# Medivir

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

## EU Road Show May 2013

**Charlotte Edenius EVP Development**
**Rein Piir, EVP Corporate Affairs / IR**

# Medivir - the emerging European pharma

- Research driven pharmaceutical company **focused on infectious disease,** with a strong track record in **partnerships as part of the business model** located in Sweden with 170 employees (out of which 50 in Cross Pharma – parallel import of pharmaceuticals in Sweden )

- **World leading expertise in polymerase and protease drug targets** – strong pipeline of innovative infectious disease drugs

- **First in-house developed product on the market**, a cold sore product with unique profile

- **Strong position in HCV drug development**, four programs including all three validated target classes, two in-house driven.

- **Simeprevir** (TMC435) in partnership with Janssen is considered as the best in class PI, **global filing done during Q1-2013**

- **Fifteen marketed products in the Nordics,** generating annual sales of ~85 MUSD with an EBITDA of ~16MUSD

- **Solid financial position**

- **Broad institutional shareholder base,** ~30% outside Nordic region

# Consolidated profit performance*

| (SEK m) | 2013 Jan-Mar | 2012 Jan-Mar | 2012 Jan-Dec |
|---|---|---|---|
| Net turnover | 282.6 | 137.9 | 555.0 |
| Gross profit | 171.3 | 40.9 | 152.3 |
| EBITDA | 84.7 | -29.9 | -151.0 |
| EBIT | 83.0 | -38.3 | -185.8 |
| Profit/loss before tax | 83.0 | -37.5 | -192.9 |
| Profit/loss after tax | 77.6 | -37.7 | -219.1 |

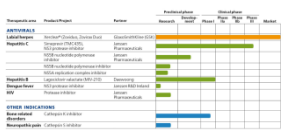
*The BioPhausia corporate group is included from 31 May 2011.

# Net turnover breakdown*

| (SEK m) | 2013 Jan-Mar | 2012 Jan-Mar | 2012 Jan-Dec |
|---|---|---|---|
| Outlicensing and partnership agreements/Non-recurrent payments | 126.8 | - | 4.4 |
| Pharmaceutical sales | 51.3 | 46.3 | 164.9 |
| Parallel imports | 104.5 | 91.6 | 384.4 |
| Other services | 0.0 | 0.0 | 1.3 |
| **Total** | **282.6** | **137.9** | **555.0** |

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

# 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

BioPhausia® – a Medivir sales company

- 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

## Solid financial position

- Present liquid assets are solid and will take us to the time point were we are profitable

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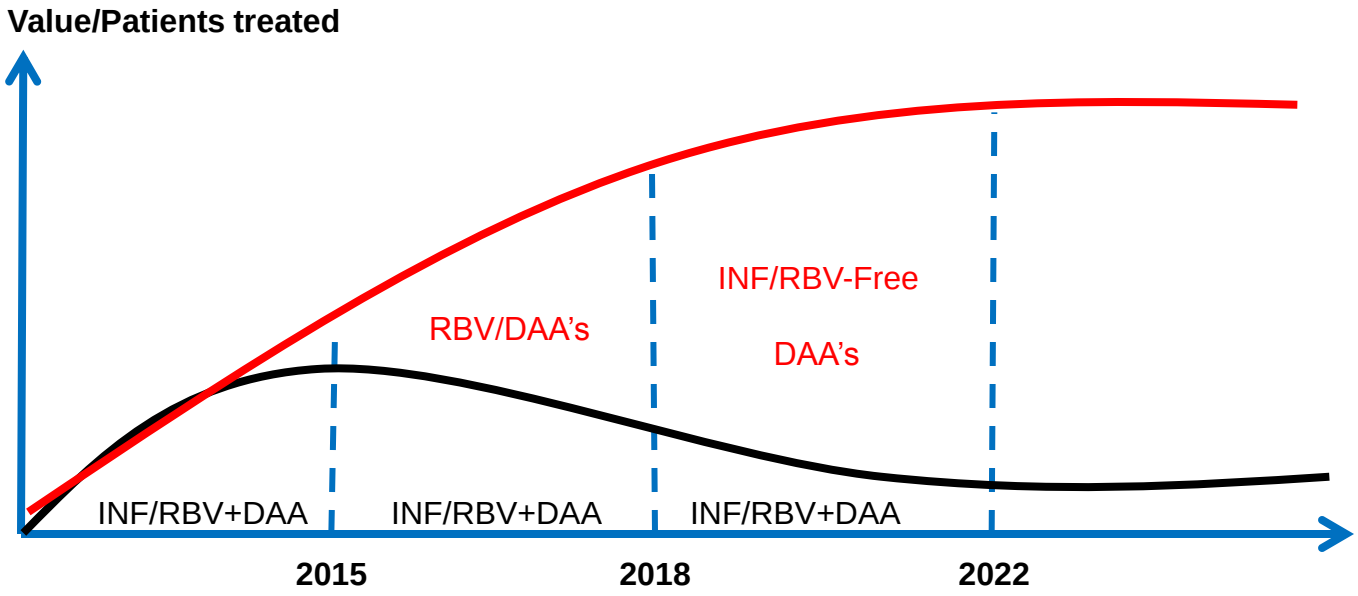
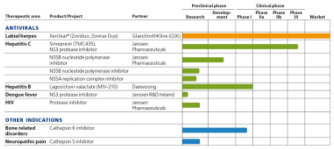
# Long term goal – eradication of hepatitis C


