Medivir

*A specialty pharmaceutical company focused on infectious diseases*

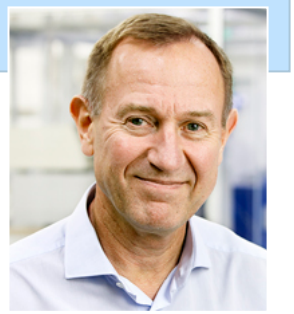
**Frukostpresentation 21 mars på IVA**

# Presenting team

**Charlotte Edenius**
VP R&D Projects

**Rein Piir**
CFO / IR

**Bertil Samuelsson**
CSO



# Flying Start to 2011

## Recent news flow highlights

- Dec-10 Private placement of SEK 280m (EUR 30m)
- Feb-11 Phase 1a start with TMC649128 HCV/POL
- Feb-11 Joint venture with Janssen Pharmaceutica on Dengue Fever
- Feb-11 Global Phase 3 studies start with TMC435 in treatment naïve patients
- Feb-11 Global Phase 3 study starts with TMC435 in treatment experienced relapser patients
- Feb-11 Japanese Phase 3 studies start with TMC435 in treatment naïve and in treatment experienced patients
- Feb-11 C205 (PILLAR) Interim SVR24 data in treatment naïve patients
- Mar-11 Launch of Xerese™ in US

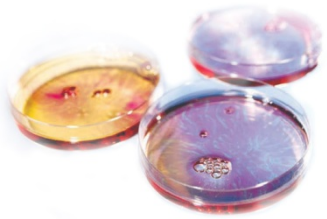
# Key Innovation and Commercialisation at Medivir

## TMC 435 - Potentially best in class hepatitis C drug

- Strong safety profile – no adverse events over SoC in P2b
- Excellent antiviral activity in P2b PILLAR and ASPIRE studies
- High convenience – one pill, once daily, no food interactions
- Global Phase 3 trials started recently


## Xerclear® / Xerese™ - in global launch phase 2011

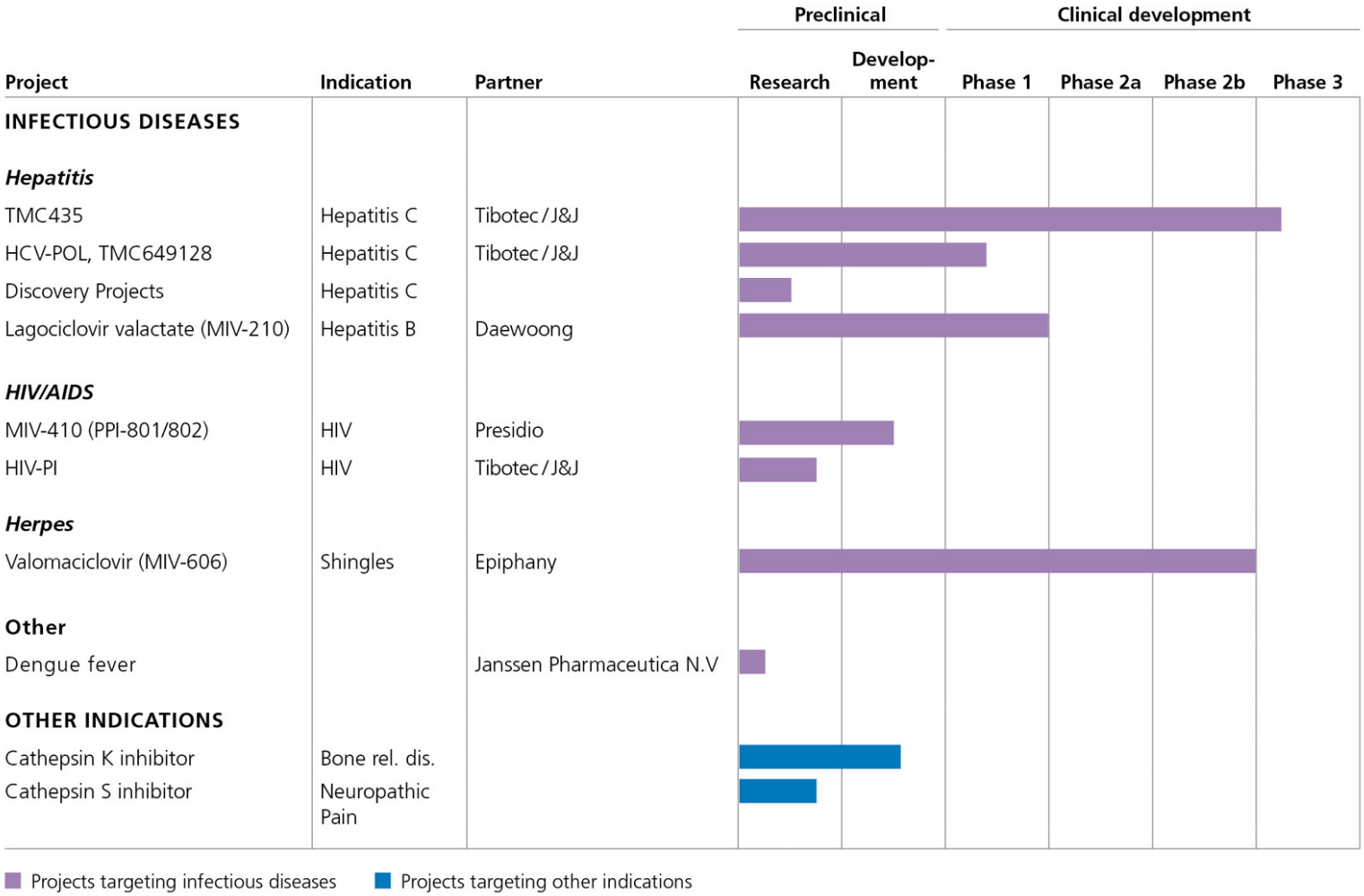
- First step towards becoming a profitable research-based pharmaceutical company
- Differentiated product profile - unique indication text
- Significant blue-chip marketing partners.



