



**Medivir** presenting at

**Rodman & Renshaw  
Healthcare Conference  
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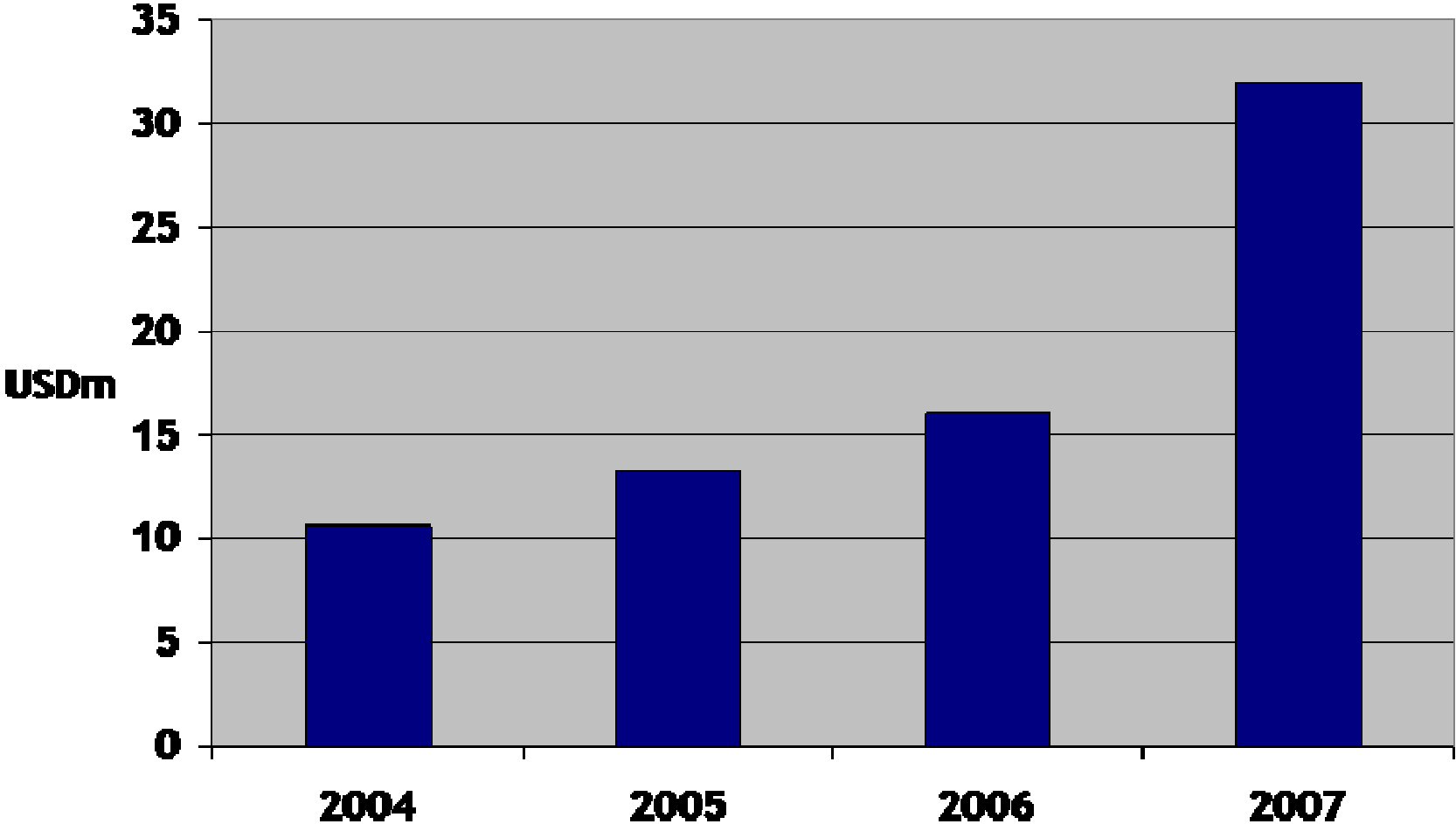


