### Medivir investor update 8 June 2009

Ron Long CEO Rein Piir, CFO / IR Bertil Samuelsson, VP Discovery & Research Eva Arlander VP Pharma

> Medivir contact <u>rein.piir@medivir.se</u> www.medivir.com



### Welcome to the investor update meeting

Program

Introduction

Operational focus 2009-2012

**Brief project updates** Lipsovir<sup>®</sup>

TMC435 HCV Polymerase BACE (Alzheimer's) Cathepsin K HIV-PI Rein Piir, CFO, VP IR

Ron Long, CEO

Eva Arlander, VP Pharma

Prof. Bertil Samuelsson VP Discovery Research



# Pipeline in June

Projekt	Indikation(er)	Partners/ Avtal ingånget	Avtalsvillkor	Medivirs marknader	Explorativ verksam- het	Optime rings- fas	Preklin. utv. fas*	Fas I	Fas II	Fas III
<b>Lipsovir®</b> (ME-609)	Läppherpes	Egen regi								
<b>TMC435</b> (HCV PI)	Hepatit C	Tibotec / 2004	80,5 MEUR + Royalty och forskningsstöd	Norden						
<b>MIV-701</b> (Cath K)	Benskörhet, Artros benmetastaser	Egen regi								
HCV POL	Hepatit C	Tibotec / 2008	142-272 MEUR+Royalty och forskningsstöd	Norden						
<b>MIV-710</b> (Cath K)	Benskörhet, Artros benmetastaser	Egen regi								
HIV PI	HIV	Tibotec / 2006	64 MEUR + Royalty och forskningsstöd	Norden						
BACE	Alzheimer's	Egen regi								
Cathepsin S	Reumatoid artrit, multipel skleros	Egen regi								
KOL PI	KOL	Egen regi		Världen exkl Kina						
Renin	Högt blodtryck	Egen regi								
Proteashämmare	e Polymeras	hämmare	Polymerashämmning/hy	drokortison						



# **Operational pipeline June 2009**

Projekt	Indikation(er)	Partners/ Avtal ingånget	Avtalsvillkor	Medivirs marknader	Explorativ verksam- het	Optime rings- fas	Preklin. utv. fas*	Fas I	Fas II	Fas III
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Valomaciclovir (MIV-606)	Bältros,körtelfeber	Epiphany Bio- sciences /2006	24,5 MUSD + Royalty Aktier i Epiphany	Norden						
Alovudine (MIV-310)	HIV	Mefuvir/2007	Royalty	Världen exkl Asien						
<b>Lagociclovir</b> (MIV-210)	Hepatit B, HIV	Hainan Noken	7 MUSD + Royalty	Världen exkl Asien						
MIV-150	HIV	Population Council / 2003		Option på 50% av västvärlden						
MIV-160	HIV	Mefuvir	Aktier i Mefuvir + Rovaltv	Världen exkl Kina, Taiwan och Macao						
MIV-410	HIV, CMV	Presidio/2006	52,25 MUSD + Royalty Aktier i Presidio	Norden och England Option på Europa						
Polymerashämma	 									





- We filed an NDA with US (FDA) and EU regulatory authorities for Lipsovir® in October 2008
- We expect to receive more feedback in the process during the summer and expect a outcome of this process during Q4 2009
- The objective is to enter partnerships to commercialize Lipsovir® globally. The partnering process is pending regulatory approval.
- The ambition is to have the first market launch in H1 2010



# Hepatitis C - Our projects in collaboration with Tibotec/JNJ

TMC-435

Phase IIb for genotype 1 treatment naïve patients has started

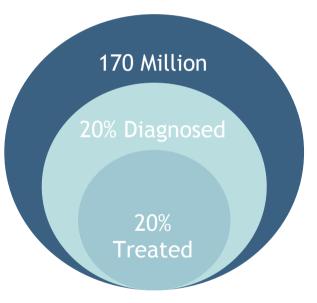
Phase IIb studies in genotype 1 treatment experienced patients to start during Q3