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

**Regional, patient and pricing differences will drive the segments in the future**



# 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

- 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

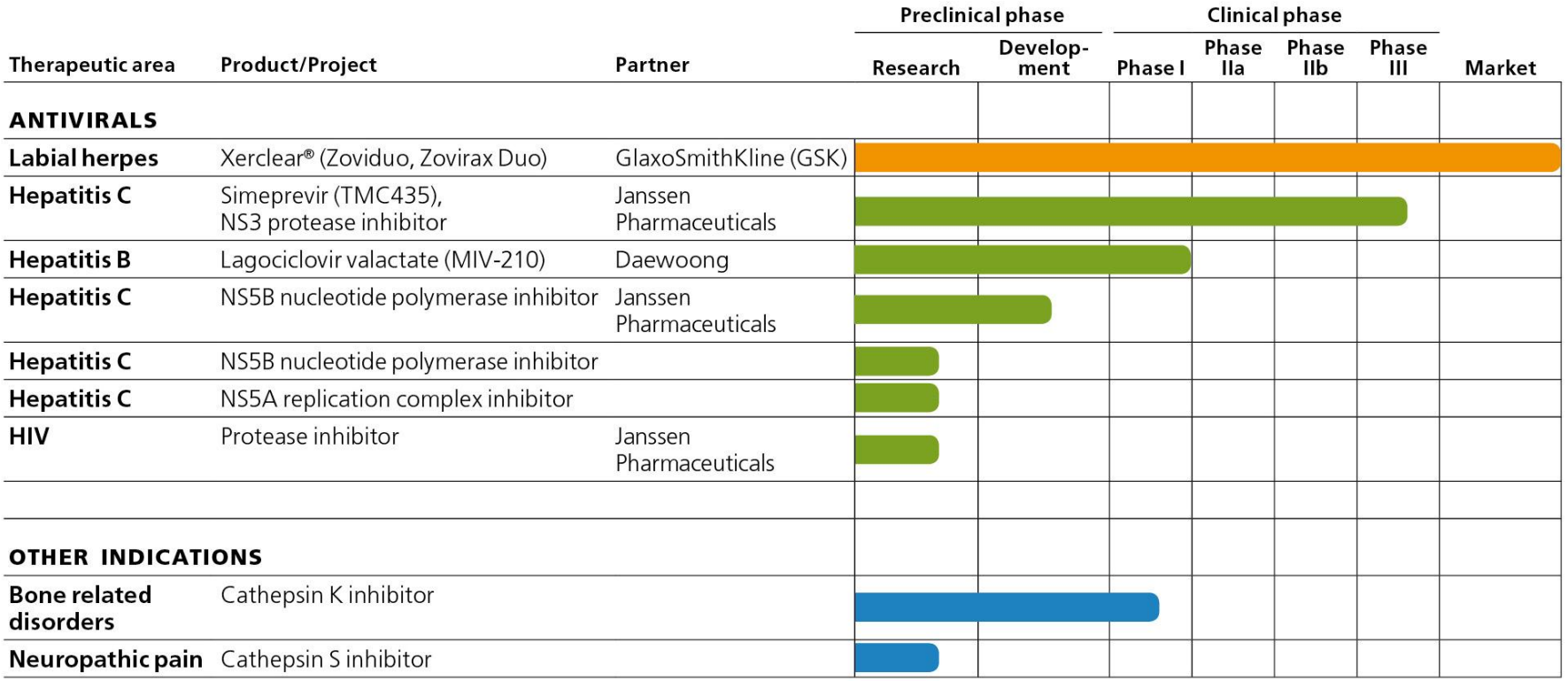
# R & D

## Charlotte Edenius, EVP Development

# Medivir – Research and Development

- Leading expertise in polymerase and protease research
- Long experience of antiviral/anti-infective research (e.g. HCV, HBV, HSV, HIV, VZV, dengue)
- Integrated, agile drug discovery unit from hit to IND with CMC, regulatory affairs and clinical capabilities
- Large network of collaborators with in academia, SMEs and CROs
- Strong deal track record with > 25 partnerships including major pharma companies