## Strong Pipeline in development

- A strong pipeline of innovative infectious disease drug candidates in development with leading pharma partners
- World class expertise in polymerase and protease drug targets and drug development

# Strong Pipeline with Multiple Paths to Value Creation



# Key programmes in our early  stag pipeline

# Cathepsin K inhibitors for bone disorders – MIV-710/711

**Creating value for shareholders by developing products further under own management**

## Disease and market

- This class of inhibitors intervene in disease states where there is excessive bone loss, e.g. osteoporosis, osteoarthritis and metastatic bone disease
- Estimated combined global market opportunity in excess of USD 12 billion

## MIV-710 and MIV-711

- Cathepsin K inhibitor program
- Maintain the beneficial bone formation, in contrast to other anti-resorptives
- Furnish potent and long duration of activity
- A low once daily human efficacious dose at 50 mg QD estimated
- Strong IP position

## Upcoming events in 2011

- Two Candidate Drugs selected, CD 1(MIV-710) and CD2 (MIV-711), which are progressing in preclinical development studies
- Start of phase 1 clinical trials for MIV-711 expected in Q3 2011

# Dengue Fever Joint Venture with Janssen Pharmaceuticals

## In February 2011 Medivir signed a co-development collaboration with Janssen Pharmaceuticals N.V. focused on dengue virus

- Strengthens Medivir's presence in infectious diseases
- Utilises strong know-how in the discovery of protease inhibitor drugs
- Approach focussed on inhibition of the dengue NS3 protease involved in viral replication

## Commercial strategy

- Both parties are contributing 50:50 resources to the research program
- Increased potential upside from co-development deal

## Market opportunity

- Dengue virus infection is a major problem in subtropical regions where the incidence has increased 30-fold over the last 50 years
- Up to 50 million infections occur annually in more than 100 endemic countries and the annual death rate from dengue infection is approximately 30,000
- This growing prevalence has not been met by any significant advances in treatment[1]

[1] World Health Organisation, Fact sheet N°117, March 2009.

# Our hepatitis C franchise

Partnered and in-house product portfolio

# TMC435 – The Leading Next Generation Protease Inhibitor

- Strong safety profile: no adverse events over SoC in the Phase 2b PILLAR and ASPIRE studies
- Excellent anti-viral efficacy shown in Phase 2b PILLAR and ASPIRE studies
- Convenient: one pill and once daily, no food interactions

# Hepatitis C - A blockbuster potential market

## The Hepatitis C Market

- Globally ~180 million (3-4% of world population) infected with hepatitis C virus, of which 80% develop chronic disease
- The difficult to treat genotype 1 (G1a/b) account for ~70% of the HCV population
  - Sustained viral response (SVR) in G1 patients is very low, 42-48% on PegIFNα/RBV, SoC
- Approximately 12 million HCV infected in the US, Europe and Japan
  - Prevalence in JPN ~1.9 million with ~55% being diagnosed (~25% worldwide)
  - Health care burden in the US ~ 5 BUSD / year

## Market Value

- Estimated market value of over USD 10 billion in 2015 and increasing
- Treatment-experienced patients, currently ~ 0.5 million, comprise ~half of the market value

