

The background of the slide is a blurred image of laboratory glassware, including a beaker and a graduated cylinder, set against a light blue background. The glassware is slightly out of focus, creating a sense of depth and scientific precision.

# Medivir

*A research based specialty pharmaceutical company focused on  
infectious diseases*

**Welcome to our Capital Markets Day  
Stockholm, 15 November 2011**



# Today's program

Welcome

Introduction

Our pipeline

Hepatitis C - A rapidly evolving treatment landscape

**Break**

Our commercial platform

The Nordic HCV market

Cross Pharma

Summary

Q/A



## Today's presenters

**Rein Piir - EVP Corporate Affairs / IR**

**Maris Hartmanis - CEO Medivir**

**Charlotte Edenius - EVP Research & Development**

**Bertil Samuelsson - Chief Scientific Advisor**

**Eva Arlander - EVP Commercial**

**Birgitta Wikman Erlandson - Director Commercial  
Development & Governmental Affairs**

**Johan Frödin - CEO Cross Pharma**



# **Introduction**

**Maris Hartmanis, CEO Medivir**

# An emerging research-based specialty pharmaceutical company

- Founded in 1988 as a spinout from AstraZeneca
- Listed in 1996, traded on Nasdaq OMX Stockholm, Mid-cap list
- World leading science in infectious diseases
- TMC435, a potential blockbuster for hepatitis C, in clinical phase 3
- Project portfolio of 11 projects, of which seven are run by partners. All rights for the Nordics are reserved
- First internally developed product, the cold sore pharmaceutical Xerclear<sup>®</sup>/ Xerese<sup>®</sup>, is in launch phase
- BioPhausia was acquired in 2011 to strengthen commercial platform
  - BioPhausia - marketing and sales of original Rx pharmaceuticals
  - Cross Pharma - marketing and sales of parallel imported pharmaceuticals



# Strategy

Our goal is to become a profitable research-based specialty pharmaceutical company focusing on infectious diseases, which creates value for our shareholders and enhances patients' quality of life

- Strengthen Medivir's position in the infectious disease area through innovation based on the company's advanced protease and polymerase R&D platform
- Strengthen the commercial platform for launch of TMC435 in the Nordic region
- In-license and/or acquire additional products or product portfolios for the commercial platform



# Key innovation and commercialisation advantages



## TMC435 – Considered “best in class” hepatitis C drug

- Excellent antiviral activity and strong safety profile
- Enhanced compliance – one pill, once daily, no food interactions
- Global phase III trials ongoing
- Interferon-free combination trials will be the next major focus



## Strong pipeline in R&D

- Strong pipeline of innovative infectious disease drugs
- World class expertise in polymerase and protease drug targets



## Commercial presence and platform in the Nordics

- Strong brand names in several therapy areas
- Established commercial platform for TMC435 launch in the Nordics
- Key competence within regulatory affairs and logistics



## Xerclear® / Xerese® - global launch in 2011/2012

- Cold sore drug with an unique, differentiated profile and blue-chip marketing partners

# Weak share price performance since this summer



SSX – Stockholm Stock Exchange

Medivir

MSI Europe

Many reasons including the Euro zone problem and setbacks in some of our Nordic peer companies

# Important key messages

- Innovation within Medivir
- Many partnerships validating core R&D platform
- Hepatitis C portfolio and TMC435 shows a broad approach in hepatitis C drug development
- Commercial Nordic platform
- Our high ambition to become a profitable specialty pharmaceutical company

**A solid platform for future growth**

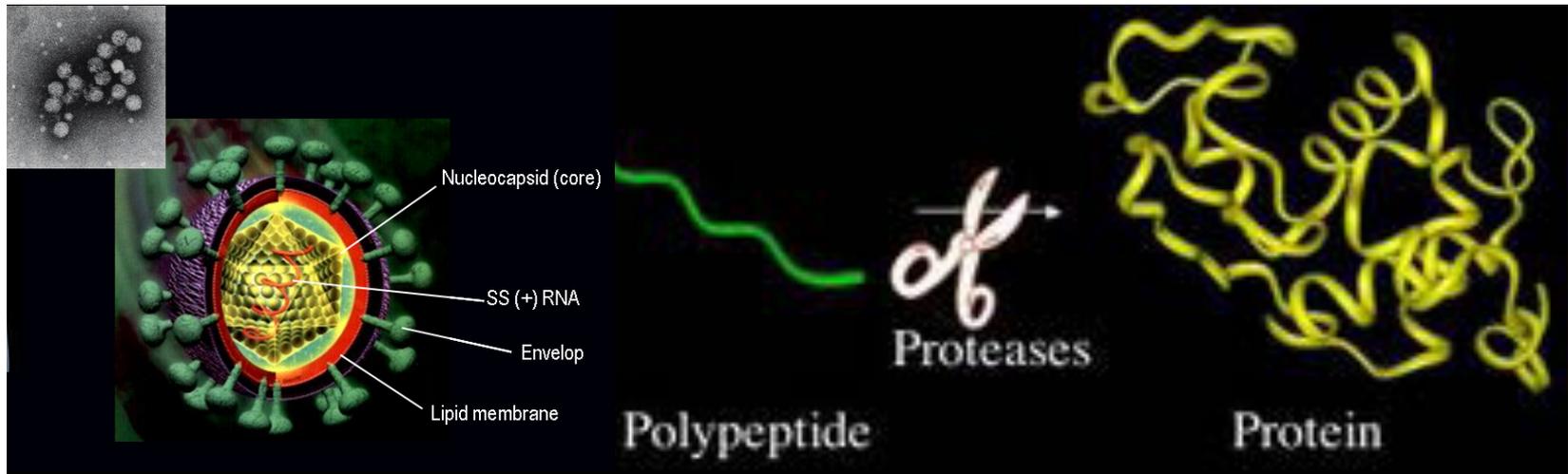


## **Our pipeline**

**Charlotte Edenius**  
**EVP Research & Development**

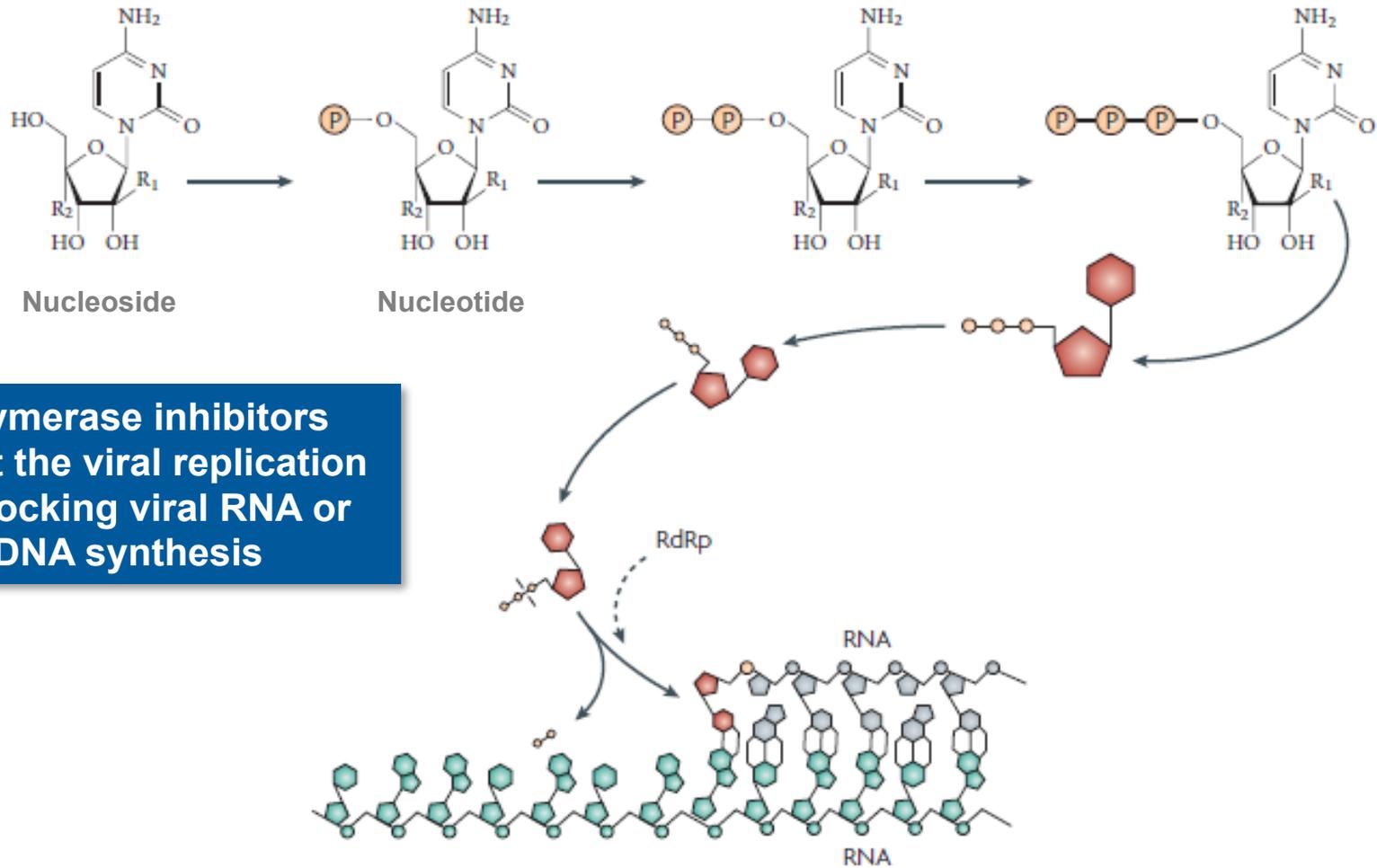
# Medivir - a leading company in the development of protease and polymerase inhibitors