## Medivir - Key achievements 2008

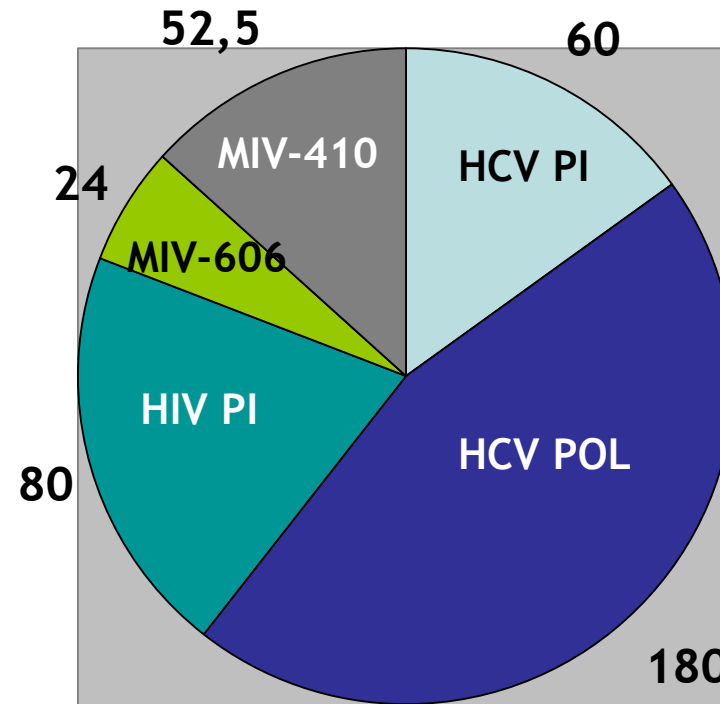


- Strong phase IIa data presented for TMC435 (hepatitis C protease inhibitor)
- Our biggest deal ever signed with JNJ/Tibotec for hepatitis C polymerase inhibitors (>USD 190m)
- Applications for approval of Lipsovir (labial herpes) filed in the US and Europe
- Co-promotion deal for GSK products in the Nordic countries
- Burn rate substantially reduced to approx. USD 7m per quarter going forward
- Strong cash position by end of Q3 (USD 38m)

# Steadily increasing revenues since 2004



~USD 400m in remaining milestone payments



- + Royalties on global sales
- + Nordic marketing rights retained
- + All future project expenses covered
- + Research funding in two collaborations

# Pipeline November 2008

## Prioritized projects

Project	Indication(s)	Partners/ Date of agreement	Terms	Medivir's markets	Exploratory phase	Optimization	Preclinical dev. *	Phase I	Phase II	Phase III
<b>Lipsovir®</b> (ME-609)	Labial herpes	In-house			[Green bar spanning from Exploratory phase to Phase III]					
<b>TMC435350</b> (HCV-PI)	Hepatitis C	Tibotec / 2004	EUR 80.5 m+ royalties and FTE funding	Nordic region	[Orange bar spanning from Exploratory phase to Phase II]					
<b>MIV-701</b> (Cath K)	Osteoporosis, osteoarthritis, bone metastases	In-house			[Orange bar spanning from Exploratory phase to Phase I]					
<b>Cathepsin K</b>	Osteoporosis, osteoarthritis, bone metastases	In-house			[Orange bar spanning from Exploratory phase to Optimization]					
<b>HIV PI</b>	HIV	Tibotec / 2006	EUR 64 m + royalties and FTE funding	Nordic region	[Orange bar spanning from Exploratory phase to Optimization]					
<b>HCV POL</b>	Hepatitis C	Roche / 2003 / In-house	Undisclosed	Nordic region	[Purple bar spanning from Exploratory phase to Optimization]					
<b>HCV POL</b>	Hepatitis C	Tibotec / 2008	EUR 142-272 m + royalties and FTE funding	Nordic region	[Purple bar spanning from Exploratory phase to Optimization]					
<b>COPD PI</b>	COPD	In-house (Hengrui)		World exc. China	[Orange bar spanning from Exploratory phase to Optimization]					
<b>Renin</b>	Hypertension	In-house			[Orange bar spanning from Exploratory phase to Optimization]					
<b>BACE</b>	Alzheimer's	In-house			[Orange bar spanning from Exploratory phase to Optimization]					
<b>Cathepsin S</b>	Rheumatoid arthritis, multiple sclerosis	In-house			[Orange bar spanning from Exploratory phase to Optimization]					

■ Protease inhibitor    
 ■ Polymerase inhibitor    
 ■ Polymerase inhibition/hydrocortisone

\* The regulated preclinical development phase.