## TMC 435 potential

- Analysts estimate TMC435 annual peak sales of 2-4 BUSD

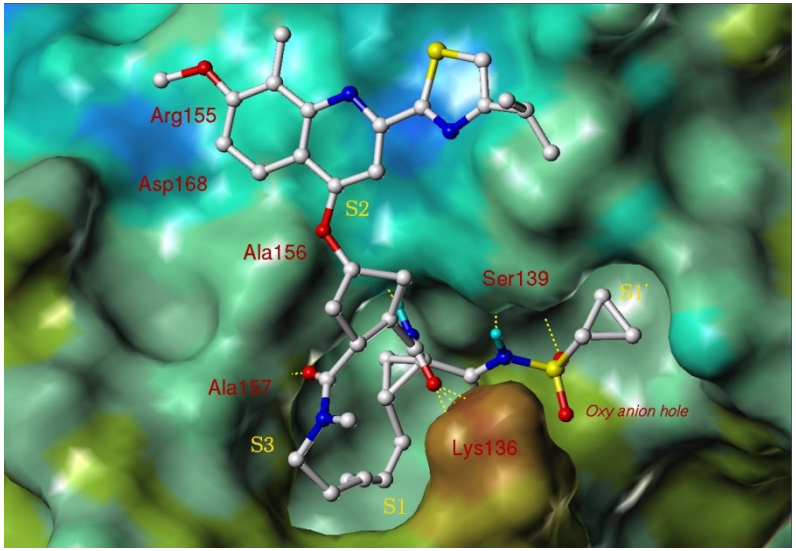
# HCV Clinical Pipeline

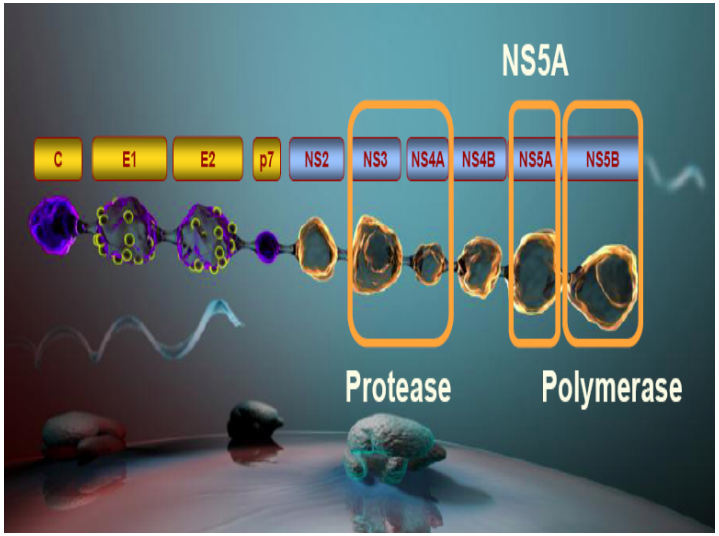
## TMC435 – major commercial opportunity

- EUR 80.5 million deal value
  - EUR 30 million outstanding
- Medivir retain Nordic rights
  - Prevalence of chronic HCV infected ~115,000
  - Current annual treatment rates ~ 3,150

## TMC435 – summary status

- Potent HCV NS3/4A protease inhibitor
- Backbone of future DAA combination therapies
  - Data expected 2011/12
- Long patent life
  - IP extending to 2026 and 2028
- Global Phase 3 trials ongoing
- Regulatory filings expected in 2013