**Proteases cut polypeptides/proteins to activate or inactivate their respective biological actions**

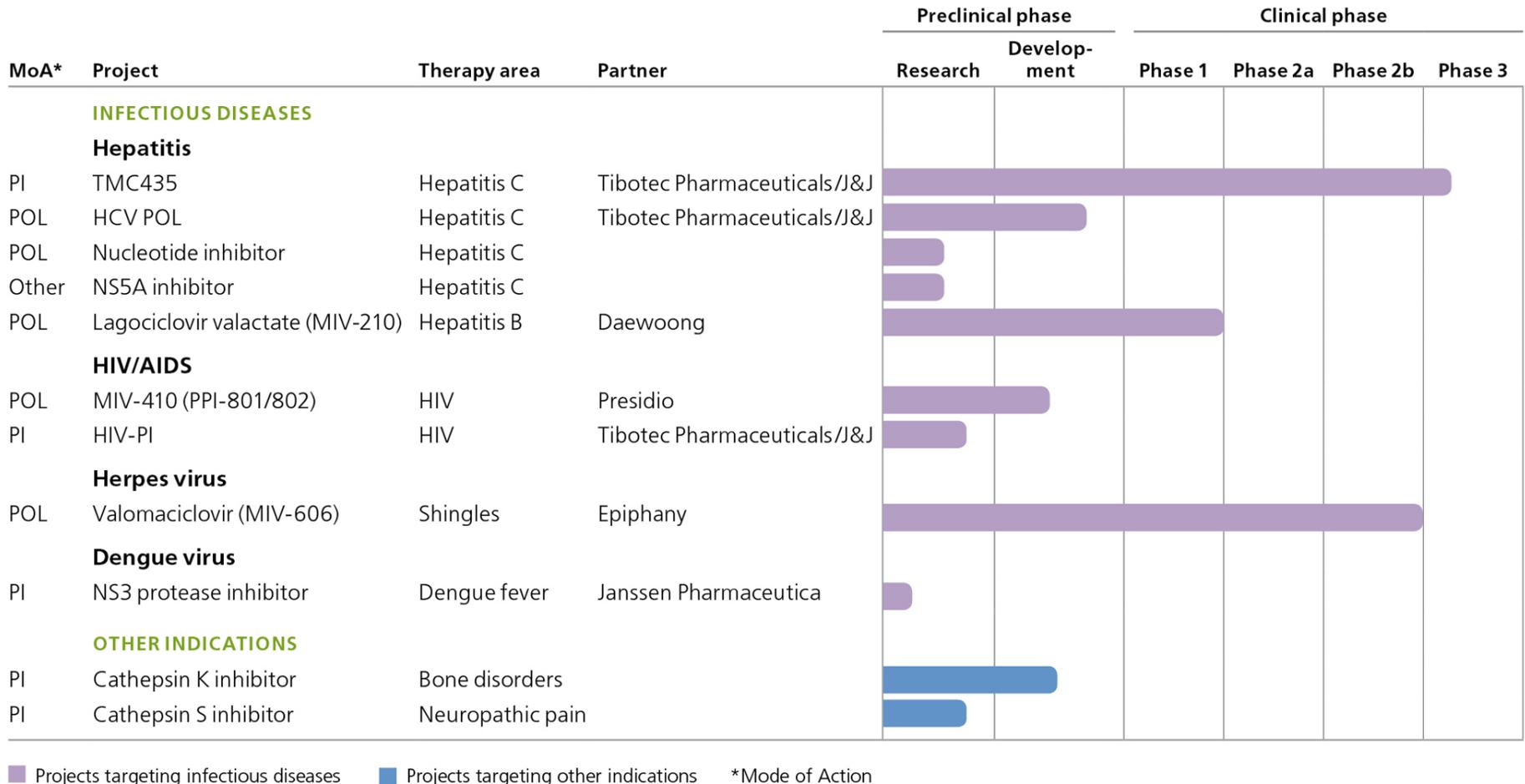


**Protease inhibitors block viral replication by blocking assembly of viral polypeptides into active viral particles**

# Medivir - a leading company in the development of protease and polymerase inhibitors



# Strong pipeline with multiple paths to value creation



# Cathepsin K inhibitors – osteoarthritis (OA) and osteoporosis

## Disease and market

- **Osteoporosis, osteoarthritis and metastatic bone disease**
- Estimated combined global market opportunity in excess of USD 12 billion

## Mechanism of Action (MoA) Cath K inhibition

- Reduced bone resorption and cartilage breakdown
- Maintained bone formation in contrast to other anti-resorptives

## Dog OA model - Results

Urinary biomarkers for bone and cartilage resorption reduced by 86% and 80% respectively ( $p < 0.001$ )

Gross scores of bone and cartilage pathology reduced by 13-37 % in OA model in dog ( $p < 0.05$ )

## Next decision point

- MIV-711 in preclinical development aiming for start of phase I clinical trials in H1 2012



**Preclinical support for beneficial effects of cathepsin K inhibition in both osteoarthritis and osteoporosis**

# Cathepsin S inhibitor – neuropathic pain and rheumatoid arthritis

## Disease and market

- Approximately 25 million patients worldwide suffer from neuropathic pain
- Estimated global market opportunity for neuropathic pain in excess of USD 2.3 billion, and rheumatoid arthritis (RA) is estimated to USD 7 billion

## MoA for Cathepsin S inhibitor

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

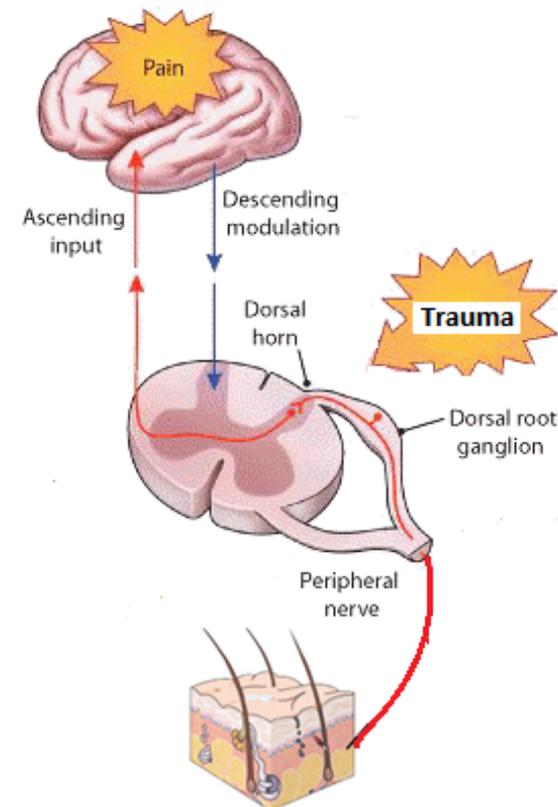
## Cathepsin S inhibitor program

- Potent, selective and orally bioavailable inhibitors developed by Medivir

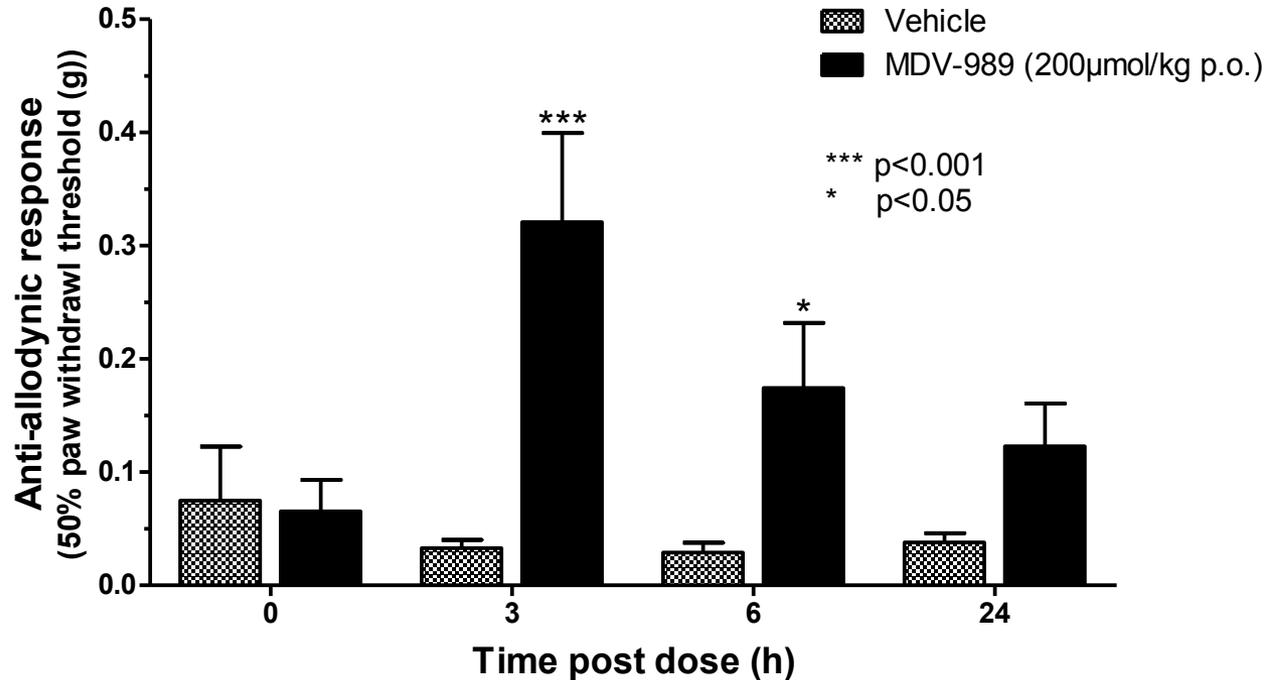
## Next decision point

- Candidate drug selection

## Principle for neuropathic pain



# Cathepsin S inhibitor efficacious in a model of neuropathic pain



**Excellent efficacy of a Medivir cathepsin S selective inhibitor in a murine neuropathic pain model**

# Dengue Fever – an increasing global threat

## Medical need and market opportunity

- Dengue virus is a mosquito-borne infection causing a severe flu-like illness, and sometimes a potentially lethal complication - dengue haemorrhagic fever
- Up to 50 million infections occur annually in over 100 endemic countries (death rate approx. 30,000/year)
- Appr. 40% of world population are now at risk<sup>1</sup>