# A focused project portfolio



| Therapeutic area | Product/Project | Partner | Preclinical phase: Research | Preclinical phase: Develop-ment | Clinical phase: Phase I | Clinical phase: Phase IIa | Clinical phase: Phase IIb | Clinical phase: Phase III | Market |
|---|---|---|---|---|---|---|---|---|---|
| **ANTIVIRALS** | | | | | | | | | |
| **Labial herpes** | Xerclear® (Zoviduo, Zovirax Duo) | GlaxoSmithKline (GSK) | | | | | | | |
| **Hepatitis C** | Simeprevir (TMC435), NS3 protease inhibitor | Janssen Pharmaceuticals | | | | | | | |
| **Hepatitis B** | Lagociclovir valactate (MIV-210) | Daewoong | | | | | | | |
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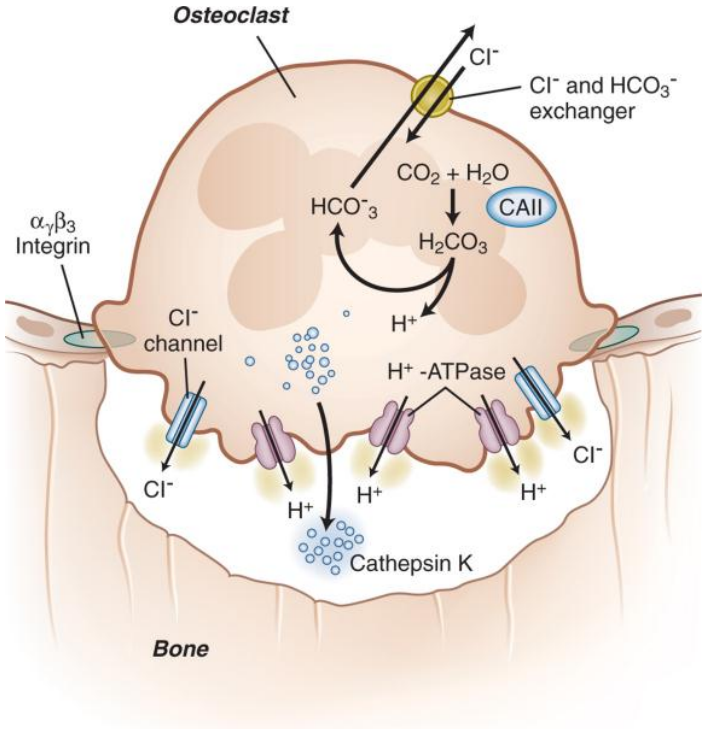
| **Hepatitis C** | NS5A replication complex inhibitor | | | | | | | | |
| **HIV** | Protease inhibitor | Janssen Pharmaceuticals | | | | | | | |
| **OTHER INDICATIONS** | | | | | | | | | |
| **Bone related disorders** | Cathepsin K inhibitor | | | | | | | | |
| **Neuropathic pain** | Cathepsin S inhibitor | | | | | | | | |

# Cathepsin K inhibitors - mechanism of action

## Osteoporosis/osteoarthritis/metastatic bone disease




**Osteoporosis and osteoarthirits**

- cathepsin K dissolves collagen I in bone and collagen II in cartilage
- genetic, animal and human data shows that cat K inhibition improves bone quality

**Metastatic bone disease**

- invasive tumour cells express high levels of cathepsin K, which increase bone resorption and the invasiveness of cancer cells

**Recent data suggest that cat K inhibitor reduces fracture risk in humans**

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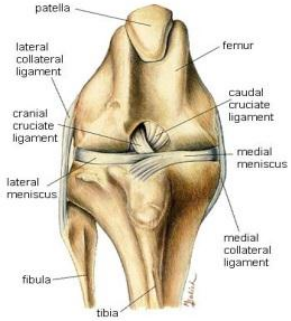
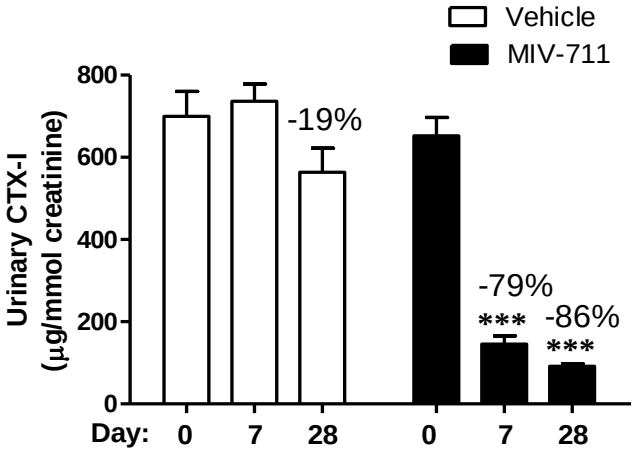
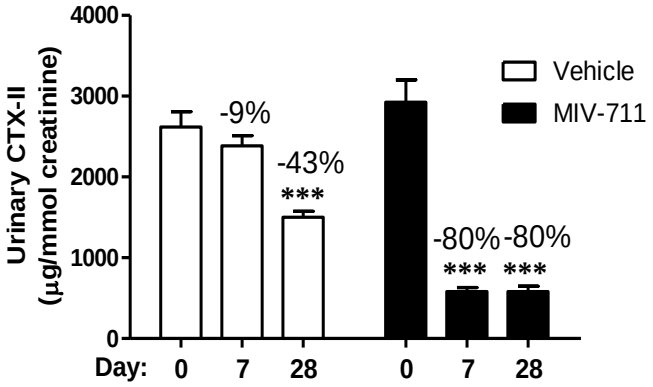
# MIV-711 – Partial medial meniscectomy; an experimental osteoarthritis model in dog