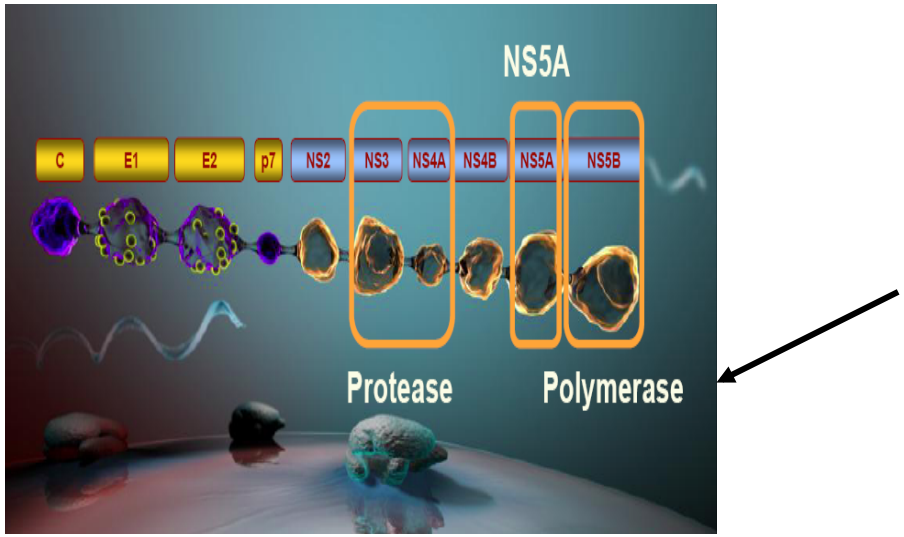
# HCV Clinical Pipeline

## TMC649 (HCV Pol) - major commercial opportunity

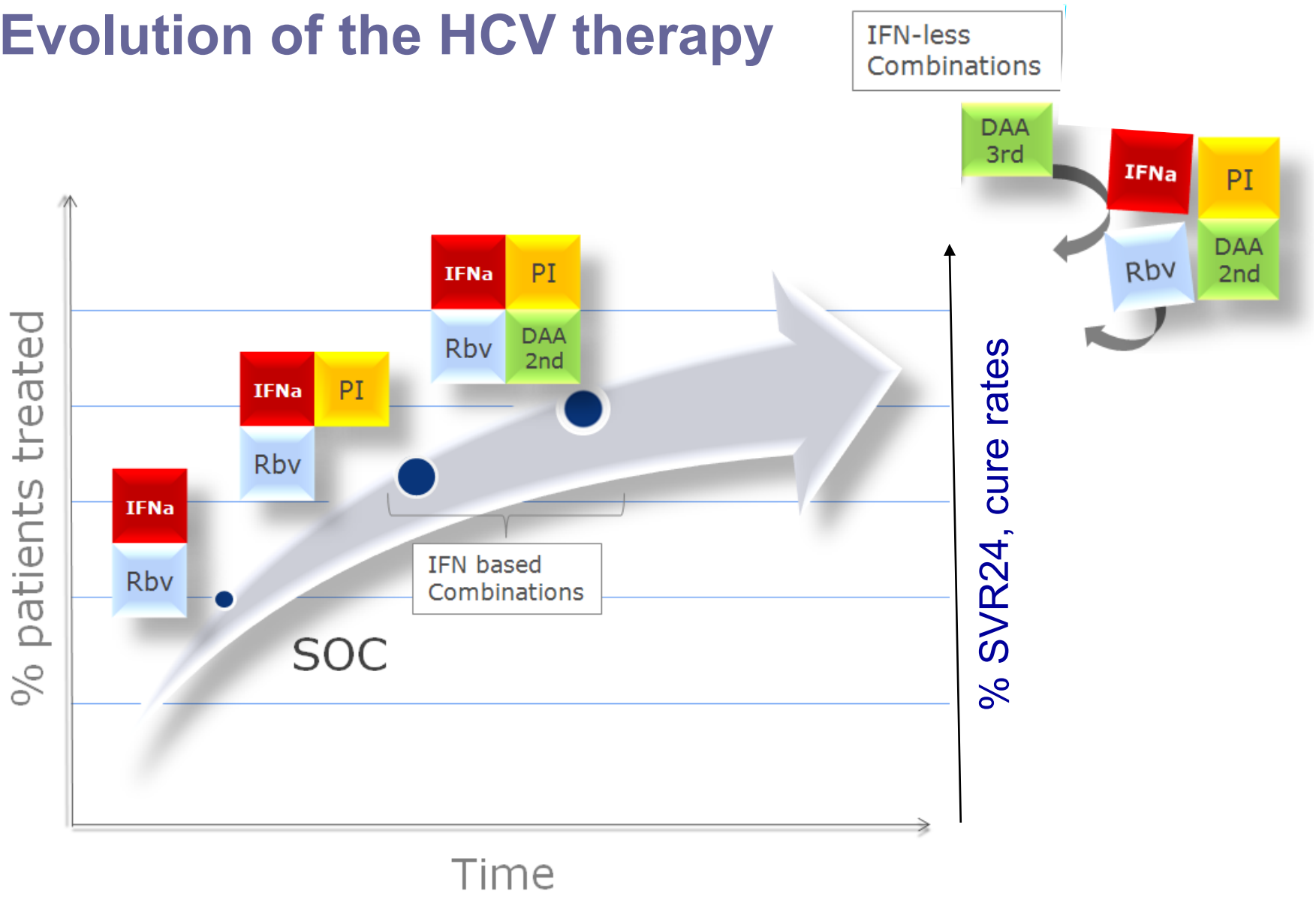
- EUR 147 million deal value
  - EUR 95 million outstanding
- Medivir retain Nordics rights
  - Prevalence of chronic HCV infected ~115,000
  - Current treatment rates ~ 3,150

## TMC649 (HCV Pol) – summary status

- Nucleoside/tide NS5B inhibitor
- An ideal DAA agent for future TMC435 combination regimens
- High barrier to resistance and broad genotype coverage
- Long patent life
  - IP extending to 2027 and 2029
- Phase 1 trails ongoing



# Evolution of the HCV therapy



# Hepatitis C PI – the competitive landscape

| Phase 1a | Phase 1b | Phase 2a | Phase 2b | Phase 3 | Registration |
|---|---|---|---|---|---|
| VPY-376 | ACH-1625 | ABT-450 | Danoprevir<br>R-7227**?** | **TMC435** | Telaprevir<br>VX-950 |
| PHX1766 | | | BMS-650032 | | Boceprevir<br>SCH-503034 |
| IDX320 | | | GS-9256 | | |
| MK-5172 | | | Vaniprevir **?**<br>MK-7009 | | |
| | | | BI201335 **?** | | |
| | | | Narlaprevir**?** | | |