## Development strategy

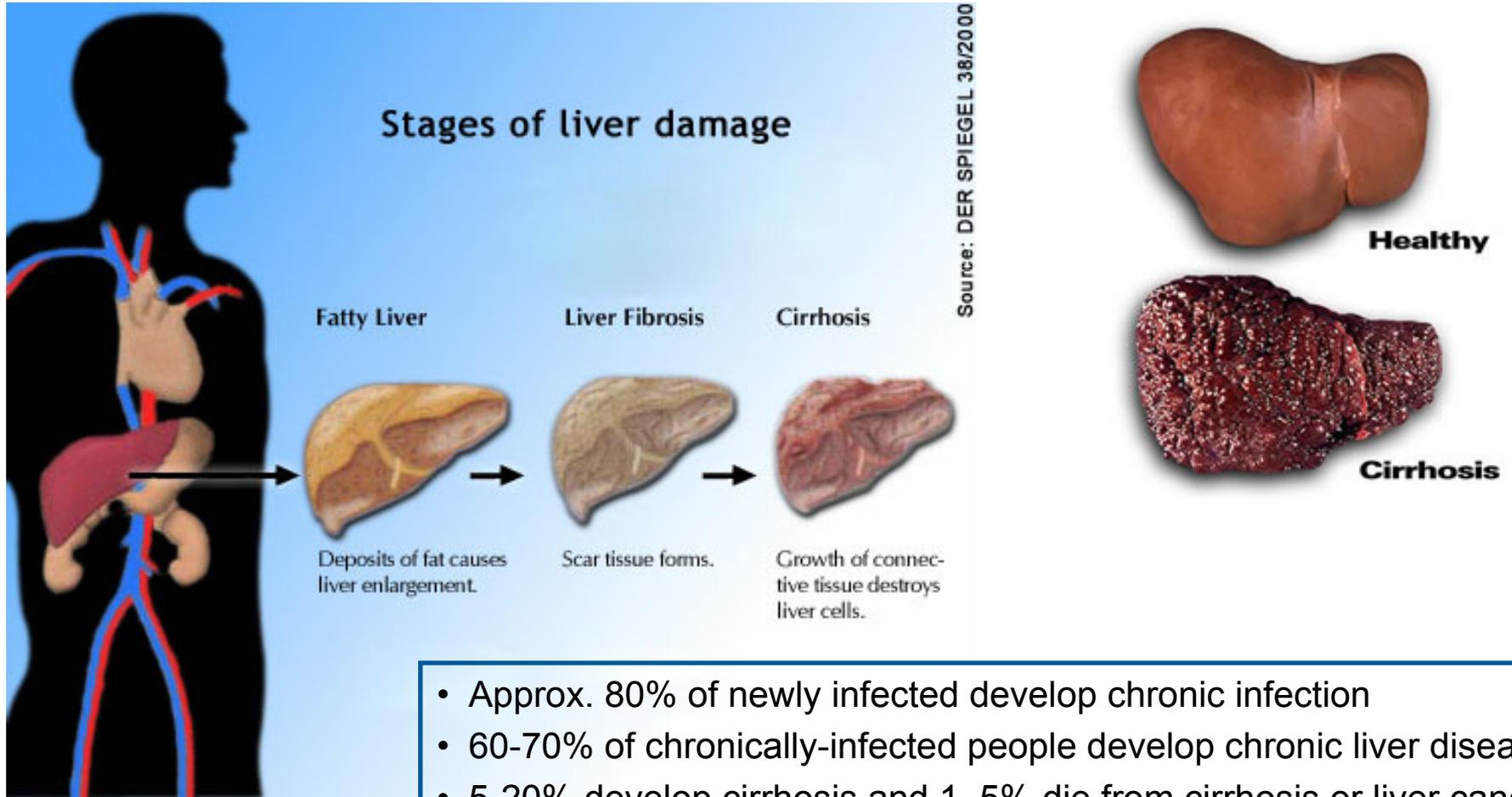
- Several viral targets exist in the dengue virus including both protease and polymerase targets, where Medivir has strong core competences
- First focus on inhibition of the dengue virus NS3 protease essential for viral replication
- Joint venture with Janssen Pharmaceutica

<sup>1</sup> World Health Organisation, Fact sheet N°117, March 2009.



# Hepatitis C

# Hepatitis C and Liver Cirrhosis



- Approx. 80% of newly infected develop chronic infection
- 60-70% of chronically-infected people develop chronic liver disease
- 5-20% develop cirrhosis and 1–5% die from cirrhosis or liver cancer

# Hepatitis C – a large and global disease

- 170 million (3-4% of world population) are estimated chronically infected with hepatitis C virus, approx. 3–4 million people newly infected by HCV each year
- Approx. 10-12 million are chronic HCV infected in the US, EU and Japan
- Over 350 000 people die from hepatitis C-related liver diseases each year
- There is still a major unmet need for novel treatments that present improved outcomes in the form of:
  - Increased viral cure rates
  - Shorter treatment durations
  - Minimal side effects

**HCV genotype-1, the most difficult-to-treat, accounts for estimated 70% of world-wide HCV infections**

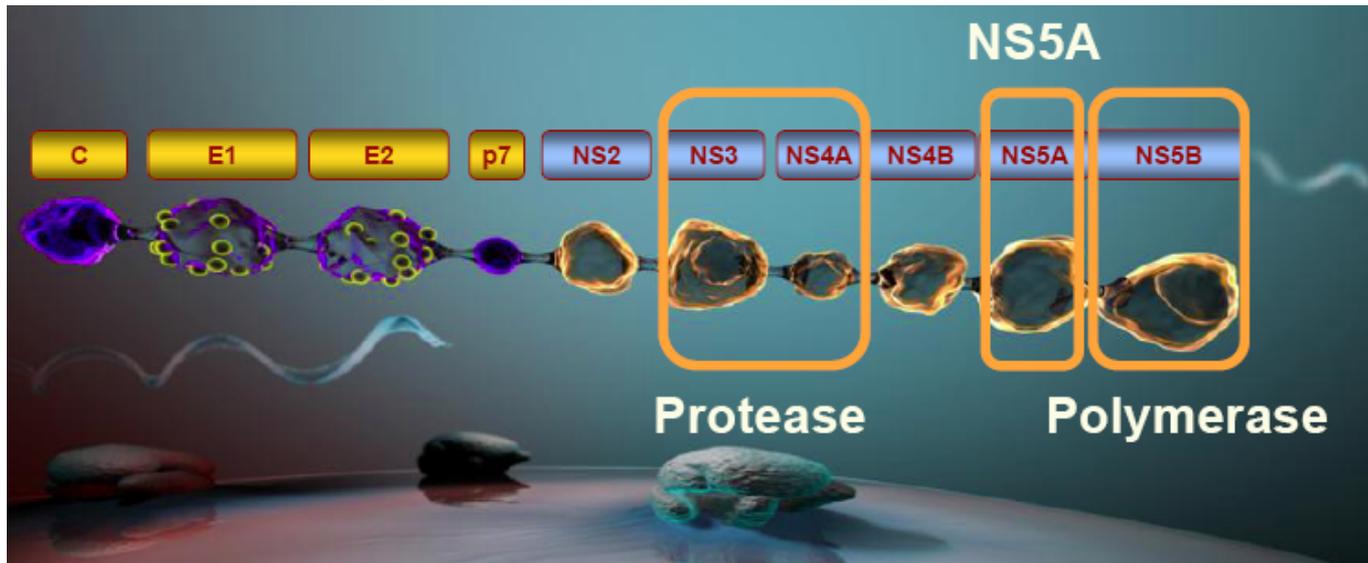


## **Our hepatitis C franchise**

Medivir is committed to building a leading position in hepatitis C

# Medivir is committed to building a leading position in Hepatitis C

Three major targets for Direct Acting Antivirals (DAAs) in HCV:



Kwong A, et al. Drug Discovery Today: Therapeutic Strategies 2006;3:211-220 Schmitz U, Tan SL. Recent Pat Antiinfect Drug Discov 2008;3:77-92

**Medivir has active programs versus all three HCV targets**

# Medivir commitment to build a leadership position in Hepatitis C

## Protease inhibitor (PI) – tibotec

**TMC435**, a potent, once-daily, safe and efficacious PI with broad genotypic coverage (1,2,4,5 and 6)

- Broad global phase III development program ongoing in genotype 1 infected patients

## Polymerase inhibitors – tibotec

A nucleoside/nucleotide inhibitor program

## Polymerase inhibitors – In-house/unpartnered

A novel liver targeting nucleotide inhibitor program

## NS5A inhibitors – In-house/unpartnered

A next generation NS5A inhibitor with high barrier to resistance

# The joint polymerase inhibitor program

## The Nucleoside program - TMC649128

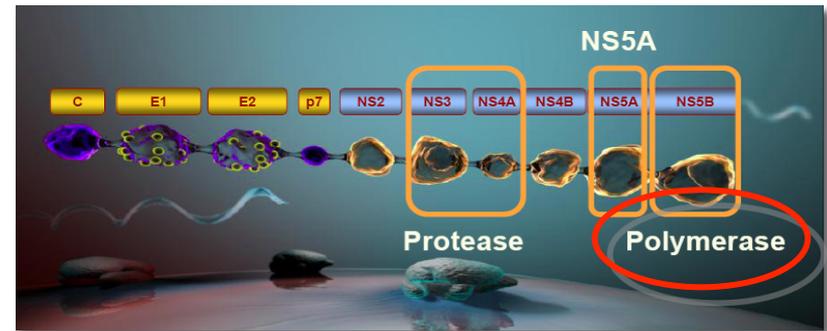
The first polymerase inhibitor under the collaboration entered clinical development (Q1-11)

- In Phase I TMC649128 was safe and well tolerated, but did not meet the target product profile with regards to efficacy in HCV genotype I infected patients
- Clinical development discontinued
- Full focus on nucleotide program

## The Nucleotide program: Clinical Candidate selected

A next generation, liver targeted nucleotide polymerase inhibitor program as part of this partnership

- Clinical Drug (CD) selected
- In preclinical development - approaching clinical development



# In-house hepatitis C related programs

## Polymerase nucleotide inhibitors – in-house/unpartnered

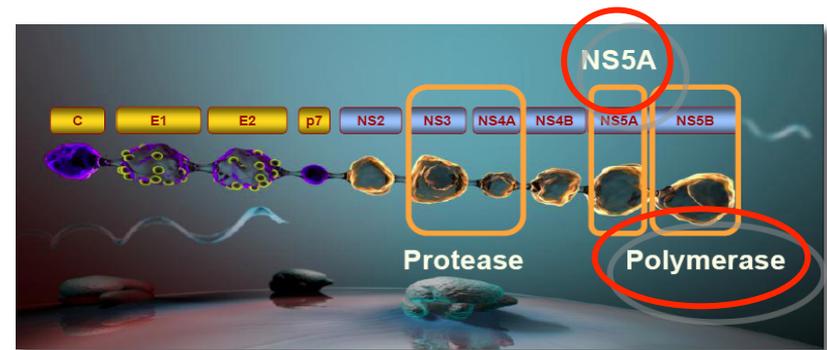
A novel liver targeting nucleotide inhibitor program - in preclinical phase

## NS5A inhibitors – In-house/unpartnered

A next generation NS5A inhibitor with high barrier to resistance - in preclinical phase

## Additional HCV activities

- Host factors as therapeutic targets
- Pharmacological tools and models





## **TMC435**

**The once-daily, safe and  
efficacious protease inhibitor**

# Commercializing TMC435 – our core product



- **Favorable safety profile**, comparable with placebo in phase IIb clinical trials
- **Excellent anti-viral efficacy**, shown in phase IIb program
- **High convenience**, one-pill, once-daily treatment
- **Broad regulatory filing in H1-2013**, all Phase III clinical trials fully enrolled

