Welcome to Medivir breakfast presentation at EASL 2009

Börje Darpö VP Development

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Åsa Rosenquist Director MedChem

Rein Piir CFO / IR
Medivir Pipeline April 2009

- "We has a large interest and strong commitment in HCV drug development"

<table>
<thead>
<tr>
<th>Prioritized projects</th>
<th>Project</th>
<th>Indication(s)</th>
<th>Partners/ Date of agreement</th>
<th>Terms</th>
<th>Medivir’s markets</th>
<th>Exploratory phase</th>
<th>Optimization</th>
<th>Preclinical dev.*</th>
<th>Phase I</th>
<th>Phase II</th>
<th>Phase III</th>
<th>NDA</th>
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<tr>
<td></td>
<td>Lipsovir® (ME-609)</td>
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<td>TMC425 (HCV-R1)</td>
<td>Hepatitis C</td>
<td>Tibotec / 2004</td>
<td>EUR 80.5 m+ royalties and FTE funding</td>
<td>Nordic region</td>
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<td>MIV-791 (Cath K)</td>
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<td>HCV POL</td>
<td>Hepatitis C</td>
<td>Tibotec / 2008</td>
<td>EUR 142-272 m+ royalties and FTE funding</td>
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<td>Tibotec / 2006</td>
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<td>In-house</td>
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<td>Renin</td>
<td>Hypertension</td>
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Inhouse preclinical program

Inhouse preclinical program

Inhouse preclinical program
HCV POL - In collaboration with Tibotec / JNJ

Nucleoside HCV Polymerase Inhibitors
HCV Nucleoside Competitive Landscape

- **Pre-clin**: Biocryt, Biota/Bl, Tibotec/Medivir, Pharmasset, PSI-7851
- **Ph I**: MK-0608, R-1626
- **Ph IIa**: Biocryt, Biota/Bl, Tibotec/Medivir, Idenix (IDX-184), PSI-7851
- **Ph IIb**: NM-283
- **Ph III**: R-7128, R-1626

Medivir
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
- Selected CD in preclinical development phase towards phase I

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, ends May 2009
- All development costs covered by JNJ
- Nordic rights retained by Medivir
TMC435 - in collaboration with Tibotec / J&J

Presently in final stage of phase IIa for genotype 1 treatment naïve patients and treatment experienced patients

Data from Opera-1 (Phase IIa) in treatment naïve and treatment experienced patients presented

Phase IIb will start in Q2
HCV PI Competitive Landscape

Pre-clin

Ph I

Ph Ib/IIa

Ph IIb

Ph III

Protease Inhibitors

Abbott

Vertex-500

Phenomix

Telaprevir
J&J/Vertex

Boceprevir
SGP

TMC435
J&J/Medivir

ITMN-191/R7227
Roche/ITMN

BI 201335

MK7009

Schering
SCH900518

Vertex-500
Hepatitis C protease - TMC435 - Medivir/Tibotec

- Non-covalent binding NS3/4A protease inhibitor
- EC$_{50}$ = 8 nM in genotype 1 replicon
- In vitro: Synergistic with IFNα and additive with RBV
Hepatitis C protease - TMC435 - Medivir/Tibotec

Status
• Phase IIb will start Q2 2009

Results from IIa
• Data from 25 and 75 mg dose groups in treatment naïve patients presented in November 2008.

New data presented at EASL in April 23-25 2009
• Data from 25 mg, 75 mg and 200 mg at week 12 in treatment naïve patients
• Data in previous non-responders and relapsers from the 75, 150 and 200mg dose groups at week 4

Licensing agreement
• Upfront & milestones of EUR 80.5m (EUR 47m remains)
  + royalties on sales
• All development costs covered by Tibotec
• Nordic rights retained by Medivir
OPERA-1 (Study TMC435-C201)

- Phase IIa, double-blind, placebo-controlled, proof-of-concept trial
  - treatment-naïve and treatment-experienced patients, genotype-1 infection

- Data presented for treatment-naïve patients
  - Cohort 1: TMC435 25 and 75 mg QD
  - Cohort 2: TMC435 200 mg QD

- Standard entry criteria for PEG-IFN/RBV studies
  - documented chronic HCV infection
  - compensated liver disease including cirrhosis
OPERA-1 (Cohorts 1 and 2): study design
Treatment-naïve, genotype-1 HCV-infected patients