HCV-Pol Nucleoside HCV Polymerase Inhibitors in preclinical development towards phase I



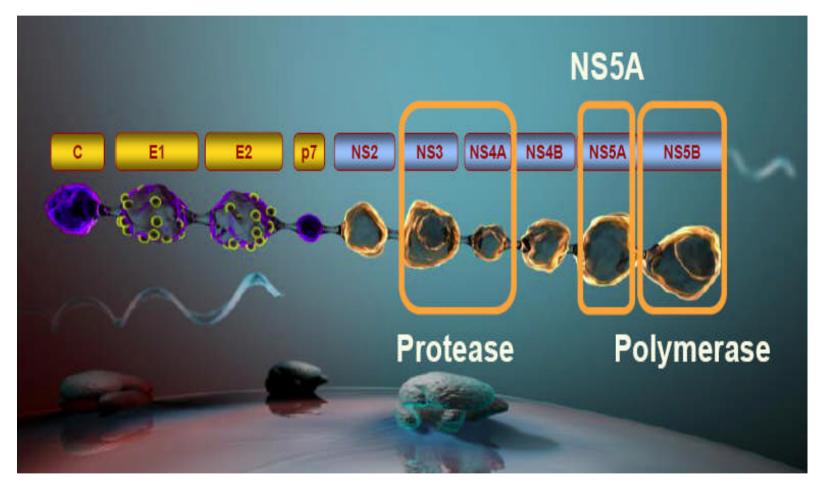
# Hepatitis C: Eliminating a deadly disease

- Affects 170 MM people worldwide (3% of population)
- Majority of patients are not diagnosed
- HCV can be cured but cure rates low with SoC
  - 40-50% cure rates for G1 with 48 weeks of treatment
- Most diagnosed patients remain untreated
- New antiviral drugs attack specific enzyme targets in HCV replication





### STAT-Cs: Paradigm Shift in HCV Treatment

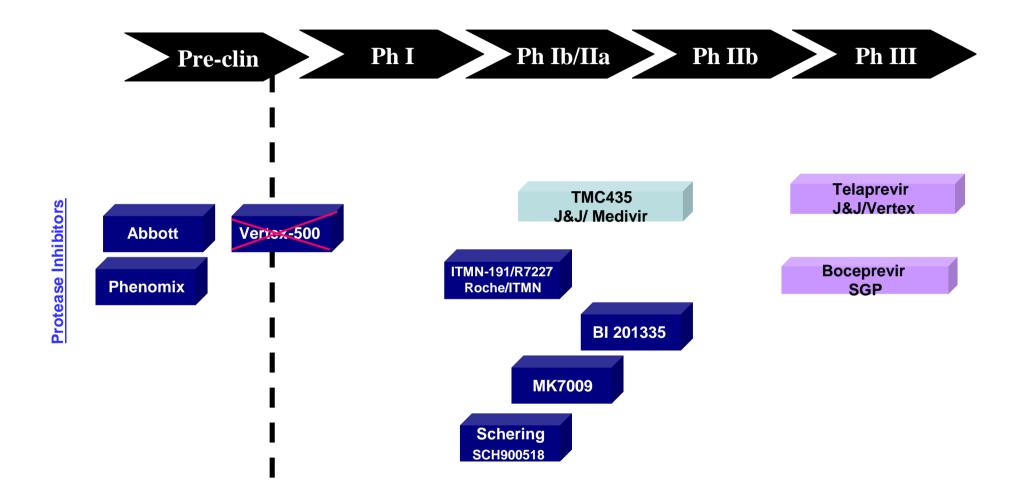


Kwong A, et al. Drug Discovery Today: Therapeutic Strategies 2006;3:211-220 Schmitz U, Tan SL. Recent Pat Antiinfect Drug Discov 2008;3:77-92