# TMC435 – Broad clinical development program in HCV genotype 1 infected patients

## Phase IIb

**PILLAR (C205)** n=386  
G1 infected treatment-naïve patients

**DRAGON (C215)** n=92  
G1 infected treatment-naïve patients in Japan

**ASPIRE (C206)** n=462  
G1 infected *treatment-experienced* patients

## Phase III

**QUEST1 and QUEST2**  
n=375 per study  
G1 infected treatment-naïve patients

**PROMISE (C3007)** n=375  
G1 infected *prior relapsed* patients

**Japan phase III program**  
Genotype-1 infected *naïve and treatment experienced* patients (four studies)

**C3001**  
Genotype-1 infected *prior partial and null responders*  
To be initiated

## IFN free combinations

**TMC435 and TMC647055**, a non-nucleoside NS5B inhibitor developed by Tibotec Pharmaceuticals

**TMC435 and PSI-7977\***, a nucleotide NS5B inhibitor. A Phase II, interferon-free, 12 or 24 weeks, +/- ribavirin PoC study in G1 prior null responders

**Others to be communicated**

For additional information please see [www.clinicaltrials.gov](http://www.clinicaltrials.gov)

**Regulatory filings anticipated H1-2013**



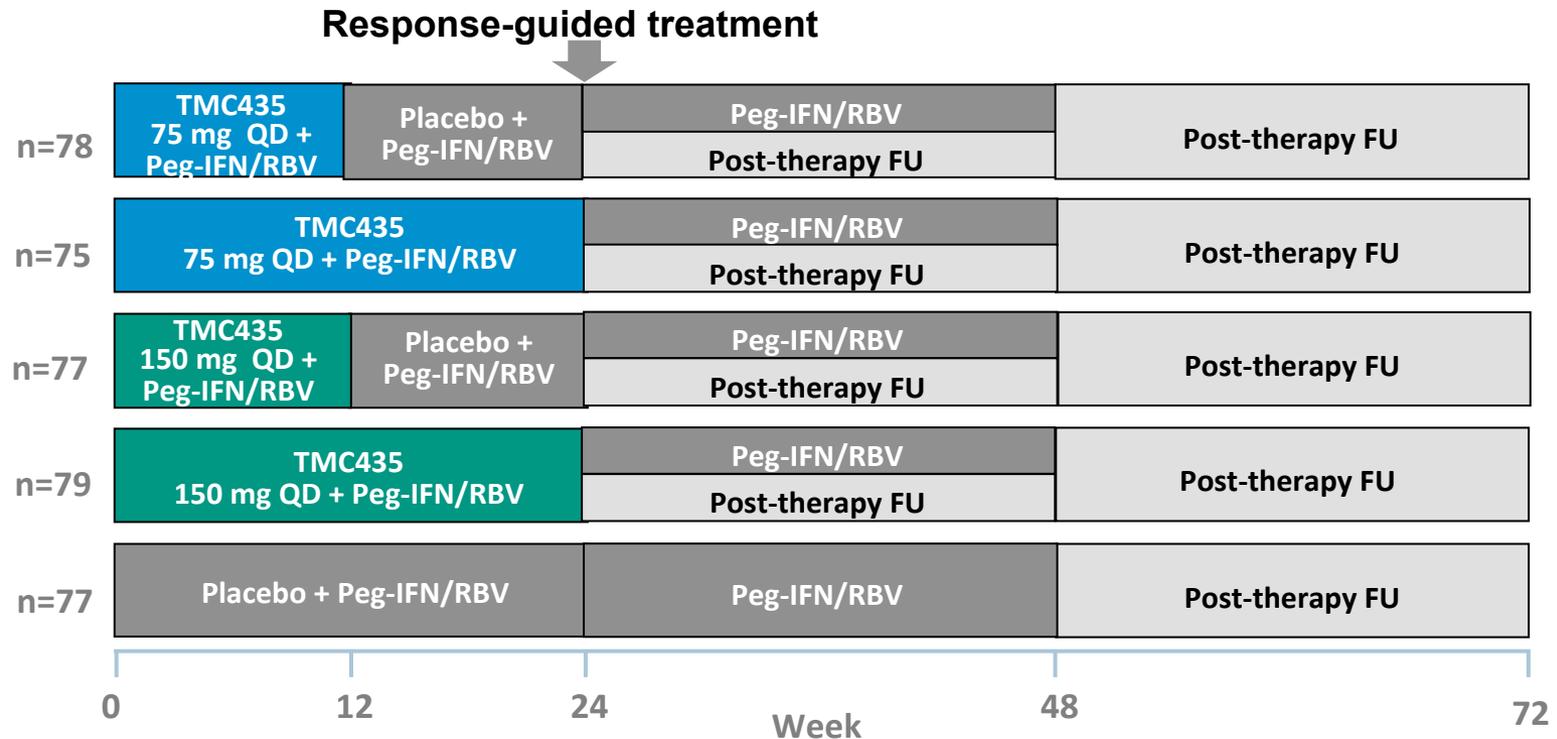
# **TMC435**

## **Clinical phase IIb results**

# TMC435 Phase IIb (PILLAR) in treatment naïve patients - *study design*

**Patients:** 386 HCV genotype I infected patients

**Dosage:** Once daily TMC435 (75 or 150 mg) added to PegIFN/RBV for 12 or 24w



# TMC435 Phase IIb (PILLAR) in treatment naïve patients - *efficacy results*

Response % (n/N)	TMC435 150 mg 12W P/R RGT N=77	TMC435 150 mg 24W P/R RGT N=79	Placebo 48W P/R N=77
RVR <sup>1</sup>	75(58/77)	75 (59/79)	5.2 (4/77)
EOT <sup>2</sup>	92 (71/77)	94 (74/79)	79 (61/77)
<b>SVR24<sup>3</sup></b>	<b>81 (62/77)*</b>	<b>86 (68/79)**</b>	<b>65 (50/77)</b>
Viral relapse	8.7 (6/69)	8.0 (6/75)	18 (11/62)

\*  $p < 0.05$ , \*\* $p < 0.005$ , significant difference versus placebo control; P/R, peginterferon  $\alpha$ -2a + ribavirin; RGT: Response guided treatment

- 81-86% SVR24 rates in TMC435 (150 mg) dose arms
- 79-86% of patients could shorten IFN/RBV-treatment duration from 48 to 24 weeks and 93-96% of these achieved SVR24

# TMC435 Phase IIb (PILLAR) in treatment naïve patients - *safety & tolerability results*

Number of subjects with AE: n (%)	All TMC435 N=309	Pbo/P/R 48W N=77
AE leading to permanent stop of TMC435/Pbo & PegIFN/RBV	11 (3.6)	4 (5.2)
Grade 3 or 4 AE	99 (32.0)	27 (35.1)
Serious AE	20 (6.5)	10 (13.0)
Five most common AEs		
Fatigue	131 (42.4)	37 (48.1)
Influenza-like illness	98 (31.7)	29 (37.7)
Pruritus	96 (31.1)	35 (45.5)
Headache	142 (46.0)	40 (51.9)
Nausea	86 (27.8)	21 (27.3)
AEs of interest		
Rash (any type)	65 (21.0)	18 (23.4)
Anemia	63 (20.4)	16 (20.8)
Neutropenia	75 (24.3)	16 (20.8)

No difference between TMC435 and placebo groups in incidence of:

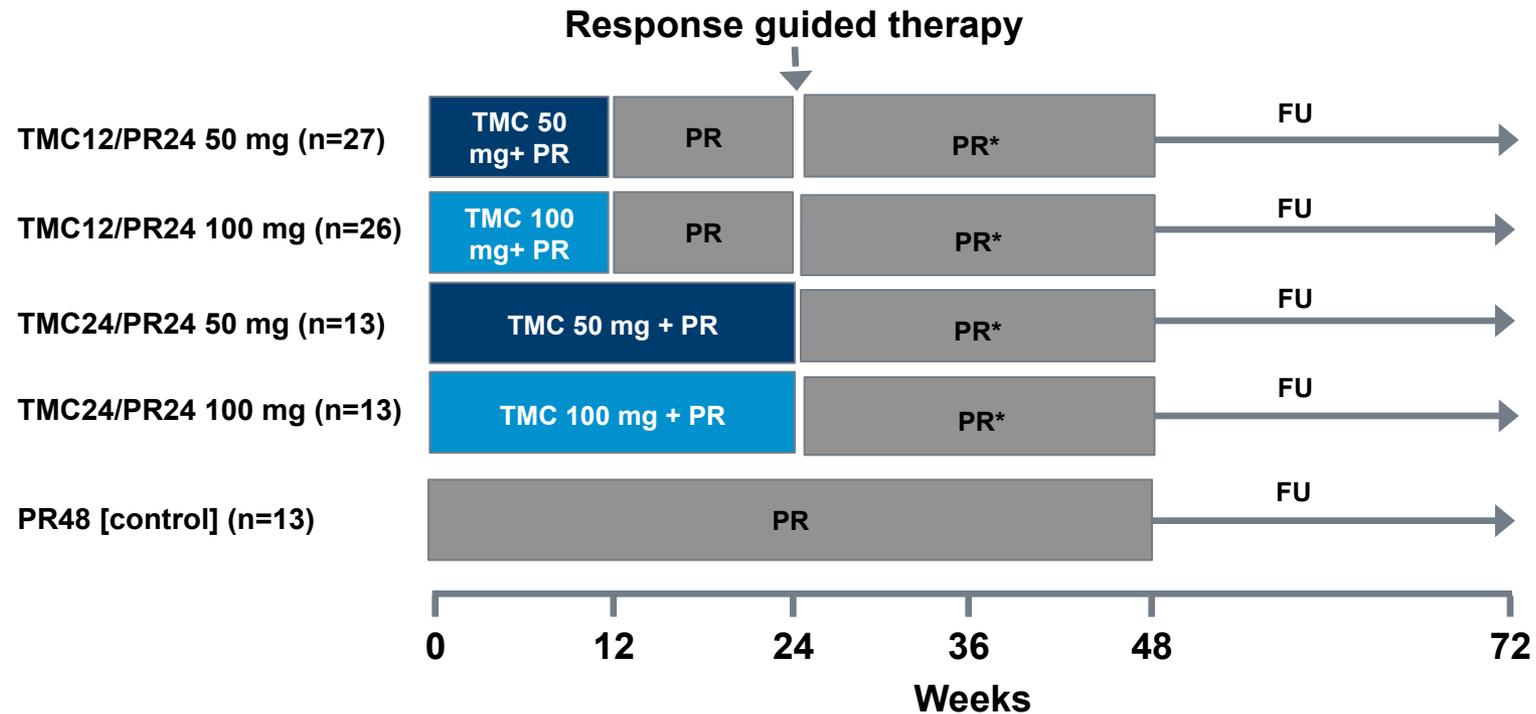
- AEs leading to discontinuations
- SAEs
- Grade 3 or 4 AEs or
- rash, anemia, or neutropenia