**Reduced urinary levels of CTX-I, a bone resorption biomarker**



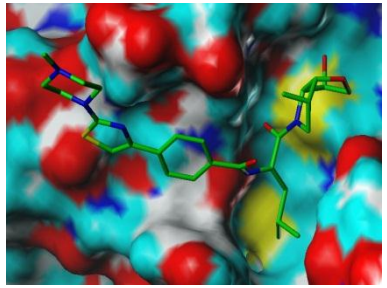

**Reduced urinary levels of CTX-II, a cartilage resorption biomarker**




MIV-711 dosed at 30 µmol/kg (p.o.) once daily for 28 days, n=15

**MIV-711 reduced bone and cartilage degradation biomarkers in dog osteoarthritis model**

# Cathepsin K inhibitor
## - a phase I clinical program



### Disease

Osteoporosis, osteoarthritis and metastatic bone disease

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

- Adaptive, placebo controlled, double-blind study in healthy volunteers incl. post meno-pausal women
- Ascending single and multiple (7 - 28 days) once daily dosing
- Biomarkers for bone and cartilage turnover

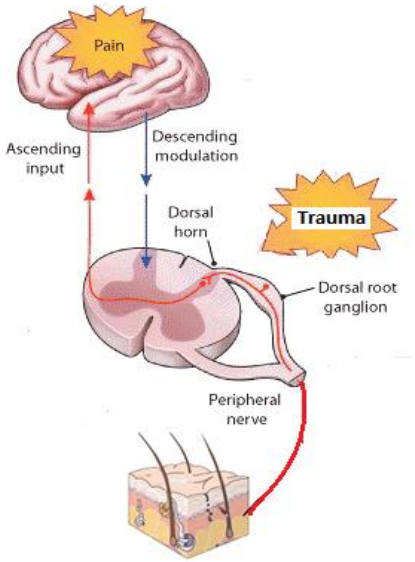
- Phase I completed and data available Q2-2013
- Single ascending dose data will be presented at the European Calcified Tissue Society (ECTS) annual meeting in Lisbon 18-21/5

**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
- 25M people in the 7 MM suffer from NP

## Mechanism of action:

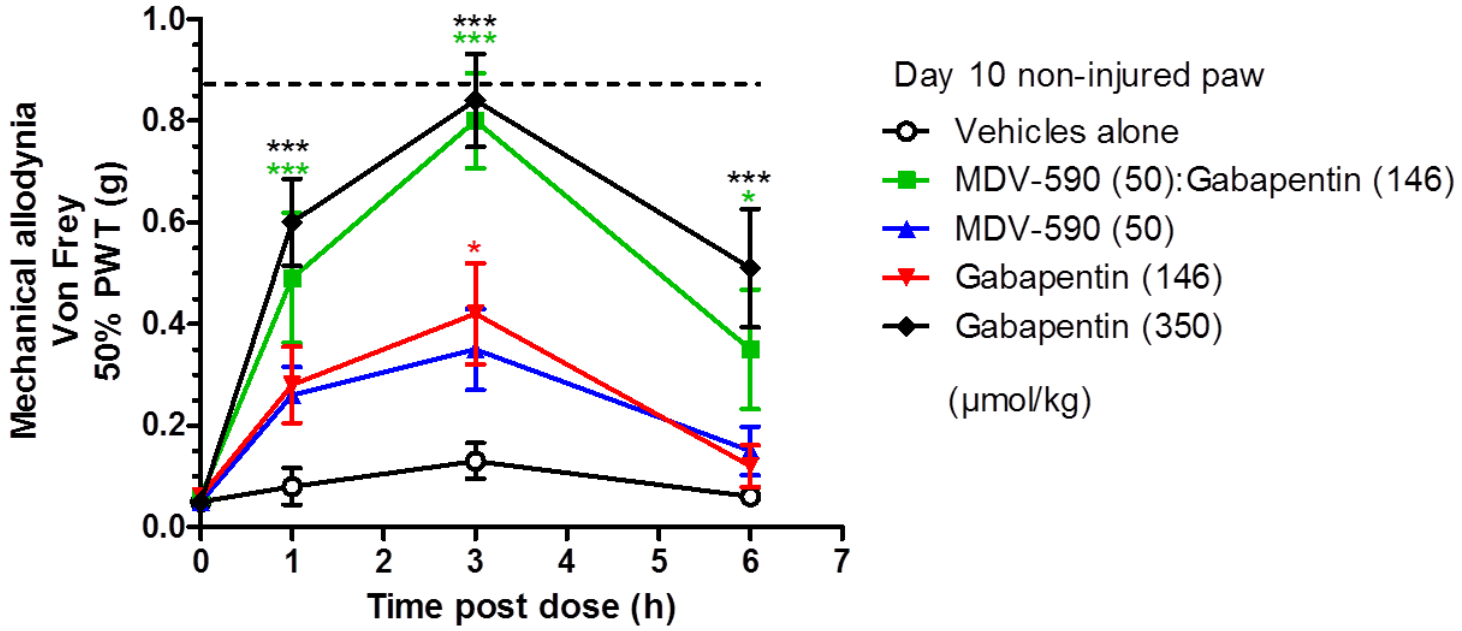
- Inhibition of Cathepsin S prevents inflammatory damage to the sensory system in the spinal cord by blocking fractalkine activation