Filed for approval

Phase IIb to be initiated

New deal

Prioritised preclinical program

# Pipeline (continued)

Two active phase II trials

## Medivir HIV Franchise AB

Project	Indication(s)	Partners/ Date of agreement	Terms	Medivir's markets	Exploratory phase	Optimization	Preclinical dev. <sup>1</sup>	Phase I	Phase II	Phase III	NDA
<b>Valomaciclovir (MIV-606)</b>	Shingles, herpes virus	Epiphany Biosciences / 2006	24.5 MUSD + royalties. Epiphany shares	Nordic region	█	█	█	█	█		
<b>Alovudine (MIV-310)</b>	HIV	Mefuvir/2007	Royalties	World excl. Asia	█	█	█				
<b>MIV-210</b>	Hepatitis B, HIV	Hainan Noken/2007	7 MUSD + royalties	World excl. China, Taiwan and Macao	█	█	█				
<b>MIV-150</b>	HIV	Population Council/2003		Option on 50% of Western world	█	█	█				
<b>MIV-160</b>	HIV	Mefuvir/2007	Mefuvir shares and royalties	World excl. China, Taiwan and Macao	█	█	█				
<b>MIV-410</b>	HIV, CMV	Presidio/2006	52.25 MUSD + royalties. Presidio shares	Nordic region and UK. Option on Europe	█	█	█				
<b>MIV-170</b>	HIV				█	█	█				

● Polymerase inhibition/hydrocortisone    ● Protease inhibitor    ● Polymerase inhibitor    <sup>1)</sup> The regulated preclinical development phase.

## Commercial focus in the coming 6-12 months

<b>LIPSOVIR</b>	<ul style="list-style-type: none"><li>◆ Secure optimal partnership structure for both US &amp; EU</li></ul>
<b>HEPATITIS C</b>	<ul style="list-style-type: none"><li>◆ TMC435: start phase IIb trials</li><li>◆ HCV-Polymerase inhibitors: candidate drug selection(s)</li></ul>
<b>CATHEPSIN K</b>	<ul style="list-style-type: none"><li>◆ Select follow-on candidate drug</li><li>◆ Start partnering process</li></ul>
<b>HIV PI</b>	<ul style="list-style-type: none"><li>◆ Candidate drug selection</li></ul>
<b>Other preclinical</b>	<ul style="list-style-type: none"><li>◆ Initiate partner discussions for at least one program</li></ul>
<b>PHARMA SALES</b>	<ul style="list-style-type: none"><li>◆ Continue selling GSK products in Sweden</li><li>◆ Secure new co-promotion deals and potential own product(s)</li></ul>

# Lipsovir<sup>®</sup>





## Lipsovir<sup>®</sup> summary

- Topical product for the treatment of recurrent labial herpes (cold sores)
- Active ingredients: 5% acyclovir + 1% hydrocortisone in a proprietary cream formulation
- Hits the virus AND the immune reaction
- Phase III program completed, including biggest labial herpes trial ever
- Filed for approval in EU/US October 2008
- First product to prevent cold sores
  - Currently marketed products reduce healing time modestly without preventive effect on emerging lesions

## Market opportunity

- At any given time 60 million people have a cold sore
- Sufferers experience pain, self-consciousness, social isolation, anxiety
- Current treatments offer marginal benefits
- Global Rx/OTC market for cold sore treatments approximately USD 700m
- Strong annual growth: OTC +\$11.6% and Rx +\$9%
- US, UK, Germany, France and Italy account for 45% of Rx and OTC markets
- Strong consumer and physician interest in Lipsovir<sup>®</sup>



## Phase III results: Lipsovir prevents cold sores and shortens episodes

- **Primary endpoint = prevention**

Lipsovir<sup>®</sup> prevents cold sores in 42% of subjects with an emerging lesion

- Lipsovir<sup>®</sup> > acyclovir in our vehicle ( $p < 0.01$ )
- Lipsovir<sup>®</sup> > vehicle ( $p < 0.05$ )

Proportion of subjects with non-ulcerative recurrences

- **Secondary endpoint = episode duration**

- Lipsovir<sup>®</sup> > vehicle on episode duration ( $p < 0.05$ )
- Lipsovir<sup>®</sup> reduces the healing time by 1.6 days

Time from treatment start until loss of hard crust for an *ulcerative* recurrence and from start of treatment to time of no signs or symptoms for a *non-ulcerative* recurrence