**TMC435 was safe and well tolerated at all doses and durations**

# TMC435 Phase IIb (DRAGON) in treatment naïve Japanese patients - *study design*

**Patients:** 92 HCV genotype I infected patients in Japan

**Dosage:** Once daily TMC435 (50 or 100 mg) added to PegIFN/RBV for 12 or 24w



# TMC435 Phase IIb (DRAGON) in treatment naïve Japanese patients - *study design*

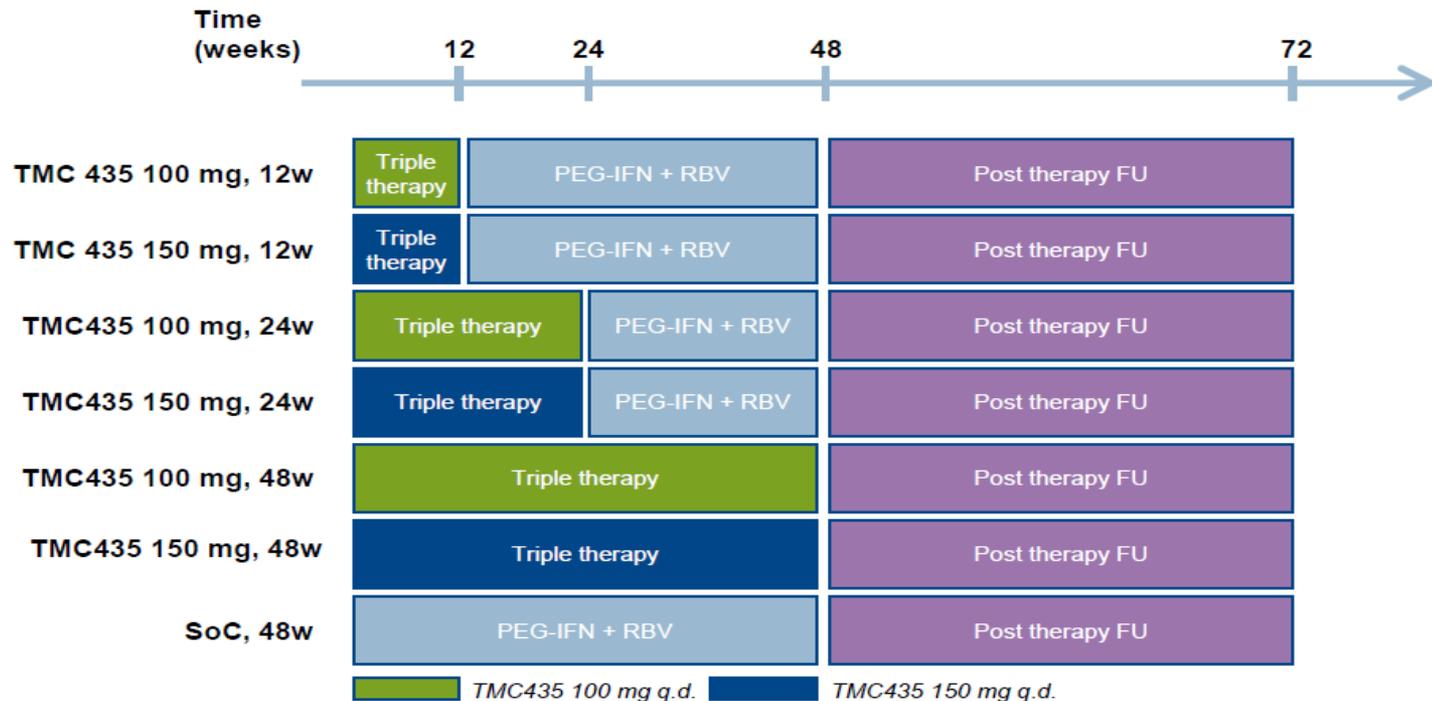
- **82% of patients achieved SVR24** in the 100 mg TMC435 versus 46% in the placebo control group
- **87% of patients received shortened treatment** duration of 24 weeks based on RGT criteria,
- TMC435 was safe and well tolerated

**Phase III clinical trials well underway in Japan (fully enrolled) in both treatment naïve and treatment experienced patients**

# TMC435 Phase IIb ASPIRE study in genotype 1 treatment experienced patients\* - *study design*

**Patients:** 462 HCV genotype 1 infected prior relapser, partial or null responder patients

**Dosage:** Once daily TMC435 (100 or 150 mg) added to PegIFN/RBV for 12, 24 or 48 weeks in combination with PEG-IFN/RBV



# TMC435 Phase IIb ASPIRE study in genotype 1 treatment experienced patients\* - *results*

SVR24 in TMC435 (150 mg q.d.) vs placebo dose groups					
% (n/N)	TMC435 <b>12w</b> PR48 N=66	TMC435 <b>24w</b> PR48 N=68	TMC435 <b>48w</b> PR48 N=65	<b>All TMC435</b> PR48 N=199	<b>Placebo</b> PR48 N=66
<b>Relapser</b>	77 (20/26)	89 (24/27)	89 (23/26)	<b>85</b> (67/79)	<b>37</b> (10/27)
<b>Partial Responder</b>	65 (15/23)	75 (18/24)	86 (19/22)	<b>75</b> (52/69)	<b>9</b> (2/23)
<b>Null Responder</b>	53 (9/17)	41 (7/17)	59 (10/17)	<b>51</b> (26/51)	<b>19</b> (3/16)

\*62 % of patients (287/462) had advanced liver disease (Metavir F2-F4)

- TMC435 once daily at 150 mg induced high SVR24 rates in prior partial and null responders
- TMC435 was safe and well tolerated

# TMC435 Phase IIb program in HCV G1 infected patients - *summary*

Study	Patient population	SVR24	IFN/RBV treatment shortened from 48 to 24 weeks
<b>PILLAR</b>	Treatment naive	<b>81 - 86%</b>	<b>79 - 86%</b>
<b>DRAGON</b>	Treatment naive (Japan)	<b>82%</b>	<b>87%</b>
<b>ASPIRE</b>	Relapsers	<b>85%</b>	-
	Partial responders	<b>75%</b>	-
	Null responders	<b>51%</b>	-

## TMC435 added once daily to PegIFN/RBV treatment

- Is safe and well tolerated
- Significantly increases cure rates (SVR24) in HCV G1 infected patients



# **TMC435**

**Phase III programs and other  
clinical activities**

# TMC435 – Phase III clinical development program in HCV G1-infected patients

## QUEST 1 (C208) and QUEST 2 (C216)

- 375 x 2 *treatment-naïve* patients
- Once daily 150 mg TMC435 for 12 weeks plus IFN/RBV, RGT
- Primary endpoint: SVR12 (*as recently agreed with FDA*)

## PROMISE (C3007)

- 375 *treatment-relapsed* patients per study
- Once daily 150 mg TMC435 for 12 weeks plus IFN/RBV, RGT
- Primary endpoint: SVR12 (*as recently agreed with FDA*)

## Japan

- Four separate studies in naïve and treatment experienced patients including prior partial and null responders, all RGT

## C3001 (To be initiated)

- *prior partial and null responder* patients
- Non-inferiority study TMC435 (150 mg, once daily) vs telaprevir (750 mg every 8 hours)
- Primary endpoint SVR12 (*as recently agreed with the FDA*)

All studies fully enrolled in Aug 2011

Regulatory filing for HCV G1-infected patients anticipated H1-2013

# TMC435 – embarking on IFN (and ribavirin) free development programs

## C2002

### A Phase II Trial of TMC435 in Combination With PSI-7977\* in Prior G1 Null Responders to Peg-IFN/RBV, Hepatitis C-Infected Patients

- 180 prior null responder HCV G1-infected patients
- Four arms: 12 or 24 weeks and +/- ribavirin
- Primary endpoint SVR12
- Status: To be initiated in a near future

# TMC435 – Robust clinical data package in HCV G1-infected patients

- More than 3 years clinical experience in HCV G1-infected patients\*
- Significantly higher SVR rates in all patient populations studied in phase IIb, when added to IFN/RBV
  - In treatment naïve
  - In treatment experienced, including null responders
  - Including patients with advanced liver disease
  - In Japan
- Very good safety and tolerability profile – no additional AEs
- One pill, once-daily – “convenience translates into compliance”

**Regulatory filing for the treatment of HCV genotype-1 infected patients anticipated H1-2013**



# **Hepatitis C - A rapidly evolving treatment landscape**

**Bertil Samuelsson, Chief Scientific Advisor**

# Hepatitis C

## Disease Background

- HCV is a large and global disease
- HCV genotype-1, the most difficult-to-treat, accounts for estimated 70% of world-wide HCV infections and even higher, ~75%, in US/EU
- Approx. 10-12 million are chronic HCV infected in the US, Europe and Japan
- Recent estimates (S. Saab, *et al*, Liver International 2011) suggest that a more accurate rate of chronic infection in the US is 5.2 million, up from the current estimate of 3.2 million.