## Cathepsin S inhibitor program

- Potent, selective and orally bioavailable inhibitors available
- Aiming for candidate drug selection in Q2 2013

# Cathepsin S inhibition – a novel mechanism for pain releaf

Combining minimal effective doses of a cathepsin S inhibitor (MDV-590) and gabapentin in a neuropathic pain model leads to synergistic effects




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

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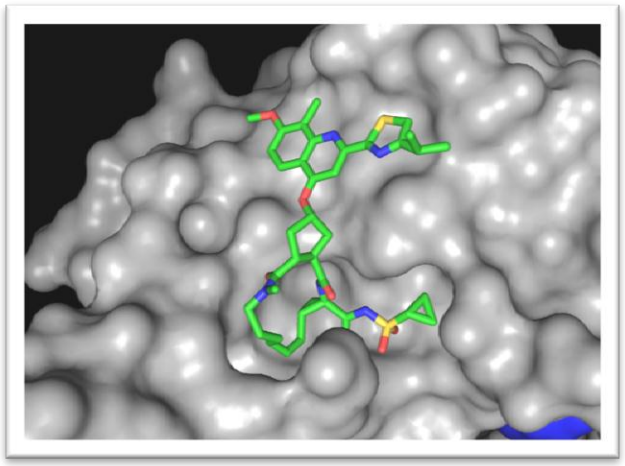
# Simeprevir (TMC435) soon to reach the market in a rapidly evolving treatment landscape

# 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**

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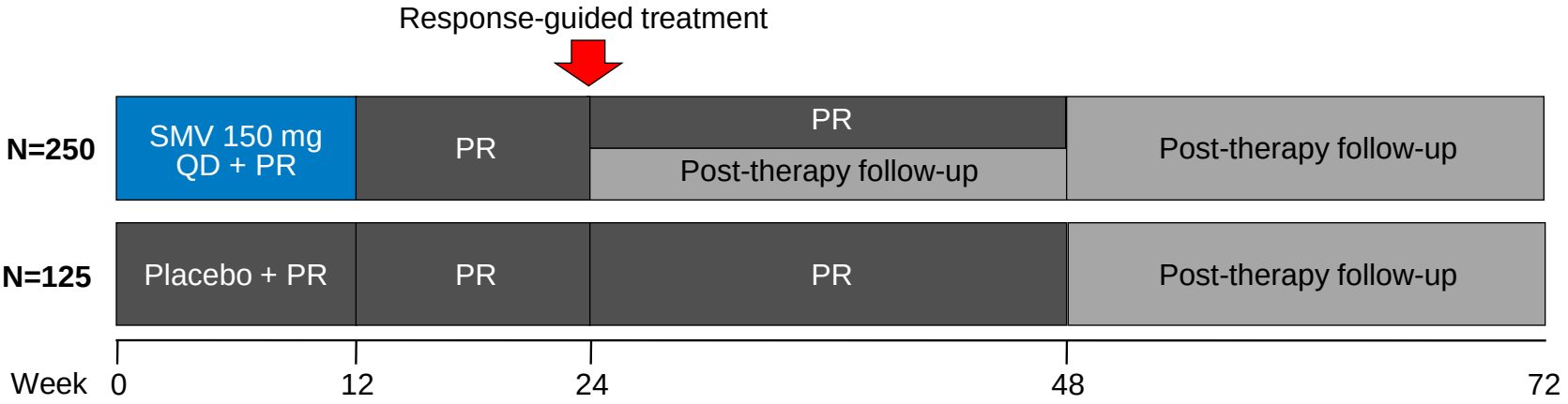
**For additional information, please see www.clinicaltrials.gov**

# 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




**PR:** PegInterferon + Ribavirin

**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 | **80** | 50 | **81** | 50 |
| SVR12 with 24 wks treatment (% pat meeting RGT criteria) | **91 (85)** | N/A | **86 (91)** | N/A |
| CC / CT / TT | **94 / 76 / 65** | 78 / 42 / 24 | **96 / 80 / 58** | 81 / 41 / 19 |
| GT1a & other / GT1b | **71 / 90** | 49 / 52 | **80 / 82** | 46 / 53 |
| F0-F2 | **83** | 60 | **85** | 51 |
| F3-F4 | **70** | 28 | **66** | 47 |