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

- Combinations of DAA agents:
  - Telaprevir in phase 2a in combination with VX-222 (NNRTI) +/- SoC
  - Danoprevir in phase 2a in combination with R7128 (NI) +/- SoC
  - BMS-650032 in phase 2a in combination with BMS-790052 (NS5A inh) +/- SoC
  - GS-9256 in combination with GS-9190 (NNRTI) +/- Ribavarin

Note: nanoprevir and ABT-450 require ritonavir-boosting

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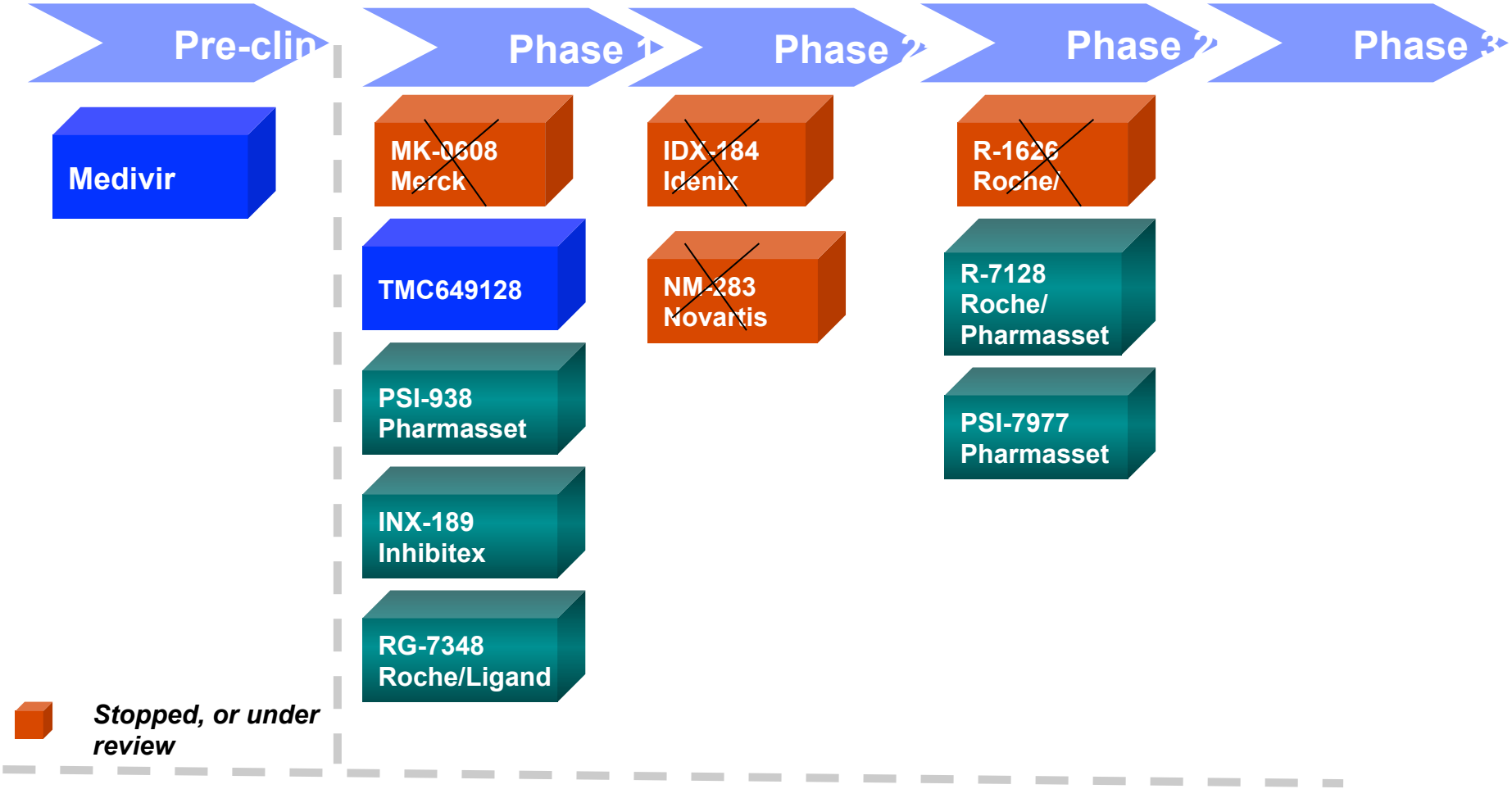
# HCV Nucleosides & Nucleotides – Competitive landscape



# TMC435 Late Stage Clinical Trial Programme

| Follow Up Phase | Recently Initiated |
|---|---|
| Phase 2b studies | Phase 3 studies |