## Medivir has a broad interest in the HCV area

- TMC435, a protease inhibitor in collaboration with Tibotec/J&J - in later part of phase IIa clinical trials  
Planning for phase IIb has started
- HCV POL collaboration with Tibotec/J&J signed May, 2008
  - Nucleoside analogue in lead optimization phase
  - Back-up nucleosides
  - Screening of Medivir library of nucleoside analogues

# Opportunities with new antivirals in HCV

- **Improved efficacy (improved cure rates)**
  - Only 50% of treatment naive G1 patients are cured today
  - Non-responders and relapsers to current standard-of-care - increasing population
- **Shorter treatment time**
- **Improved side effect profile**
- **More convenient dosing**
- **Longer term - treatment shift in SoC**



**TMC435 - a protease inhibitor in  
collaboration with Tibotec**

**Presently in the final stage of phase IIa  
for genotype 1 naïve patients**

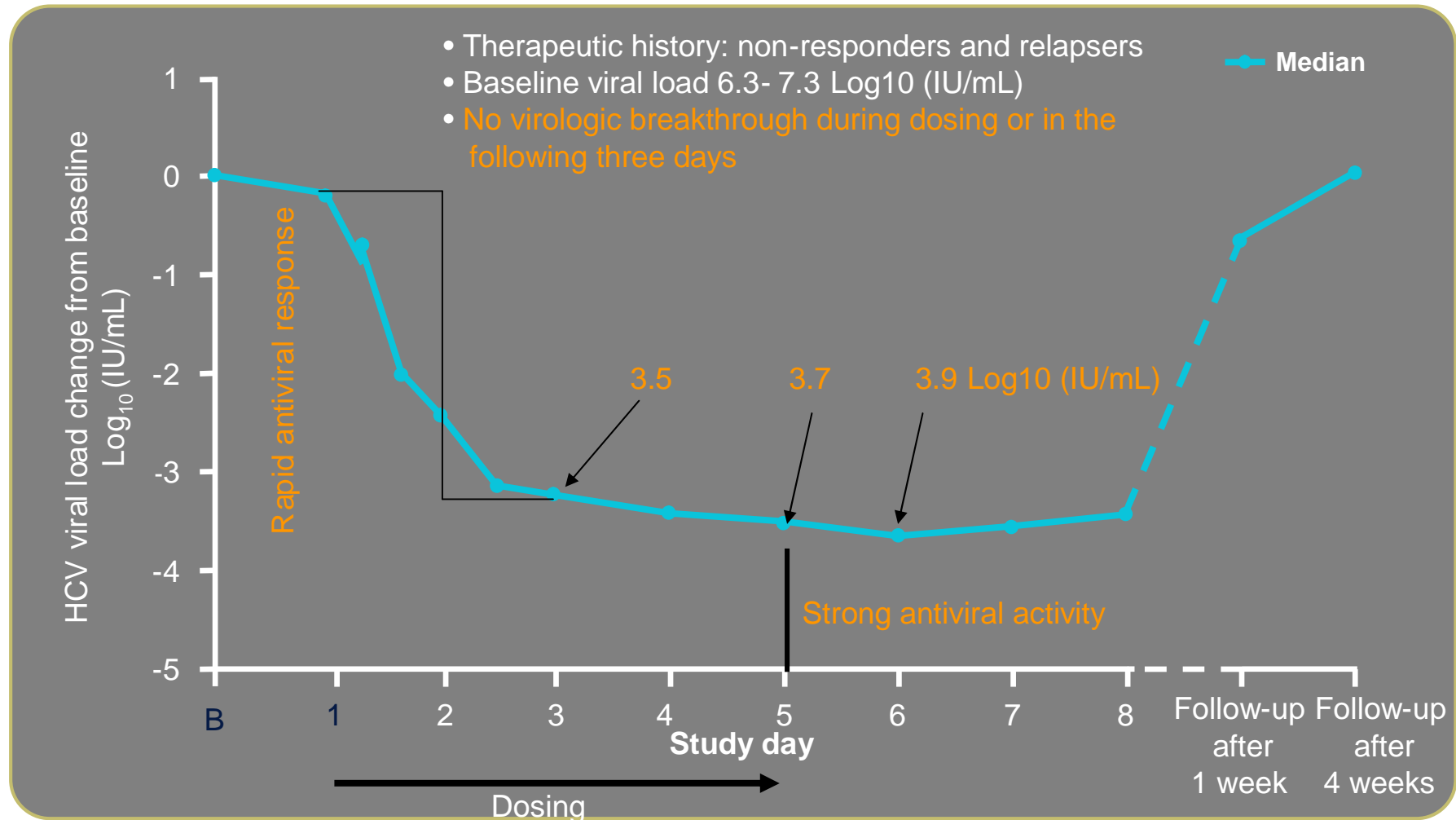
**Phase IIb planning has started**



## TMC435 Phase I trial conclusions

- High potency + favourable PK