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

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# 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) |
| **Most common AEs (≥25% in SMV arm)** | | | | |
| Fatigue | 42 | 41 | 37 | 42 |
| Pruritus | 26 | 16 | 25 | 25 |
| Headache | 33 | 39 | 39 | 37 |
| Pyrexia | | | 31 | 40 |
| Influenza-like illness | | | 26 | 26 |
| **Other AEs of interest** | | | | |
| Rash (any type) | 34 | 32 | 27 | 20 |
| Anemia | 20 | 28 | 21 | 28 |

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

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# Simeprevir - Phase III triple therapy
## Summary

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

- Naive and relapser patients in three large global studies: 79-81%[1]
- Confirmed in Japan program, where high cure rates where demonstrated[2]

✓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**

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1 All three trials included hard-to-cure patients with advanced liver fibrosis/cirrhosis (METAVIR score F3-F4)
2 To be presented at an upcoming medical meeting

# 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)

***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

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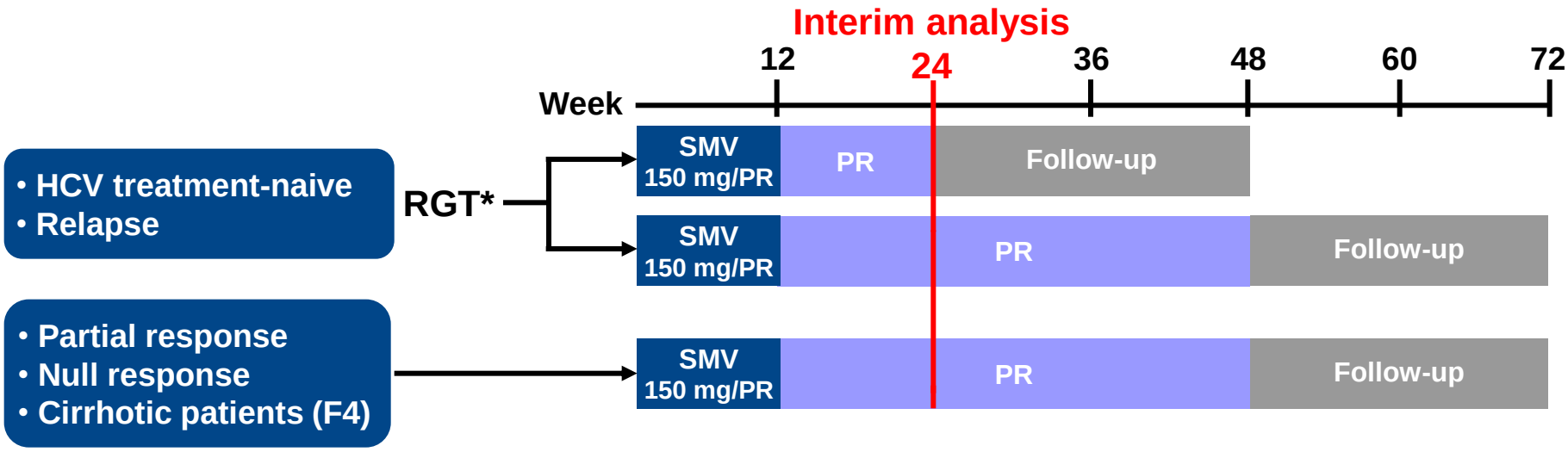
**For additional information, please see www.clinicaltrials.gov**

