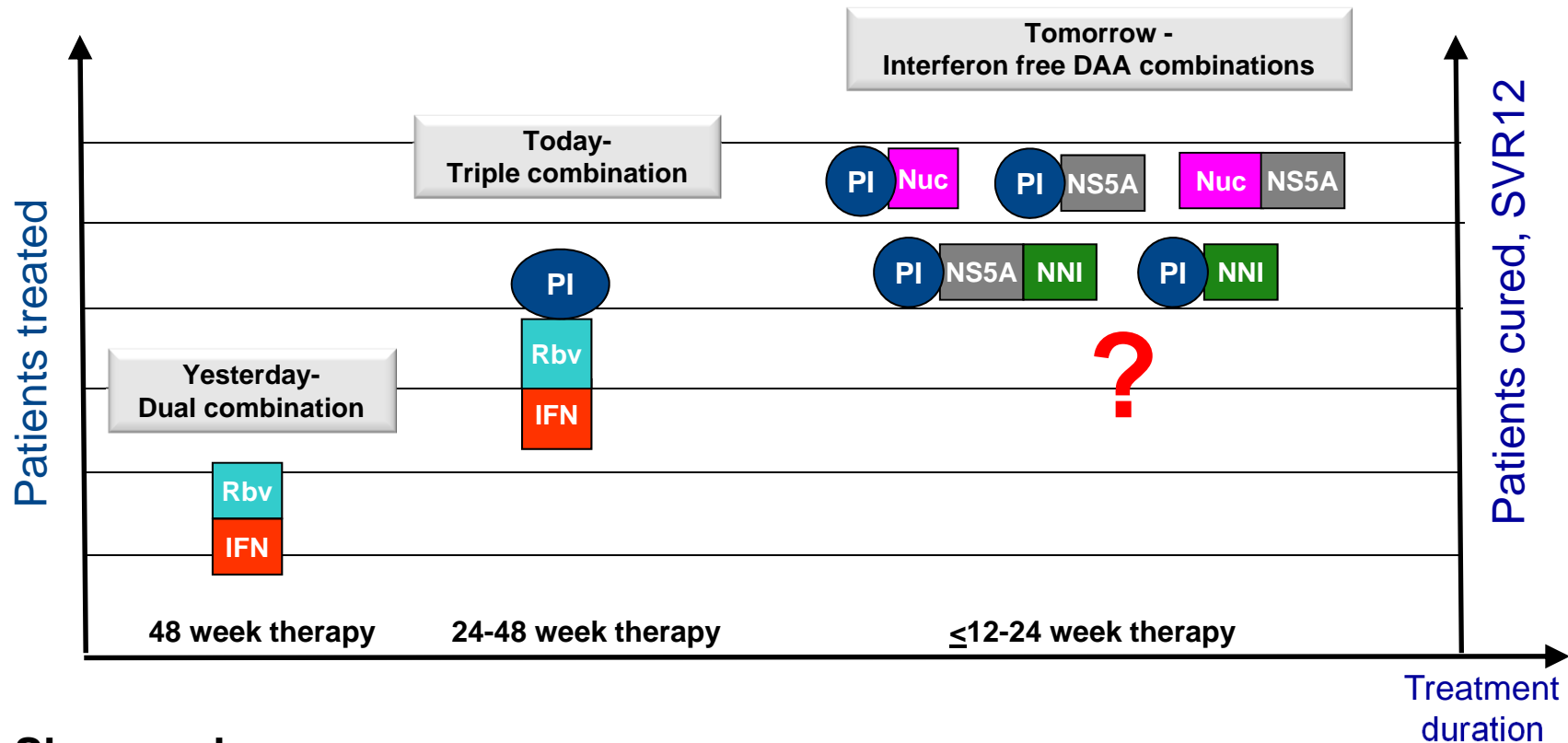
### Excellent safety and tolerability

- Overall incidence of adverse events, including rash and anemia, similar to placebo
- Confirmed in Japan program in which favourable safety profile was demonstrated

**Phase III data support simeprevir as a new treatment for G1 HCV, with advantages vs marketed 1<sup>st</sup> generation PIs**

**Regulatory filings for simeprevir triple combination H1- 2013 in US, EU & Japan**

# Evolution of HCV therapy in HCV G1 infection



## Simeprevir

- ✓ a tolerable 2<sup>nd</sup> generation protease inhibitor leading to high SVR rates
- ✓ well positioned for triple as well as future interferon free combination therapies

# Simeprevir (TMC435) – interferon free combinations

Ribavirin

**Simeprevir + Sofosbuvir**  
(nucleotide)

+/-

12w

+/-

24w

N= 90 + 90

Cohort b initiated Nov-12

Cohort a: nulls, F0-F2

Cohort b: nulls + naives; **F3/4 (cirrhotics)**

**Simeprevir + Daclatasvir**  
(NS5A inhibitor)

+/-

12w

+/-

24w

N=180

Fully enrolled Nov-12

Naives and nulls

**Incl. F3/4 up to 35 %**

**Simeprevir + TMC647055/r**  
(NNI; non-nucleoside)

+/-

12w

Naives/relapser and nulls

Non-cirrhotics

**Simeprevir + VX-135**  
(nucleotide)

+/-

12w

DDI study to start Q1-13

**Simeprevir + IDX719**  
(NS5A inhibitor)  
+/- TMC647055/r

+/-

12w

DDI study started (SMV + IDX719)

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



## News flow - highlights



- ✓ 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 Potential CD selection in Cathepsin S (neuropathic pain) program
- H1-13 Filing of simeprevir in US and EU
- H1-13 Results from the phase I-study with MIV-711, a cathepsin K inhibitor (bone related disorders)
- H1-13 Start of phase II study 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 1 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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