# New treatments beyond Incivek and Victrelis

## The Big Bang in hepatitis C

### Current Disease Management of HCV Genotype-1

- Incivek and Victrelis
  - Approved in 2011 in G1 patients in combination with “SoC”, a weekly injectable pegylated interferon (PegIFN) and twice-daily oral ribavirin (RBV) for up to 48 weeks
  - US prices for Incivek™ is 49,200 USD and Victrelis™ 26,400-48,400 USD
  - Cost of PegIFN/RBV based therapy ~ 30k USD for a 48 week treatment
- Significantly increased cure rates in the HCV genotype 1, 66-79% versus 40-50% for SoC
- However, they leave **significant room for improvement!**
  - PegIFN/RBV are associated with severe side effects
  - Compliance for treatment reduced by:
    - 3 times daily dosing and high doses (over 2g drug per day)
    - Additional side effects (severe pruritus, severe rash, severe anemia, nausea and vomiting)
    - 21-34% still not cured

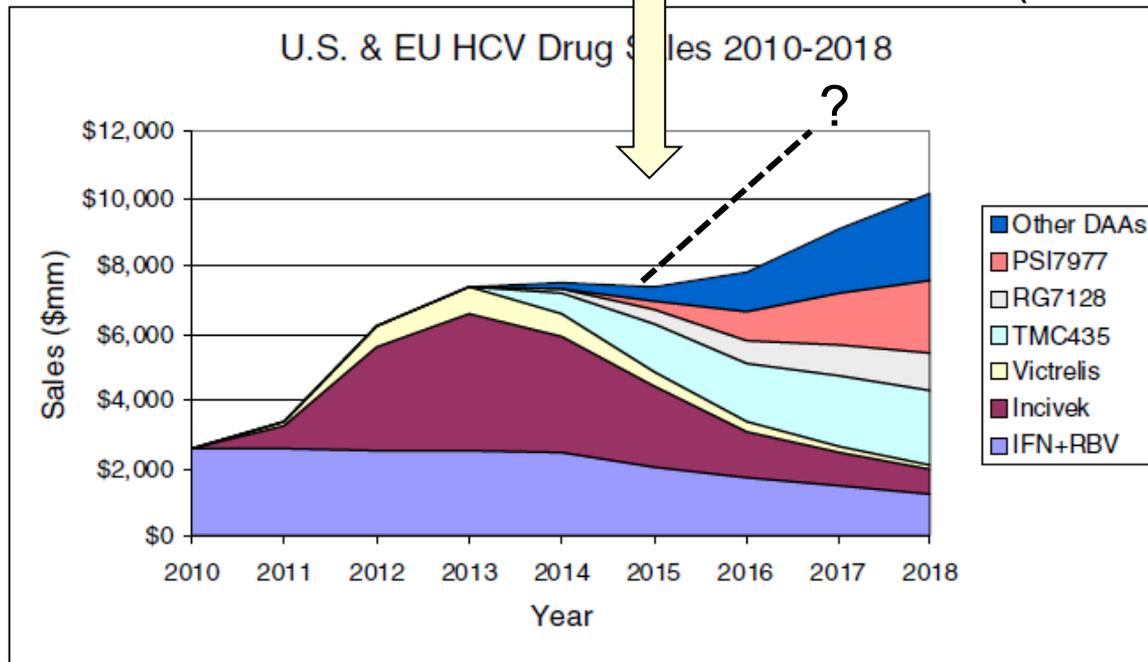
# The Big Bang in Hepatitis C

Introduction of new competitive all-oral PegIFN-free treatment regimens, would be the largest driver for an increased market by triggering:

- increased treatment rates
- increased diagnosis rates
- new pool of eligible treaters

Introduction PegIFN-free?

Exhibit 1: We Explosive Growth in the HCV Drug Market (18% CAGR from 2010-2018) (Ex. JPN)



Source: Credit Suisse 2011

- The market is expected to more than triple over the next 3-4 years
- Next stage in market expansion is triggered by introduction of PegINF free therapies

# Evolution of patient treatments in HCV

The market is expanding and in several phases

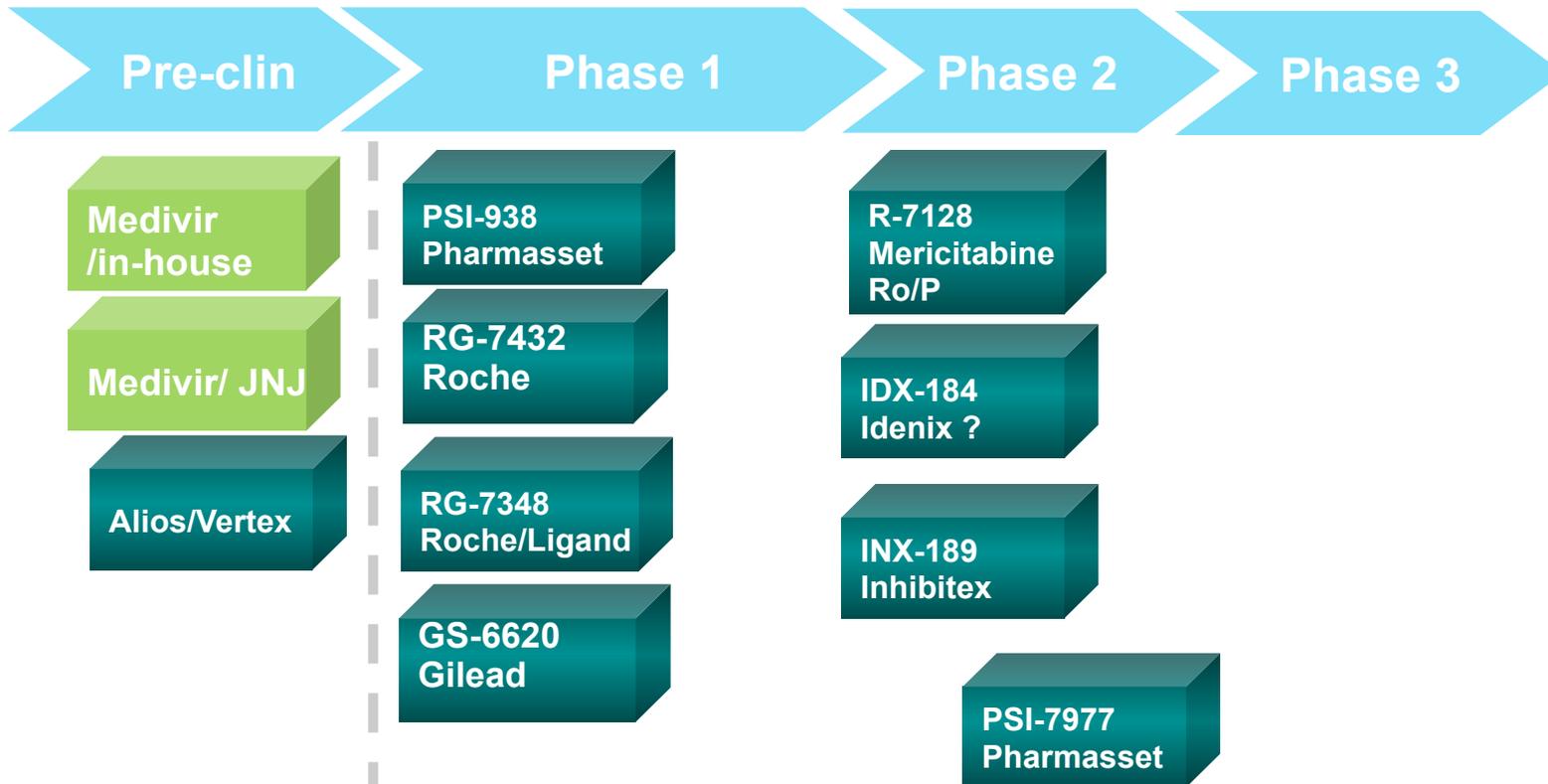
US data	2010	2015	2020
Treated total	50k	92k	120k
Naïves	30k	-	70k
Experienced	20k	-	50k
Influx new patients	19k	increase	increase

- **Early market growth:**
  - Driven by improved treatment options for the large “in waiting” experienced population, ~700k in the US, Europe and Japan (~300K in the US)
- **Market growth in later years:**
  - Driven by the huge treatment naïve patient population, HCV PegIFN-ineligible, deferred patient segments and new treatment experienced patients
- **Increased diagnosis rate will be key for sustainable market growth**



# **Competitive Environment & Evolution of HCV Therapy**

# HCV Nucleosides & Nucleotides – Competitive landscape



The transformation of clinical HCV polymerase landscape:  
Nucleosides, with high failure rates, replaced by liver targeted nucleotides

# Hepatitis C Protease Inhibitors

## - The competitive landscape



# Hepatitis C Protease Inhibitors in combinations

## - The competitive landscape

### HCV PI's in combination with DAAs and SoC

- Example of combinations of DAA agents:
  - TMC435 + PSI-7977 (NI)
  - TMC435 + XXX
  - Telaprevir + VX-222 (NNI)
  - Danoprevir + R7128 (NI)
  - BMS650032 + BMS790052 (NS5A inh)
  - GS9256 + GS-9190 (NNI)
  - GS9265 + GS9451
  - ABT450 + ABT333 (NNI)/ABT072 (NNI)

Note: danoprevir and ABT-450 require ritonavir-boosting

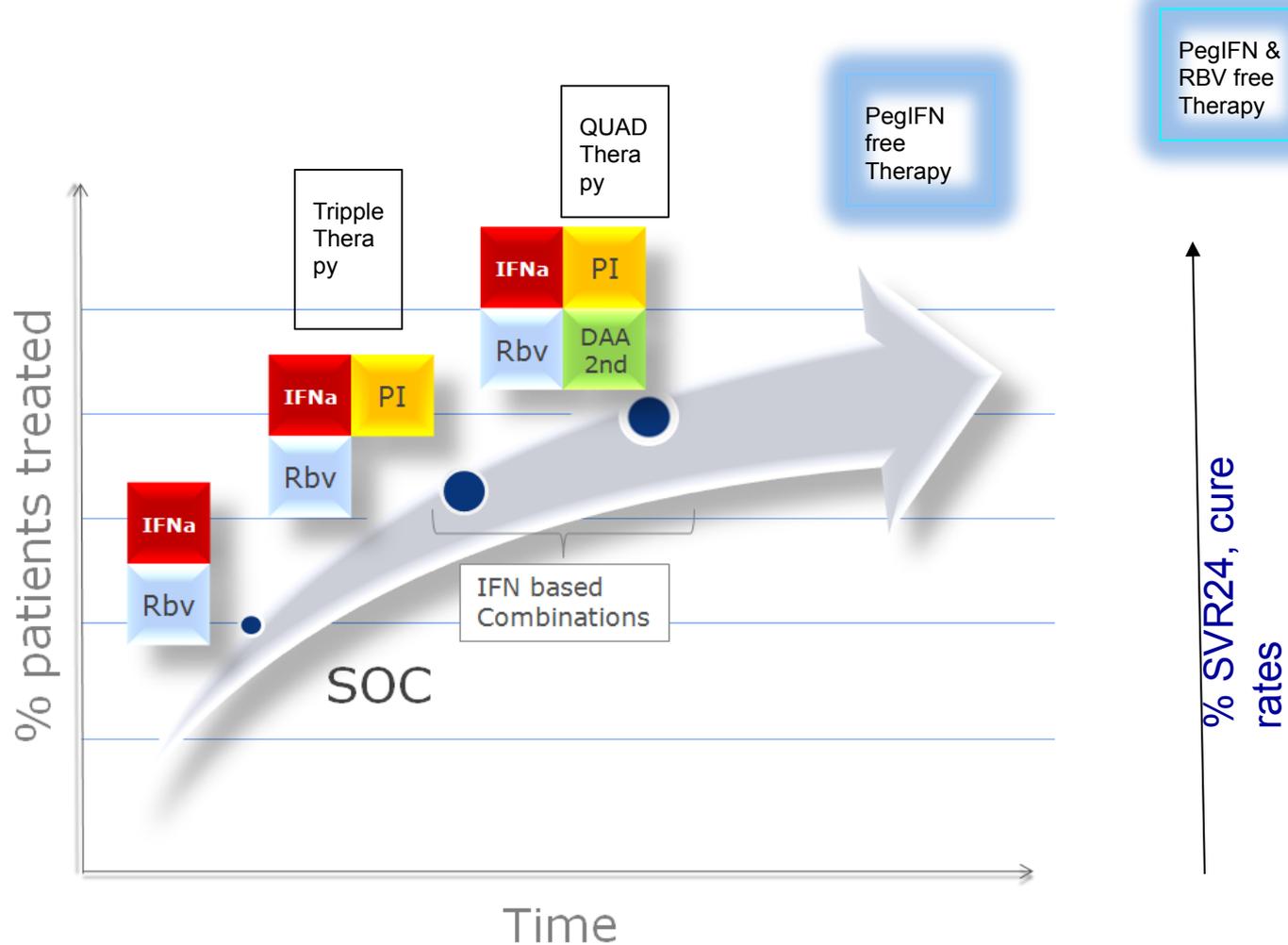
### Conclusion:

**HCV PIs are viewed as a key component  
of new combination treatments.  
TMC435 is the leading next generation HCV PI**

# HCV genotype-1 infection is the most common and has the poorest treatment prognosis

- There are six main genotypes, G1-G6:
- **Genotype 1** infection is the most common, and accounts for > 70% of worldwide HCV infections and ~75% in the US, EU and JPN.  
Genotype 1 chronic infection is also the most difficult to treat and to cure
- **Genotype 1** cure rates (SVR) are very poor, only ~45%, with PegINF/RBV after 48 week treatment in treatment naïve patients
- **Genotype 1** cure rates in treatment experienced patients is substantially worse
- **Genotype 2 and 3** have generally a good treatment prognosis with PegINF/RBV and half the treatment duration (24 weeks) compared with genotype 1
  - G2: 80-93% SVR (cure rates)
  - G3: 66-80% SVR

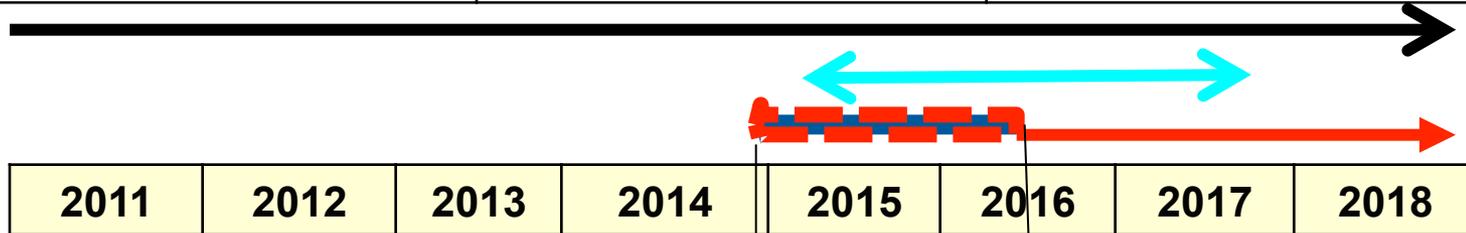
# Evolution of HCV therapy in genotype 1 infection



There are multiple paths leading to a PegIFN & RBV free therapy!!

# HCV Treatment Horizon – Genotype-1 focus of PegIFN free therapies

	Triple Therapy	QUAD Therapy	PegIFN free +/- R
<b>Selected Competition</b>	Telaprevir (Protease) +P/R Boceprevir (Protease) +P/R  TMC435 (Protease) +P/R BI201335 (Protease) +P/R DEB025 (Cyclophilin Inh) +P/R BMS790052 (NS5A) +P/R MK7009 (protease, JPN) +P/R	Two DAAs + P/R	One DAA + R or Two DAAs +/- R or Three DAAs •TMC435 + PSI-7977 •TMC435 + XXX •PSI-7977 + BMS-790052 •PSI-7977 + R  Other combinations: Abbott, BMS, BI, Gilead
<b>Main Populations</b>	Naïve & P/R treatment experienced	Null & partial responders Difficult to treat Naïve Triple Failure High price – high unmet need populations	PegIFN ineligible Treatment deferred Treatment experienced Naïve diagnosed patients (largest segment)
<b>Key Attributes</b>	Efficacy/Length of therapy Tolerability/AE profile Ease of Use	Efficacy Tolerability/AE profile Ease of use, Affordability	Efficacy, Ease of Use, FDC Length of Therapy



2011	2012	2013	2014	2015	2016	2017	2018
------	------	------	------	------	------	------	------

Some patient groups

Large patient populations

# Evolution in HCV treatment

TMC435 well positioned to become the backbone of future HCV treatment

Before 2011

- Interferon (PegIFN) + Ribavirin (RBV)

**Cure rates: 40-50 %**

2011: First generation Protease Inhibitors

- Teleprevir and Boceprevir + PegIFN and RBV

**Cure rates: 66-79 %**

2013: Second generation Protease Inhibitors

- TMC435 + PegIFN and RBV

**Cure rates: 81-86 %  
Most patients have  
shorter treatment**

2013 and forwards: More treatment options

- New DAA's (Direct Acting Antivirals)
- PegIFN free treatment
- PegIFN and RBV free treatments
- Combinations of different DAA drugs

**Even better cure rates  
Reduced side effects  
Reduced treatment time**

# Three Phase III PegIFN-free studies to evaluate PSI-7977 plus ribavirin in HCV patients

## ELECTRON informed IFN-free Phase 3 Program for PSI-7977



- FISSION:** 500 treatment-naïve pts HCV GT2/3  
➔ **PSI-7977/RBV 12 wks** vs. 24 wks PEG/RBV
- POSITRON:** 225 HCV GT2/3 patients who are interferon intolerant or ineligible  
➔ **PSI-7977/RBV 12 wks** vs. Placebo
- NEUTRINO:** 280 GT1 (& all other genotypes) patients who are interferon intolerant or ineligible  
➔ **PSI-7977/RBV 12 wks** vs. Placebo

- **FISSION:** Genotype 2/3
- **POSITRON:** Genotype 2/3, no active comparator arm
- **NEUTRINO:** Design and inclusion criteria yet to be decided, no active comparator arm?

# Selected Interferon-Free Scenarios

## TMC435 and PSI-7977/ RBV

	PSI-7977 + Ribavirin 1 <sup>st</sup> generation PegIFN-free	TMC435 + *DAA 2 <sup>nd</sup> generation PegIFN/RBV-free
Treatment duration	12 weeks	12 weeks
**Genotype Patient population	G2/3 and G1 ? naïves	G1 naïves + experienced
Market	EU + US	EU + US + JPN
Side effects/ adverse events	Ribavirin	None /low
Dosing/compliance	BID	QD
Fixed Dose Combination	No	Yes
Fibrotic HCV patients (F3 - F4)	*** To be determined	Yes
Secondary beneficial mechanism	No	Yes on IFN response

\* Direct acting antiviral agent, planning underway, 1st evaluation, PSI-7977, already communicated

\*\* Genotype 1, the most difficult to treat, ~75% in the western World

\*\*\* PSI-7977 requires activation by several liver enzymes, could be impaired in fibrotic patients

### RIBAVIRIN Adverse Events

- Hemolytic anemia, Teratogenicity, Cough and dyspnea, Rash and pruritus, Insomnia, Anorexia
- Contraindication: Pregnant women, patients with hemoglobinopathies

# 2011 – High Value HCV Deals and Collaborations

## Trends in 2011 – Positioning started for the ultimate combinations

- Vertex and Alios BioPharma announce exclusive worldwide licensing agreement for two nucleotides in preclinical development, ALS-2200 and ALS-2158
  - \$60 million upfront and research funding
  - \$715 million in milestone payments if both compounds are approved
  - \$750 million in sales milestone
  - Tiered royalties on product sales
- Merck and Roche join forces to develop and co-promote hepatitis C treatments in the US, including the latter's recently approved HCV PI Victrelis (boceprevir)
- Roche acquired Anady's HCV assets Setrobuvir, a non-nucleoside NS5B inhibitor in phase 2b, and ANA773, a TLR7 agonists, in phase 1 for HCV, chronic infections and cancer
- Selected company collaborations
  - TMC435 and PSI-7977, phase 2, oral PegIFN-free
  - BMS-790052 and PSI-7977, phase 2, oral PegIFN-free

# Evolution of New Treatment Paradigms

## TMC435 PegIFN-Free Treatments

- **TMC435 is being developed along two major development lines:**
- **TMC435 plus PegIFN/RBV – Broad regulatory approvals in the HCV genotype 1 patient populations are anticipated in H2 2013**
- **TMC435 plus a direct acting antiviral (PegIFN-free and RBV free)**
  - Tibotec/JNJ is aiming to develop the most competitive TMC435 based PegIFN-free combination, with or without ribavirin
  - TMC435 plus PSI-7977 combination in genotype 1 null responders is under way. Data will be available by mid 2012
  - TMC435 in combination with another DAA (directly acting antiviral) to be communicated
  - The aim is to achieve a broad label in both treatment experienced and in treatment naïve HCV genotype 1 infected people (with or without RBV)
- **The TMC435 development strategy is aiming to become the preferred backbone component in future HCV treatments**