# C212 HCV-HIV Co-infected

## Study design



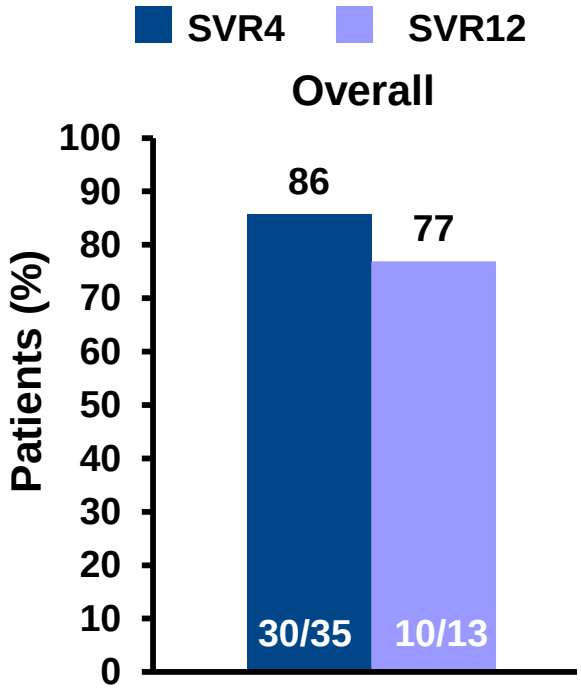

**Interim analysis:**

- **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 coinfected with HCV**

# Simeprevir

## - All oral interferon free combination update

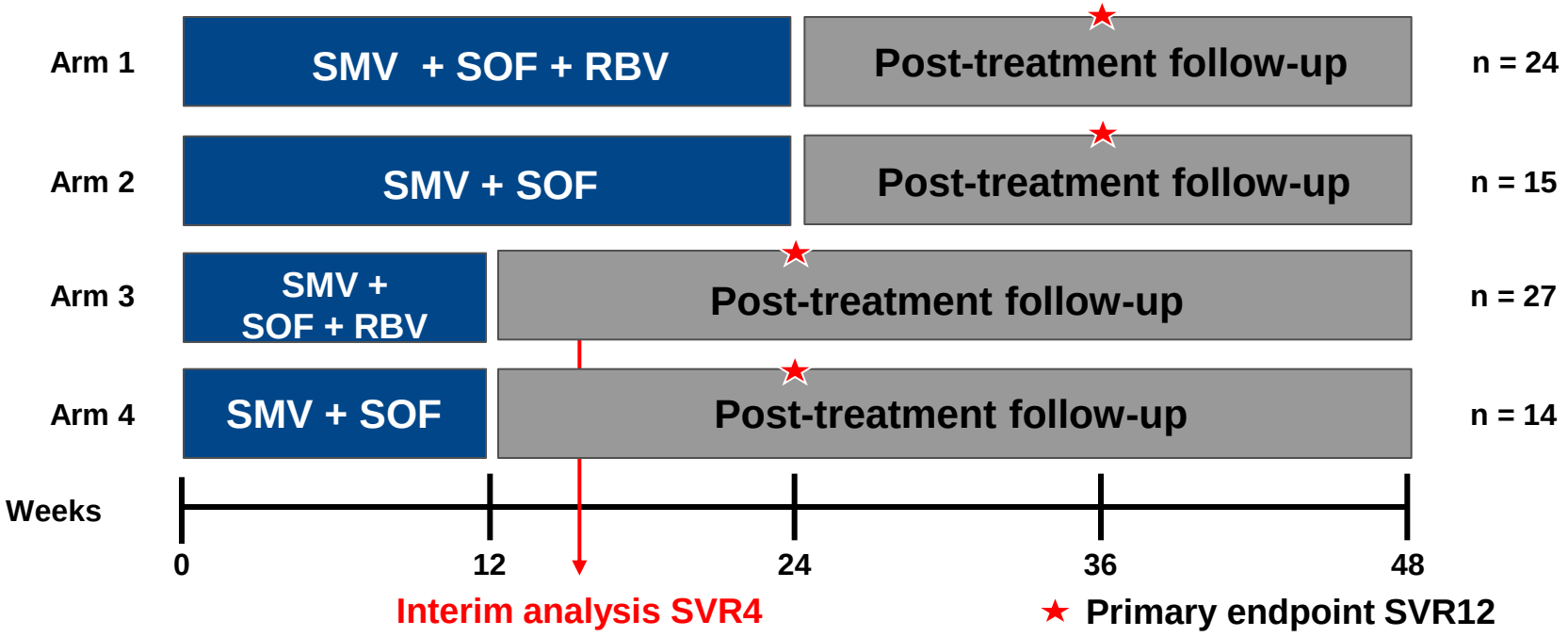
# COSMOS Study

(interim analysis)

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

*The **COSMOS** study**: CO**mbination of **SiM**eprevir and s**O**fosbuvir in HCV infected patie**ntS**

# 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**

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# COSMOS study - Baseline patient demographics and HCV disease characteristics

| Patients | | Total (n=80) |
|---|---|---|
| **Patient demographics** | | |
| Male | | 61% |
| Race | Caucasian | 71% |
| | African American | 29% |
| Ethnicity | Hispanic/Latino | 25% |
| Age, years, median | | 56.0 |
| BMI, kg/m$^2$, median | | 27.5 |
| *IL28B* | nonCC | 94% |
| **Baseline characteristics** | | |
| HCV subtype 1a | | 78% |
| HCV RNA, median, $\log_{10}$ IU/mL | | 6.8 |
| METAVIR score | F0-F1 | 41% |
| | F2 | 59% |

# COSMOS study – Efficacy results (interim analysis)

| Response rates | 12 weeks treatment | |
|---|---|---|
| | SMV + SOF+ RBV (n=27) | SMV + SOF (n=14) |
| RVR[1], n/N (%) | 23/27 (85) | 8/14 (57) |
| Undetectable end of treatment, n/N (%) | 27/27 (100) | 14/14 (100) |
| Relapse, n | 1 | 1 |
| **SVR4, n/N (%)** | **26/27 (96)** | **13/14 (93)** |
| **SVR8, n/N (%)** | **26/27 (96)** | **13/14 (93)** |

Of the patients in the **12 week arms** who achieved SVR8

– **24/24** who reached post-treatment Week 12 had achieved **SVR12**

[1]RVR is based on patients with available data at Week 4 (2 patients discontinued before Week 4)
EOT, end of treatment; RVR, rapid virologic response; SMV, simeprevir; SOF, sofosbuvir; SVR, sustained virologic response