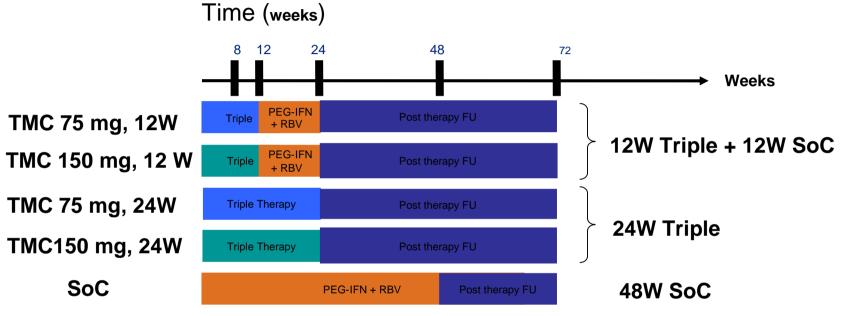


# **HCV PI Competitive Landscape**





# TMC435 - C205 - Phase IIb study in treatment-naïve HCV patients has started

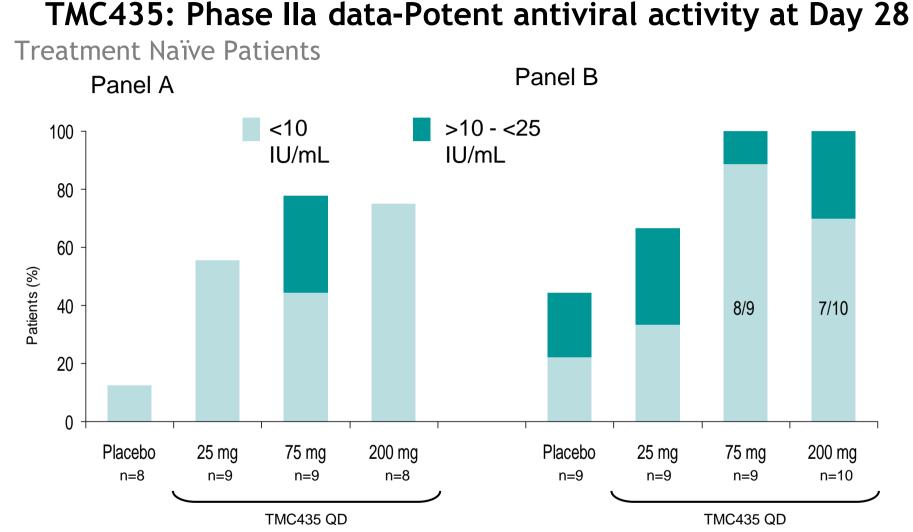


N = 400

**Primary endpoint:** Proportion of patients with undetectable virus levels 24 weeks after planned end-of-treatment (SVR24)

SoC: Ribavirin 1000-1200 mg BID + pegIFNalpha-2A 180  $\mu$ g weekly

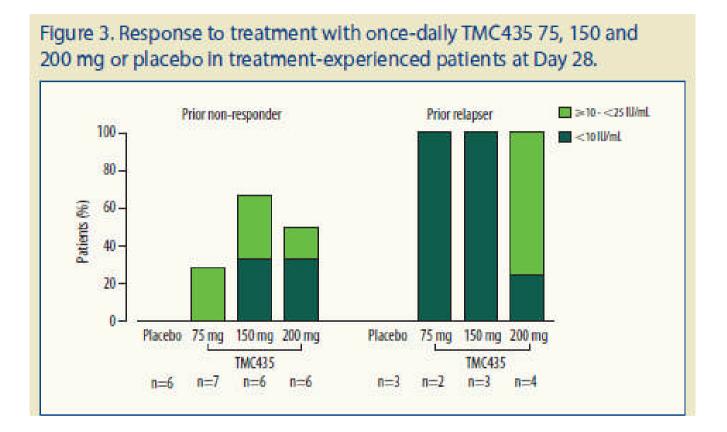




• 6/9 patients in the 25 mg arm, 9/9 (100%) patients in the 75 mg arm and 10/10 (100%) patients in the 200 mg arm of Panel B had HCV RNA <10 IU/mL at Week 12 (4-weeks TMC435 + SoC, 8-weeks SoC only)



# Viral load reduction in treatment-experienced patients



2/9 (22%), 5/9 (56%) and 3/10 (30%) patients in 75, 150 and the 200 mg groups reached undetectable levels (< 10 IU/mL) after 4 weeks of treatment, compared to 0/9 patients on placebo.