  - allow once daily dosing
  - plasma levels far in excess of predicted effect levels in HCV patients
- Five-day treatment with 200 mg once daily resulted in a marked antiviral effect in non-responding HCV G1 patients
- Has been well tolerated in healthy volunteers and HCV patients over 5 days of dosing

# Rapid decline in HCV viral load observed in all HCV-infected individuals (Genotype 1a and 1b) in phase Ib



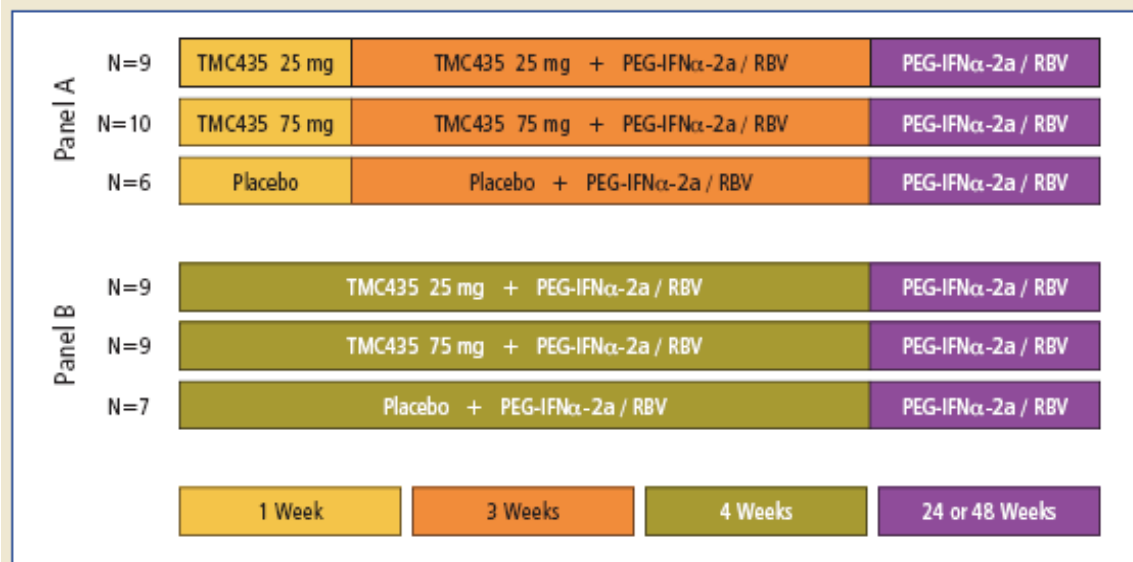


## TMC435: Data presented at AASLD 2008

1. Safety data from 25 and 75 mg once daily groups in phase 2a study Opera-1
  - Study is still on-going
  - 200 mg once daily evaluated in treatment naïve patients
  - several doses evaluated in treatment experienced HCV G1 patients
2. PK data from same patient groups in Opera-1
3. In-vitro characterization of inhibitory activity on proteases from genotype 1 to 6

# Opera-1: Design of Study, 1st cohort (25 and 75 mg once daily or placebo)

Figure 3: Overview of Study Design of cohort 1 of OPERA-1 trial in treatment-naïve patients.