- Cohort 1: TMC435 25 and 75 mg QD
- Cohort 2: TMC435 200 mg QD

SoC = pegylated interferonα-2a + ribavirin (PEG-IFNα-2a + RBV)
ITT, intent-to-treat population
OPERA-1 (Cohorts 1 and 2): mean change in HCV RNA from baseline to Day 28 (mono- and triple therapy)

Panel A: 1 week of TMC435 monotherapy followed by 3 weeks combined with SoC
Panel B: 4 weeks of TMC435 combined with SoC
OPERA-1 (Cohorts 1 and 2): response to treatment at Day 28

- 6/9 patients in the 25 mg arm, 9/9 patients in the 75 mg arm and 10/10 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)

Panel A: 1 week of TMC435 monotherapy followed by 3 weeks combined with SoC
Panel B: 4 weeks of TMC435 combined with SoC
OPERA-1 (Cohorts 1 and 2): virology findings during the first 4 weeks of treatment

- No viral breakthroughs were observed in Panel B (4 weeks TMC435 + SoC)
- 5 viral breakthroughs were observed in Panel A (1 week TMC435 monotherapy followed by 3 weeks TMC435 + SoC)
  - 2 patients in 25 mg group
  - 2 patients in 75 mg group
  - 1 patient in 200 mg group

- Among the viral breakthroughs in Panel A, emerging NS3 mutations† were observed in all 5 patients
  - R155K (intermediate FC‡)
  - R155K + D168N (intermediate FC‡)
  - D168E (intermediate FC‡)
  - Q80R/K + D168E (high FC‡)
  - D168V (high FC‡)

Viral breakthrough: >1 log_{10} IU/mL increase in HCV RNA from nadir or >100 IU/mL in patients with previous HCV RNA <10 IU/mL

FC, fold change; intermediate FC: >10-100; high FC: >100

†based on in vitro passage experiments; ‡based on in vitro replicon SDM data for TMC435
### OPERA-1 (Cohorts 1 and 2): adverse event (AE) summary

<table>
<thead>
<tr>
<th>Parameter, %</th>
<th>Placebo (N=13)</th>
<th>25 mg QD (N=18)</th>
<th>75 mg QD (N=19)</th>
<th>Placebo (N=6)</th>
<th>200 mg QD (N=18)</th>
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</thead>
<tbody>
<tr>
<td>Any AE</td>
<td></td>
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<tr>
<td>Grade 3 or 4</td>
<td>0</td>
<td>0</td>
<td>10.5*</td>
<td>0</td>
<td>11.1*</td>
</tr>
<tr>
<td>Discontinuation due to AE</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
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<tr>
<td>Serious AE</td>
<td>7.7</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Death</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Most common AEs†</td>
<td></td>
<td></td>
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<tr>
<td>Headache</td>
<td>38.5</td>
<td>50.0</td>
<td>47.4</td>
<td>50.0</td>
<td>16.7</td>
</tr>
<tr>
<td>Fatigue</td>
<td>30.8</td>
<td>44.4</td>
<td>21.1</td>
<td>16.7</td>
<td>27.8</td>
</tr>
<tr>
<td>Nausea</td>
<td>7.7</td>
<td>27.8</td>
<td>26.3</td>
<td>16.7</td>
<td>27.8</td>
</tr>
<tr>
<td>Influenza-like illness</td>
<td>15.4</td>
<td>27.8</td>
<td>31.6</td>
<td>0</td>
<td>22.2</td>
</tr>
</tbody>
</table>

No evidence of hepatobiliary, renal, haematopoietic or cardiac disturbances

*Neutropenia in 4 subjects, related to PEG-IFNα -2a, not or doubtfully related to TMC435

†Reported in >10 patients (all TMC435 groups combined)
OPERA-1 (Cohorts 1 and 2): Total bilirubin at baseline (Day 0) and Day 28

- Bilirubin levels decreased after the end of treatment with TMC435
- Elevations in direct and indirect bilirubin levels were also observed, particularly in the highest dose group

*Baseline sample missing from 1 patient; ULN, upper limit of normal = 21 μmol/L
OPERA-1 (Cohorts 1 and 2): ALT at baseline (Day 0) and Day 28

Panel A

Panel B

Mean U/L (± SE)

Day 0 28 0 28 0 28 0 28 0 28 0 28 0 28

Placebo 25 mg 75 mg 200 mg Placebo 25 mg 75 mg 200 mg

n=6 n=9* n=10 n=8 n=6 n=9** n=10 n=8

*Baseline sample missing from 1 patient; **baseline sample missing from 2 patients

ALT, alanine aminotransferase
TMC435 demonstrated potent antiviral activity in monotherapy and in combination with SoC over 4 weeks of treatment