**PILLAR (C205)** – 386
genotype-1 infected
treatment-naïve patients

**DRAGON (C215)** – 92
genotype-1 infected
treatment-naïve patients

**ASPIRE (C206)** – 462
genotype-1 infected
treatment-experienced
patients

**QUEST 1 (C208)** 375
genotype-1 infected
treatment-naïve patients

**QUEST 2 (C216)** 375
genotype-1 infected
treatment-naïve patients

**PROMISE (C3007)** 375
genotype-1 infected
relapsed patients

**Phase 3 studies started in Japan**
both in naïve and treatment experienced
genotype-1 infected
patients

For additional information on inclusion and exclusion criteria for these studies, please see www.clinicaltrials.gov

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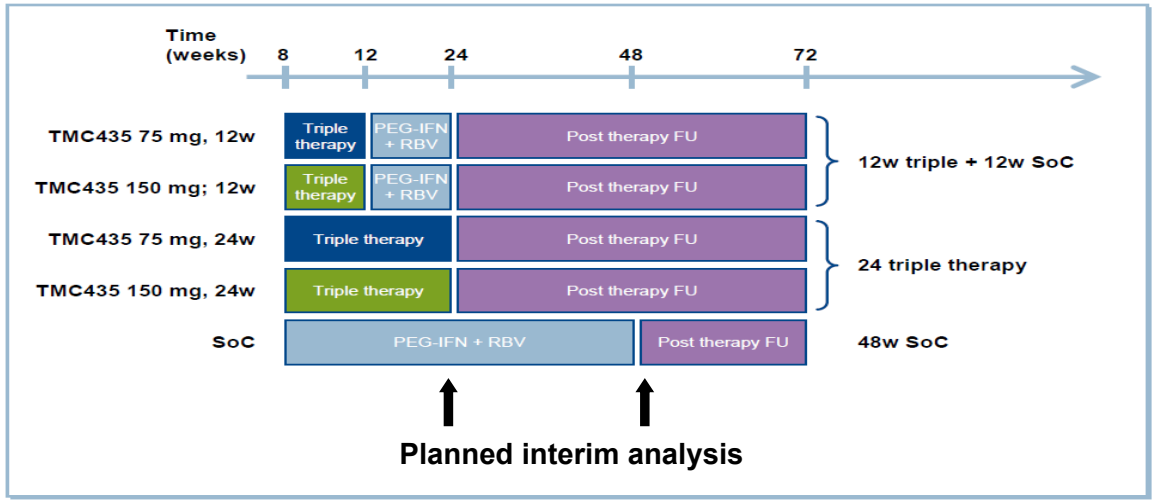
# TMC435 Phase 2b: study design & findings - 48 week interim analysis

## PILLAR (C205)

- TMC435-C205 is a global phase 2b study in 386 genotype-1 treatment-naïve patients
- Once daily (*q.d.*), 75 mg and 150 mg, of TMC435 + SoC:
  - 12-week triple therapy followed by SoC alone up to week 24
  - 24-week triple therapy
- Response-guided treatment duration in TMC435 arms
  - End treatment at Week 24, if
    - HCV RNA <25 IU/mL detectable or undetectable at Week 4, *and*
    - HCV RNA <25 IU/mL undetectable at Weeks 12, 16, and 20
  - All other patients continued Peg/RBV for up to 48 weeks



# PILLAR C205 week 48 interim analysis – safety and efficacy

1. **Phase 2b 48-week (SVR24) Interim Results of TMC435 in Treatment-naïve Patients Chronically Infected with Genotype-1 Hepatitis C Virus**
2. **In the TMC435 treatment groups 83% of patients were able to stop all therapy at week 24**
3. **Potent and consistent antiviral efficacy was demonstrated with SVR24 rates of up to 84%**
4. **No clinically relevant difference in safety and tolerability between TMC435 and placebo groups**