PegIFN $\alpha$ -2a (180  $\mu$ g SC weekly): Pegasys®

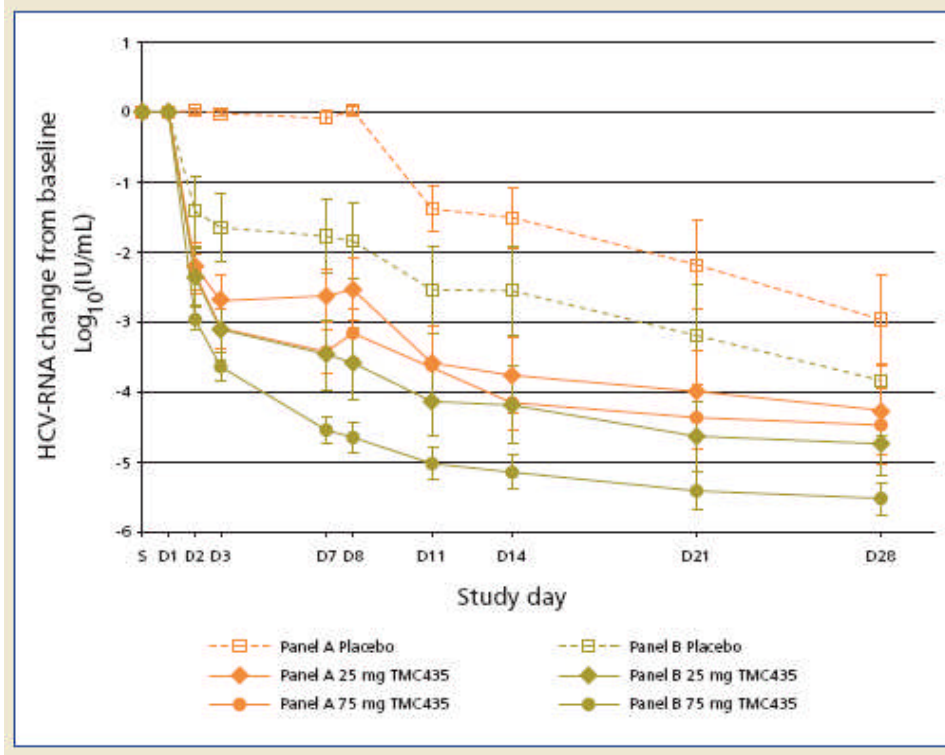
RBV (1000 to 1200 mg daily): Copegus®

SoC treatment for 24 or 48 weeks at the discretion of the investigator

## Opera-1 (cohort 1): Antiviral efficacy (1)

- Strong dose dependent, antiviral effect, which was more pronounced with 4-weeks triple therapy
- No viral breakthrough observed with 4-week triple therapy with 25 and 75 mg TMC435
- Largest viral load reduction observed in the 75 mg OD:  $-5.5 \log_{10}$  IU/mL

Figure 5: Mean HCV-RNA change per treatment arm from baseline to Day 28



## Opera-1 (cohort 1): Antiviral efficacy (2)

Table 3: Mean HCV RNA changes from baseline and number of patients with HCV RNA levels below lower limit of quantification (LLQ) and detection (LLD) per treatment arm.

Dose/Treatment	Time point (Day)	Mean HCV-RNA change (Log <sub>10</sub> IU/mL)	< LLQ n/N <25 IU/mL	< LLD n/N <10 IU/mL
Panel A Placebo	7	-0.08	0/6	0/6
Panel A TMC435 25 mg	7	-2.63	1/9	0/9
Panel A TMC435 75 mg	7	-3.43	0/9	0/9
Panel B Placebo	7	-1.77	0/6	0/6
	14	-2.56	0/6	0/6
	28	-3.83	3/6	2/6
Panel B TMC435 25 mg	7	-3.47	1/9	0/9
	14	-4.19	3/9	1/9
	28	-4.74	6/9	3/9
Panel B TMC435 75 mg	7	-4.55	1/9	0/9
	14	-5.15	7/9	3/9
	28	-5.52	9/9	8/9

HCV RNA levels were assessed with Roche COBAS Taq Man HCV/HPS assay v2 with an LLQ of 25 IU/mL and an LLD of ~10 IU/mL. To calculate mean HCV RNA values, results below LLQ are imputed with 24 IU/mL and values below LLD with 9 IU/mL.