# Conclusions from phase IIa studies (Opera-1) in treatment naïve and treatment experienced

In both treatment-naïve and treatment experienced patients infected with HCV genotype-1, TMC435 in combination with SoC over 4 weeks of treatment:

- demonstrated potent antiviral activity
- was generally safe and well tolerated
- was not associated with AE-related treatment discontinuations.
- Mild and reversible increases in bilirubin was observed, most pronounced in the highest dose groups. The mechanism of action is under active investigation.

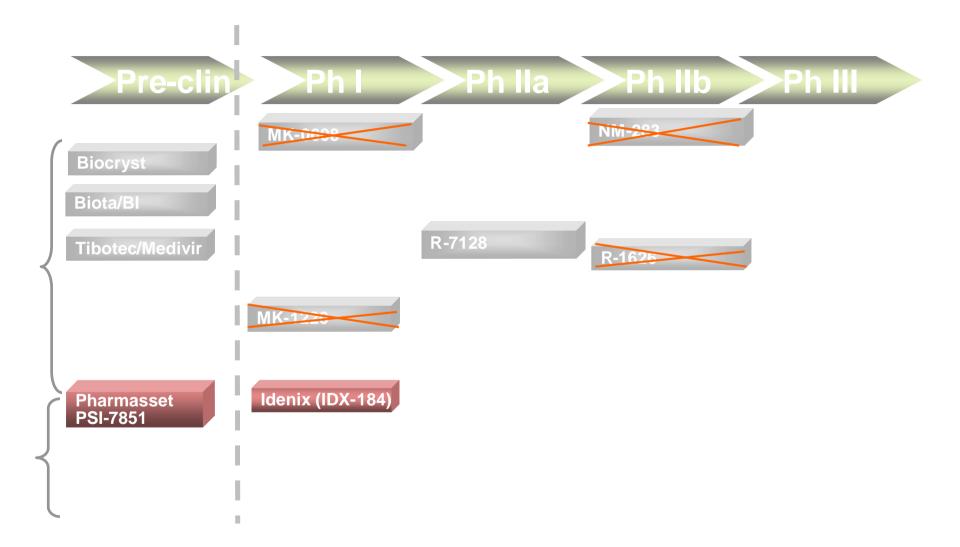


# Nucleoside HCV Polymerase Inhibitors





## HCV Nucleoside Competitive Landscape





# Hepatitis C Polymerase - Medivir/J&J program

#### Status

- Partnership with Tibotec / Johnson & Johnson since May 15 2008
- Candidate Drug selected on December 9th, 2008, triggering a milestone of € 2.6m
- Presently in preclinical development phase towards
  phase I

#### Next step

• Start of phase la

#### Patents

• Extensive and non-limiting IP filed

#### Licensing agreement

- Remaining milestones of € 137m + royalties on sales for one product reaching market.
- Additional € 130m for second compound and indication reaching market + royalties on sales.
- FTE Funding for one year, ended May 2009
- All development costs covered by JNJ
- Nordic rights retained by Medivir