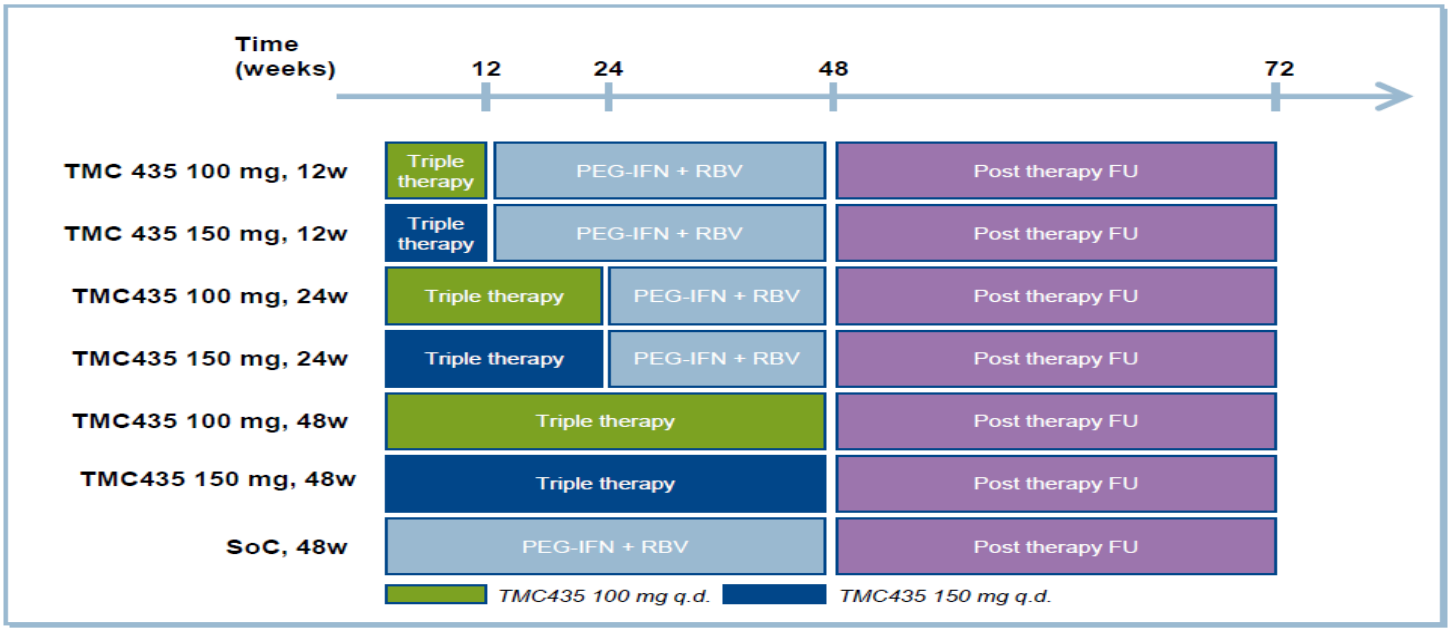
| **Sustained Virological Response 4 and 24 Weeks after Planned End of Treatment (EoT);** | | | | | |
|---|---|---|---|---|---|
| **% (n/N)** | **TMC435 12PR24 75mg q.d. N=78** | **TMC435 24PR24 75mg q.d. N=75** | **TMC435 12PR24 150mg q.d. N=77** | **TMC435 24PR24 150mg q.d. N=79** | **Placebo N=77** |
| **SVR4** | **87.2 (68/78)** | **86.5 (64/74)** | **84.9 (62/73)** | **88.5 (69/78)** | **71.2 (42/59)** |
| **SVR24** | **83.6 (61/73)** | **76.1 (51/67)** | **83.1 (59/71)** | **84.4 (65/77)** | **N/A** |

* < 25 log10 IU/mL undetectable
q.d.: once daily, PR: pegIFNalpha-2A and ribavirin,
SVR4 and SVR24: patients with undetectable HCV RNA 4 and 24 weeks after planned EoT, respectively.
N/A: Patients in the control arm continue SoC until Week 48 and SVR24 data was not available

# TMC 435 Phase 2b study design

## ASPIRE (C206)

- TMC435-C206 is a global phase 2b study in 462 genotype-1 treatment-experienced patients
- Once daily (*q.d.*), 100 mg and 150 mg, of TMC435 + SoC:
  - 12-week triple therapy followed by 36 weeks of SoC
  - 24-week triple therapy followed by 24 weeks of SoC
  - 48-week triple therapy



# Antiviral efficacy in TMC435 ASPIRE C206 - 24-week interim data

| | TMC12/PR48 100 mg (N=66) | TMC24/PR48 100 mg (N=65) | TMC48/PR48 100 mg (N=66) | TMC12/PR48 150 mg (N=66) | TMC24/PR48 150 mg (N=68) | TMC48/ PR48 150 mg (N=65) | Pbo48/PR48 (N=66) |
|---|---|---|---|---|---|---|---|
| **HCV RNA <25 IU/mL undetectable, % (n/N)** | | | | | | | |
| Overall population Week 4 (RVR) | **67.7** (44/65) *** | **59.4** (38/64) *** | **53.8** (35/65) *** | **63.1** (41/65) *** | **70.8** (46/65) *** | **66.2** (43/65) *** | **1.5** (1/65) |
| Prior null responder | **33.3** (5/15) | **50.0** (8/16) | **25.0** (4/16) | **35.3** (6/17) | **41.2** (7/17) | **41.2** (7/17) | **0.0** (0/16) |
| Prior partial responder | **65.2** (15/23) | **40.9** (9/22) | **60.9** (14/23) | **65.2** (15/23) | **69.6** (16/23) | **68.2** (15/22) | **0.0** (0/23) |
| Prior relapser | **88.9** (24/27) | **80.8** (21/26) | **65.4** (17/26) | **80.0** (20/25) | **92.0** (23/25) | **80.8** (21/26) | **3.8** (1/26) |
| Overall population Week 24 | **87.1** (54/62) *** | **84.5** (49/58) *** | **85.2** (52/61) *** | **85.7** (54/63) *** | **90.8** (59/65) *** | **90.3** (56/62) *** | **51.9** (28/54) |
| Prior null responder | **71.4** (10/14) | **83.3** (10/12) | **68.8** (11/16) | **70.6** (12/17) | **81.3** (13/16) | **93.3** (14/15) | **44.4** (4/9) |
| Prior partial responder | **86.4** (19/22) | **80.0** (16/20) | **85.7** (18/21) | **86.4** (19/22) | **90.9** (20/22) | **86.4** (19/22) | **19.0** (4/21) |
| Prior relapser | **96.2** (25/26) | **88.5** (23/26) | **95.8** (23/24) | **95.8** (23/24) | **96.3** (26/27) | **92.0** (23/25) | **83.3** (20/24) |