## Opera-1 (cohort 1): Conclusions

**TMC435 25 and 75 mg once daily in combination with SoC demonstrated dose-dependent potent antiviral efficacy and a favorable safety profile when dosed up to 28 days in treatment naïve HCV genotype 1 patients**

### **Efficacy**

- 4 weeks of triple therapy with 75 mg TMC435 once daily resulted in a viral load reduction of  $-5.5 \log_{10}$  IU/mL and 8 of 9 (89%) patients with undetectable virus

### **Safety**

- All patients completed 4 weeks of TMC435 dosing and continued on SoC
- All TMC435-related AEs were of mild or moderate intensity (grade 1 or 2)
- Most common TMC435-related AEs were headache, nausea and diarrhea
- No Tx discontinuations due to adverse events

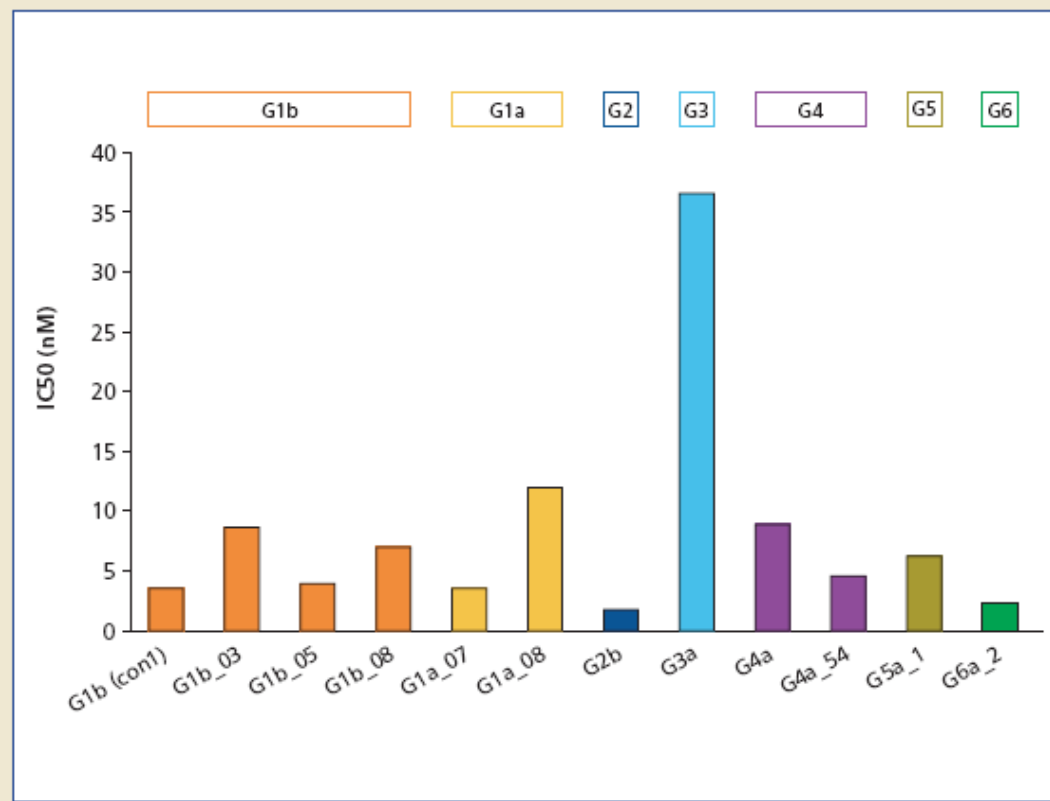
## Opera-1 (cohort 1): PK data

### PK Conclusions:

- 25 and 75 mg TMC OD generated plasma levels well in excess (12 to 44-fold) of targeted efficacious levels (replicon EC<sub>50</sub>)
- Steady state achieved within 3 days in HCV G1 patients
- Dose proportional increase of exposure from 25 to 75 mg OD
- No clinically relevant drug-interactions between SoC and TMC435