**Cathepsin K inhibitors** 

Osteoporosis, Osteoarthritis & Bone Metastases



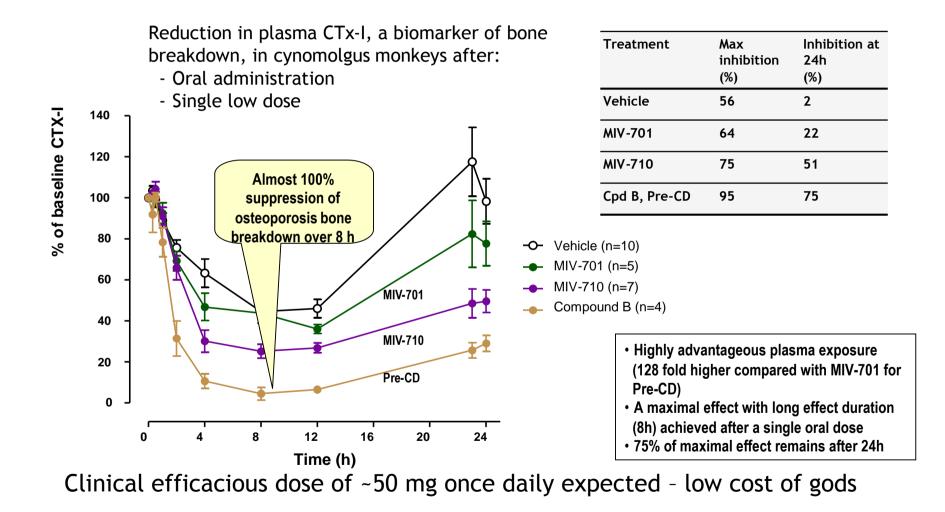


## Medivir Cathepsin K Inhibitor Program - Status

- Medivir Cathepsin K inhibitor CD's display potent and reversible anti-resorptive activity on bone whilst not suppressing the beneficial bone formation, as other anti-resorptives
- MIV-710 is a new Candidate Drug selected in February 2009. It is a follow-on to MIV-701 having superior pharmacokinetic properties
- A second CD will be selected in June 2009
- Strong IP position
- A broad program targeting multiple indications of great unmet medical need
- Partnering initiatives has commenced for the full program



### In vivo cynomolgus data of MIV-710 (CD) and Pre-CD (Cpd B) -High efficacy based on biomarkers for osteoporosis



## Key advantages of Medivir inhibitors vs odanacatib

Odanacatib is a cathepsin K inhibitor from Merck currently in phase III clinical trials for osteoporosis. There are no other competitor cathepsin K inhibitors in active clinical trials

- Potential for stronger bone (reduced fracture incidence) than that achieved with Odanacatib due to Medivir inhibitors providing beneficial daily PTH spike, essential for maintaining bone formation
- Higher potency vs odanacatib in the human osteoclast assay
- Longer duration of potency in the human osteoclasts
- Structurally different from both odanacatib (Merck) and balicatib (Novartis, Phase II, suspended) which contain nitrile 'warheads' with possible implication in skin disorders, phenomenon also shared with Novartis nitrile containing DPP-IV inhibitors whose progress was halted due to adverse skin effects
- Higher selectivity vs other cysteine proteases like cathepsin S
- Once daily dosing (Medivir) rather than once weekly dosing (Merck odanacatib) preferred in terms of patient preference and compliance



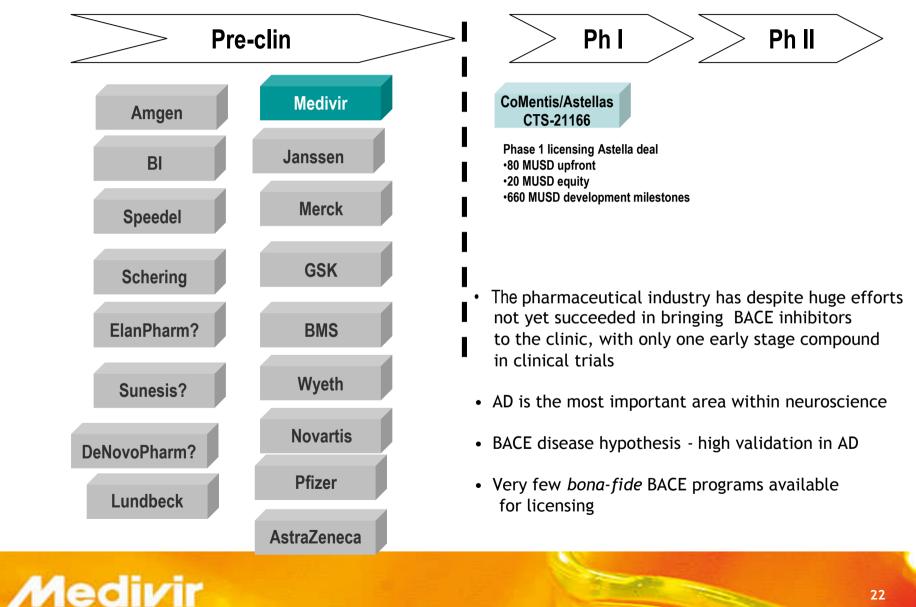
# **BACE Inhibitors**

# Alzheimer's disease





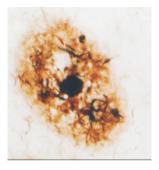
### **BACE-1** Inhibitors in development