***Statistically significant difference versus placebo, p<0.001

- **The TMC435 treatment arms demonstrate high response rates**
- **The antiviral efficacy was enhanced in all patient groups through week 12 and 24**
- **Notably, the null responder group demonstrated significant response rates**

**Excellent antiviral activity**

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# Safety and Tolerability in TMC435 ASPIRE C206 24-week interim data

- TMC435 was generally safe and well tolerated consistent with the previously reported phase 2b PILLAR C205 study
- Significant decreases in transaminases (ALT and AST) were observed in all TMC435 treatment groups
- The two most frequently reported AEs were fatigue and headache, with comparable results shown in the placebo group

| % | All TMC435 N = 396 | Placebo N = 66 |
|---|---|---|
| Fatigue | 41 | 42 |
| Headache | 33 | 33 |

**TMC435 was safe and well tolerated**

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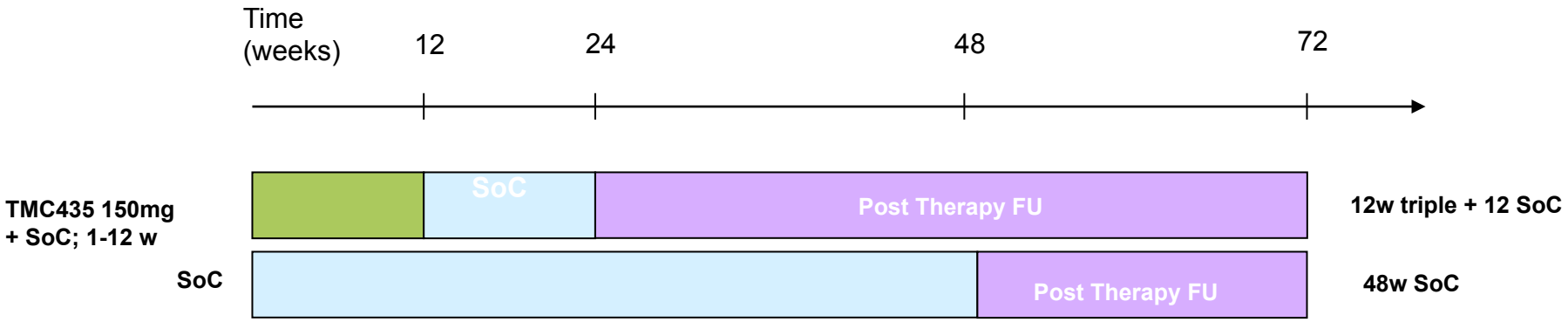
# Phase 3 trial design: Quest-1, Quest-2* and PROMISE

Approximately 1125 patients in total, 375 in each study

Response-guided treatment duration in TMC435 arms

- End treatment at Week 24 if predefined stop criteria are met
- All other patients continue on Peg/RBV for up to 48 weeks




**•Quest-1, Quest-2:**

- will evaluate a single once-daily oral tablet of TMC435 (150 mg) verses placebo in treatment naïve HCV patients

**•PROMISE:**

- will evaluate a single once-daily oral tablet of TMC435 (150 mg) verses placebo in HCV patients who experienced viral relapse after previous interferon-based therapy

**Quest 2*** – patients in this trial will either receive Pegasys® and Copegus®) or PegIntron® and Rebetol® as part of their treatment

# Conclusion

# Upcoming News Flow

## Expected key newsflow highlights during 2011

- Apr-11 EASL - additional data on TMC435
- Q211 TMC435, 48-week interim data from the phase 2b C206 (ASPIRE) trial in treatment-experienced patients
- Q3-11 C205 (PILLAR) full SVR24 data
- Q3-11 Start of phase 1 trials with MIV-711
- H2-11 Start of phase 3 trials with TMC435 in treatment-experienced non-responder patients
- H2-11 Phase 1a/1b results with TMC649
- Q4 AASLD – additional data on TMC435
- Q4-11 OTC launch of Xerclear® in Europe by GSK
- Q4-11 C206 (ASPIRE) SVR24 data