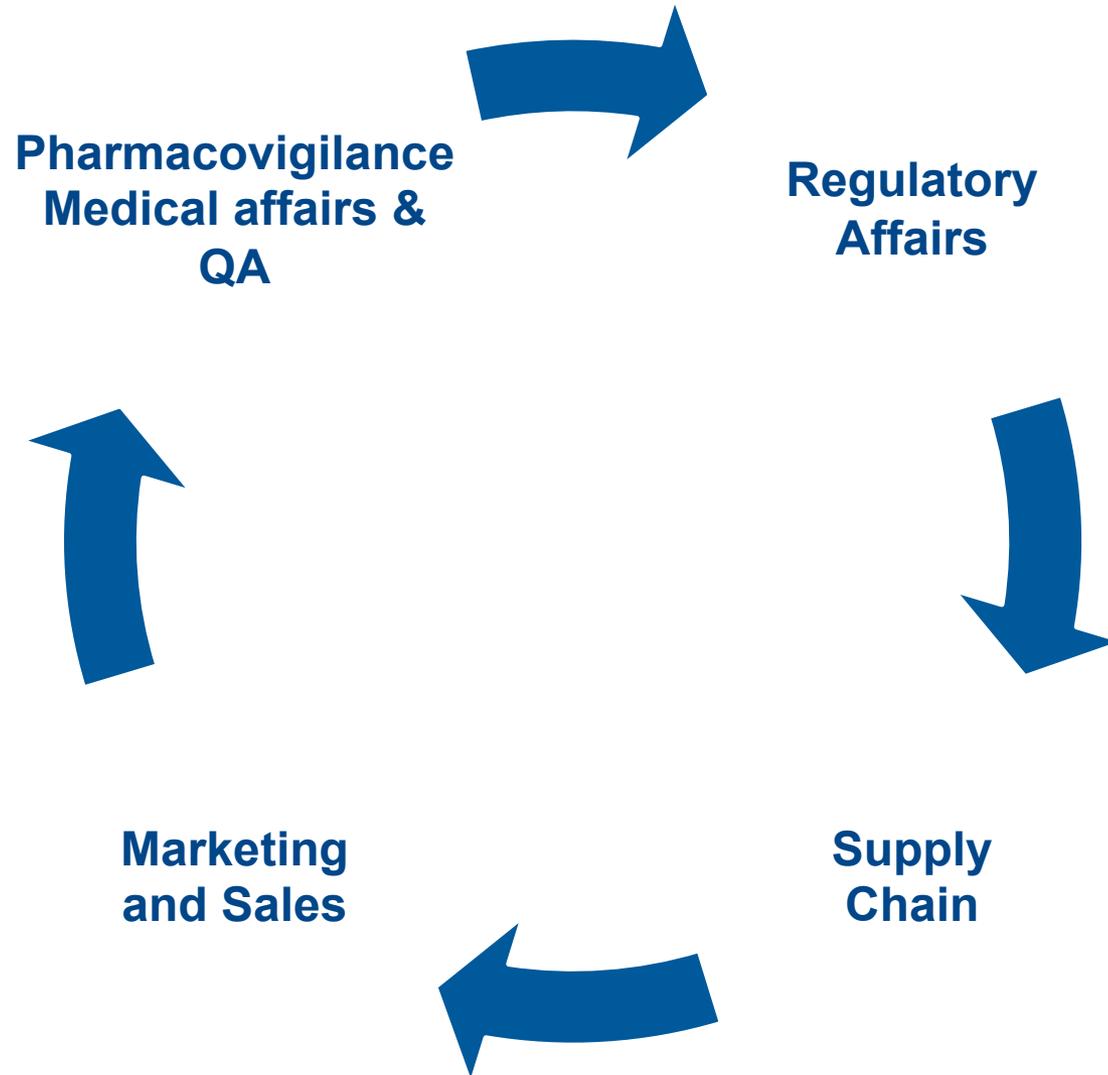
**Break 15 minutes**



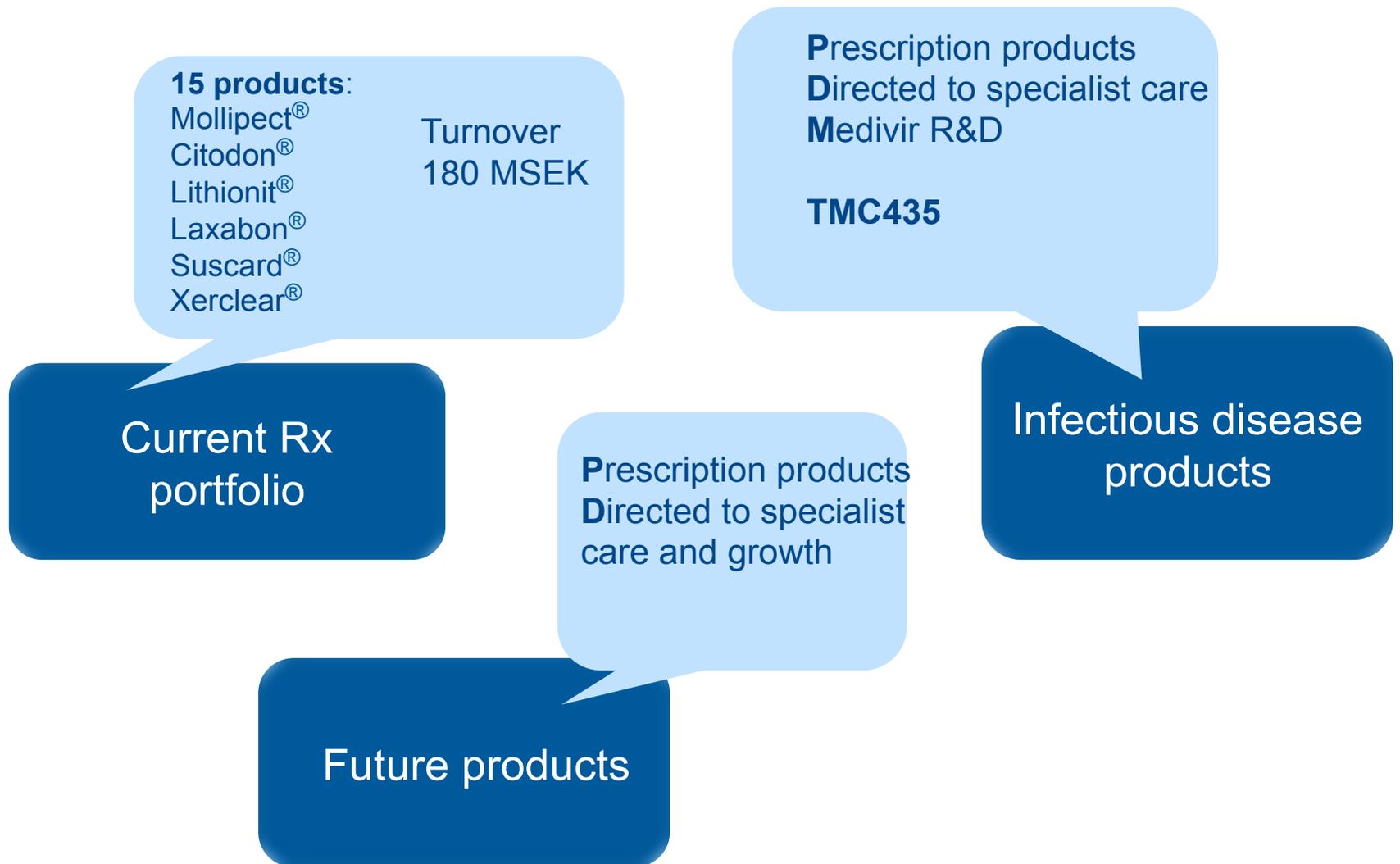
# **Commercial Platform**

**Eva Arlander  
EVP Commercial**

# Commercial Platform



# Product portfolios





# **The Nordic HCV Market**

**Birgitta Wikman Erlandson**

**Director Commercial Development &**

**Governmental Affairs**

# The Nordic HCV market

## Prevalence and incidence:<sup>1</sup>

Sweden: 50 000 patients (~2000/yr)

Denmark: 25 000 patients (~1000/yr)

Norway: 25 000 – 30 000 patients (~1000/yr)

Finland: 25 000 patients (~1000/yr)

## Genotype spread:<sup>2</sup>

1 ~ 50%

2 ~17%

3 ~ 26%

4 and other subtypes: <2%

## Transmission:<sup>3</sup>

Domestic: ~54%

Infected abroad: 18% (Eastern Europe and Asia)

Unknown: 28%

## Transmission route:<sup>3</sup>

44% intravenous drug abuse

4% sexually transmitted

5% within healthcare

2% tattoos/piercing

0,1% infected at birth

44% unknown transmission route

# Activities focussed towards a quick uptake at launch

**Differentiation vs. competition**

**Reimbursement and recommendations**

**Endorsement among stakeholders**

**Medivir - the HCV partner**



# **Cross Pharma**

**Johan Frödin CEO Cross Pharma**

# What is Parallel Trade?

- Parallel trade (PT) is based on the EU principle of free movement of goods within the EU and is a legitimate mechanism for redistribution of pharmaceuticals
- PT takes advantage of the price differences that exist within the EU
- PT within the EU started in the early 1980' s. In 2009 the value of PT was 33 000 MSEK in the top five EU countries and PT continues to develop and grow
- PT is supervised by the same authorities that supervise all other pharmaceutical companies within the EU

# Parallel Trade in Scandinavia

- PT within Scandinavia started in the early 1990 ' s. The current value of PT in that region is 6 900 MSEK, where Sweden (3 300 MSEK) and Denmark (3 000 MSEK) constitute 92%
- Sweden
  - 18 companies on the market, but it is dominated by 5 companies that have 93 % market share
  - The market has grown with 29% since 2009
  - Constitutes 12% of the Rx market
  - The pharmacy chains have a big incentive to buy PT products
- Denmark
  - 12 companies on the market, but it is dominated by 6 companies that have 96 % market share
  - Sales is achieved within a combination of lowest public price and agreements with the pharmacy chains

# Cross Pharma AB

- Facts

- Founded in 1995.
- Sweden is the main market.
- Fully owned subsidiary in Poland for repacking.
- Expected turnover 2011 is ~ 310 MSEK.
- The fourth largest PT company in Sweden with a market share of 9 %.

- Outlook

- Opportunity to expand the business:
  - The PT market is growing in Sweden.
  - Cross Pharma has strengthened the organization and the financial position.



## **Summary - Maris Hartmanis, CEO Medivir**

# Upcoming News Flow

- ✓ Q3 TMC435 Phase III enrollment completed
- ✓ Q4 Digestive week Japan - DRAGON full SVR24 data
- ✓ Q4 ASPIRE top line SVR24 data
- ✓ Q4 AASLD - PILLAR full SVR24 data
- ✓ Q4 Change of primary end point in ongoing and coming Phase 3 studies, SVR24 → SVR12
- ✓ Q4 TMC649128 compound discontinued – Nucleotide program continues towards clinical development
- Q4 TMC435 and PSI-7977 enters in DAA combination trials
- Q1-12 FY report and update on projects and financials
- Q1-12 OTC launch of Xerclear® in Europe by GSK
- Q1-12 EASL – ASPIRE full SVR24 data
- Q1-12 Start of Phase III trials with TMC435 in prior null and partial responder patients
- H1-12 Aiming to start Phase I trials with MIV-711

**Expected key news flow highlights during the coming 6 months**



**Q/A**