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

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

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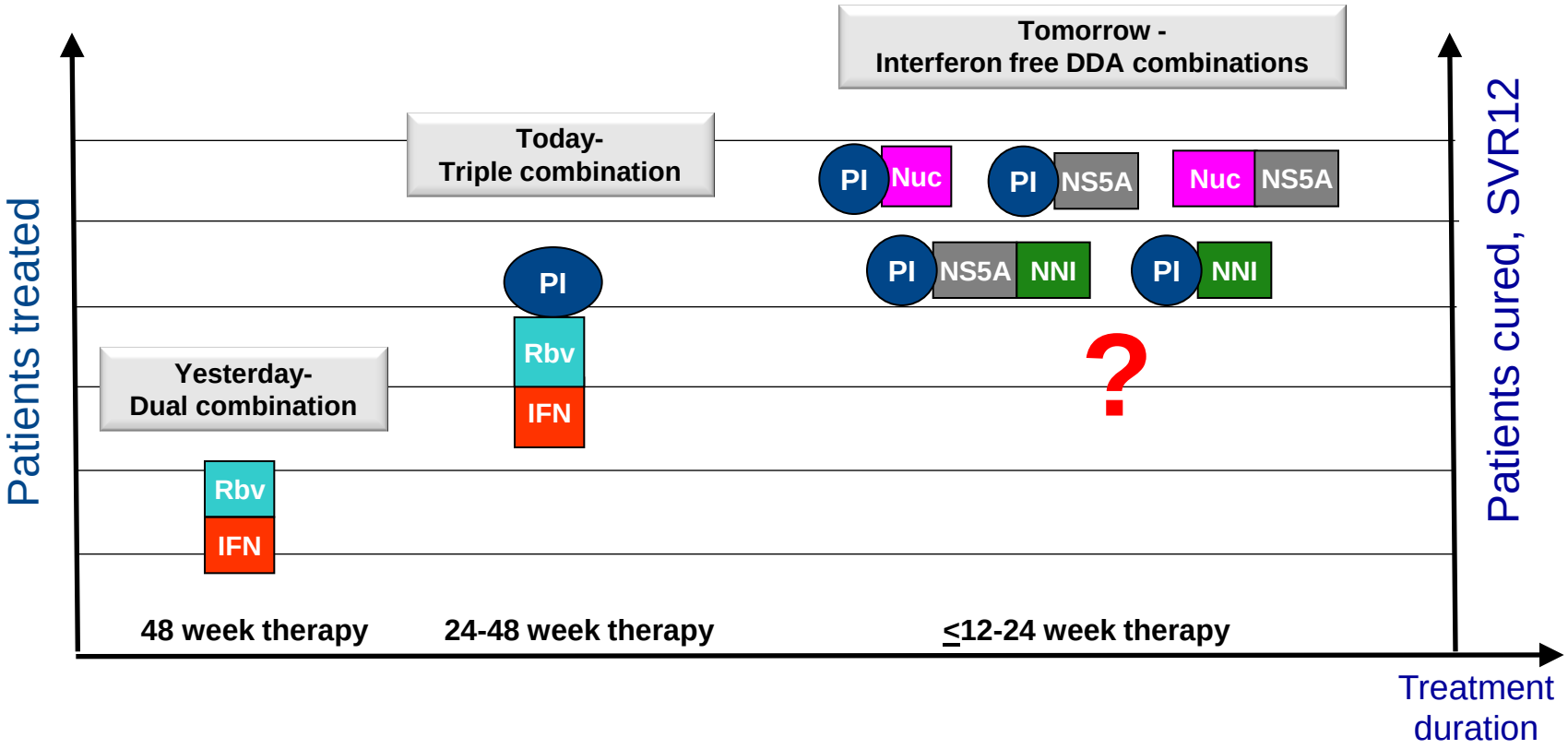
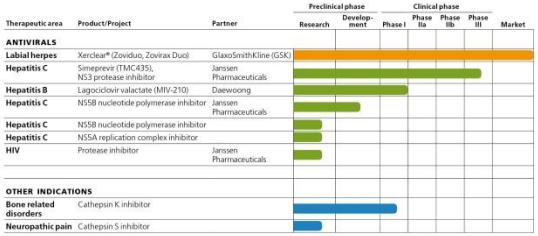
For additional information, please see www.clinicaltrials.gov

# Evolution of HCV therapy in HCV G1 infection




**Simeprevir - well positioned for triple as well as future interferon free combination therapies**

# News flow - highlights



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| **Bone related disorders** | Cathepsin K inhibitor | | | | | | | | |
| **Neuropathic pain** | Cathepsin S inhibitor | | | | | | | | |

- ✓ 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

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**For more information please contact**
**Rein Piir, EVP Corporate Affairs & IR**
**(rein.piir@medivir.com)**