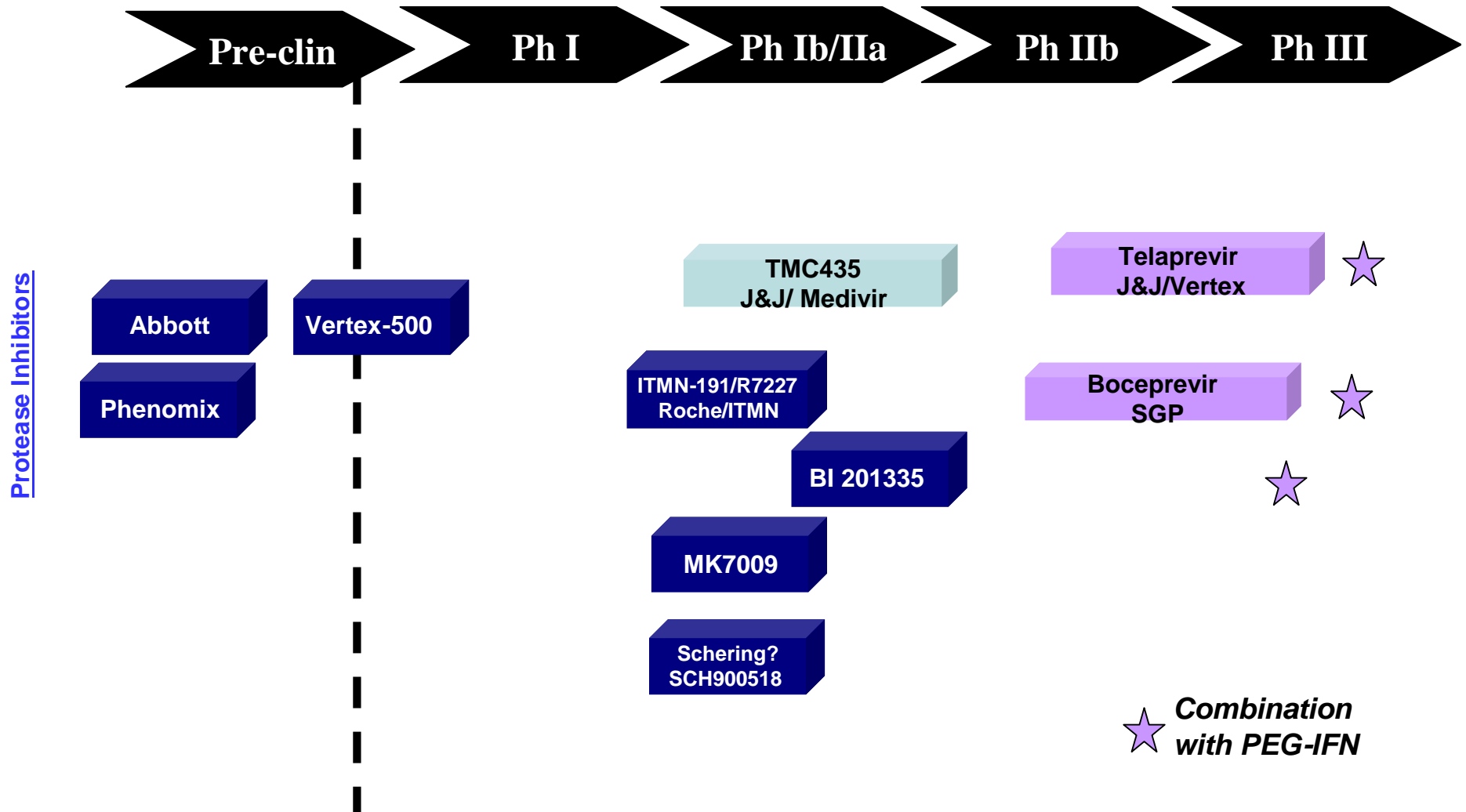
# In-vitro inhibition of genotype 1 to 6 proteases

Figure 3: Inhibition of NS3 protease by TMC435 determined in a biochemical protease assay.



TMC435 is a potent inhibitor of NS3/4A protease from genotype 1 to 6, with IC<sub>50</sub> values below 13 nM for all except genotype 3A (37 nM)

# HCV PI Competitive Landscape







In collaboration with  
Tibotec Pharmaceuticals

## HCV Polymerase

Existing HCV polymerase compounds



# Hepatitis C Polymerase - Medivir/J&J program

## Status

- Partnership with Tibotec / Johnson & Johnson since May 15 2008

## Process

- Jointly develop Medivir's existing HCV polymerase NS5B inhibitors from preclinical towards clinical development and screening of Medivir polymerase library's for HCV

## Patents

- Extensive and non-limiting IP

## Licensing agreement

- Upfront & milestones of € 147m + royalties on sales for one product reaching market.
- Additional € 130m for second compound and indication reaching market + royalties on sales. Will be based on screening of Medivir nucleoside library's
- FTE Funding
- All development costs covered by JNJ
- Nordic rights retained by Medivir



# Medivir - Project Summary 2008



- Strong phase IIa data presented for TMC435 in HCV patients
  - Phase IIb will soon start
- Initiated late preclinical collaboration with JNJ/Tibotec on hepatitis C polymerase inhibitors
- Applications for approval of Lipsovir (labial herpes) filed in the US and Europe October 2008



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