# Alzheimer's disease, AD

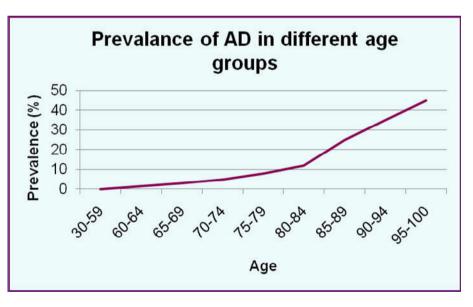
- Around 24 million AD cases world-wide
- Life expectancy from diagnosis: Approx. 10 years
- Stage 1 (1-3 y):
  - Memory impairment
- Stage 2 (2-6 y):
  - Difficulties to recognize people and objects
- Stage 3 (4-6 y):
  - Very passive, hard to reach
  - Need help with hygeine, dressing, eating
  - Psycotic problems (paranoia, aggression...)
  - Incontinence, low blood pressure, infections
- The cost for dementia care in Sweden is around 40 billion SEK/ year (≈ heart/vascular diseases and cancer together)
- 60% of all institutional care places are kept by demented persons (30% in the 70s)
- No available drugs cures/prevents the disease
  - Acetylcholine esterase inhibitors
  - Glutamate antagonist





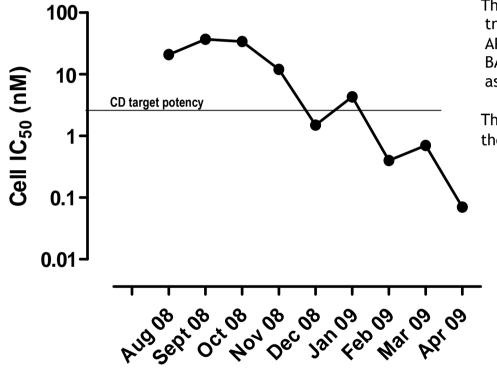
Reduced brain volume Neuronal cell death Synaptic degeneration

Plaque (Amyloid B-peptide)





### High cell-based potency achieved



The HEK293, Human Embryonic Kidney cells, transfected with and over expressing the substrate APP, Swedish variant, and naturally expressing BACE1: the industry standard assay used as a measurement of efficacy for a BACE1 inhibitor.

The lower the cell-based IC50 value, the more potent the inhibitor compound.

BACE inhibitors synthesis development by month



# Medivir BACE Program

Novel and patentable lead series

- ✓ 3 validated novel Lead Series
- ✓ 1 of the series currently at advanced Lead Optimization stage

Strong IP (patent) position

Extensive and non-limiting IP filed

Potent BACE inhibitors both on enzyme and in cell-based assay

 Lead inhibitors display robust potency, IC50<< 1 nM, in both BACE enzyme and in cell-based assay, measuring AB40 release

Activity *in vivo* on reduction of AB40 release in the CNS upon administration of BACE inhibitor Lead inhibitors display AB40 reduction in both plasma and in the CNS of wt mice

CD selection expected within 12 months

Partnering discussions initiated



# **HIV-PI Program**

- R&D collaboration with Tibotec/J&J Collaboration
  - Upfront: 2 M€ in June 2006
  - Research funding at Medivir up to December 2008
  - Development milestones similar to HCV PI license agreement
- Protease inhibitors for the treatment of HIV-1
- Highly competitive CD target profile.
- Extensive non-limiting patent portfolio
- Next milestone, selection of candidate drug