- TMC435 25, 75 and 200 mg QD resulted in marked HCV RNA reductions
- In the 75 and 200 mg groups, all patients achieved HCV RNA levels <25 IU/mL and 7/10 and 8/9 respectively were undetectable at the end of 4-week triple therapy (Panel B)
- After 4 weeks triple + 8 weeks SoC, all patients (9/9 and 10/10) in 75 and 200 mg groups achieved non-detectable HCV RNA levels

Once-daily administration of TMC435 in combination with SoC in treatment-naïve genotype-1 patients over 28 days was generally safe and well tolerated

- TMC435 was not associated with AE-related treatment discontinuations
- Most reported AEs were mild to moderate
- Most common AEs included headache, fatigue, nausea and influenza-like illness
- Bilirubin elevations were observed in some patients receiving TMC435, mostly with the 200 mg dose, and were generally mild and reversible in nature
- Substantial decreases in transaminases were observed in patients receiving TMC435
Opera-1: Data in treatment experienced HCV G1 patients

4 weeks triple (TMC + SoC) therapy, no lead in.
Lowest dose of 75 mg
Demographics

Majority of patients (68%) Were non-responders

Table 1. Patient demographics and baseline characteristics.

<table>
<thead>
<tr>
<th></th>
<th>Placebo</th>
<th>TMC435</th>
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<tbody>
<tr>
<td></td>
<td>N=9</td>
<td>75 mg QD N=9</td>
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<tr>
<td>Gender, n (%)</td>
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</tr>
<tr>
<td>Female</td>
<td>0 (100)</td>
<td>3 (33.3)</td>
</tr>
<tr>
<td>Male</td>
<td>9 (100)</td>
<td>6 (66.7)</td>
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<tr>
<td>Race, n (%)</td>
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<tr>
<td>Caucasian</td>
<td>9 (100)</td>
<td>9 (100)</td>
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<tr>
<td>Age, years</td>
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<tr>
<td>Median (Range)</td>
<td>47.0 (21–57)</td>
<td>53.0 (38–62)</td>
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<tr>
<td>Body weight, kg</td>
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<tr>
<td>Median (Range)</td>
<td>78.0 (67–94)</td>
<td>74.0 (55–92)</td>
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<tr>
<td>HCV subtype (NS3B), n (%)</td>
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<tr>
<td>1a</td>
<td>2 (22.2)</td>
<td>2 (22.2)</td>
</tr>
<tr>
<td>1b</td>
<td>7 (77.8)</td>
<td>7 (77.8)</td>
</tr>
<tr>
<td>HCV RNA (log10 IU/mL)</td>
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<td></td>
</tr>
<tr>
<td>Median (Range)</td>
<td>6.4 (6–7)</td>
<td>6.9 (6–7)</td>
</tr>
<tr>
<td>Cirrhosis, n (%)</td>
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<tr>
<td>5 (55.6)</td>
<td>5 (55.6)</td>
<td>5 (55.6)</td>
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<tr>
<td>Response to prior IFN-based therapy* for HCV, n (%)</td>
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<tr>
<td>Non-responder</td>
<td>6 (66.7)</td>
<td>7 (77.8)</td>
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<tr>
<td>Relapser</td>
<td>3 (33.3)</td>
<td>2 (22.2)</td>
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</table>

*88% of patients received PEGIFN based therapy
Viral load reduction - All patients

Marked viral load reduction that exceeded $5 \log_{10} \text{IU/mL}$ after 4 weeks in highest dose groups.
Viral load reduction categorized by previous response

Viral response pronounced in both non-responders and relapsers
Viral load reduction

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.
Adverse events

There were no treatment discontinuations due to AEs or serious adverse events.
Effect on the liver - transaminases

Figure 4. Serum aminotransferase levels for treatment-experienced patients at baseline and after 28 days of treatment with once-daily TMC435 75, 150 and 200 mg or placebo. a) Alanine aminotransferase, ALT; b) Aspartate aminotransferase, AST.

[Graph showing ALT and AST levels with mean (+/- SE) for different treatment groups at baseline and Day 28.]
Bilirubin, total

- Bilirubin elevations were generally mild, and reversible in nature and elevations were most common with the highest dose
- Bilirubin elevations have been taken into account with the dose selection for phase 2b
- Appropriate measures have been put in place in the protocols for monitoring and management of these changes
- The mode of action is being investigated
Conclusions Opera-1
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.

These results support the development of TMC435 for both treatment-naïve and treatment-experienced patients infected with HCV genotype-1