Medivir

A research based specialty pharmaceutical company focused on infectious diseases

Credit Suisse Global 1 x 1 Confereence

Charlotte Edenius, EVP Research & Development Jens Kristensen EVP Clinical

An emerging research-based specialty pharmaceutical company

- Founded in 1988 as a spinout from AstraZeneca
- Listed in 1996 and traded on Nasdaq OMX Stockholm
- World leading science base 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[®]/ Xerese[®], is currently 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

- Add new products, both short and mid term to the Nordic commercial platform which will enable Medivir to approach its goal of becoming profitable
- Fine-tune the commercial platform for launch of TMC435 in the Nordic region
- Strengthen Medivir's position in the infectious disease, but also evaluate new therapeutic areas for the future through innovation based on the company's advanced protease and polymerase R&D platform



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



Key innovation and commercialisation advantages

Medivir has a strong position in HCV drug development – both partnered and internal programs for 3 different target classes

- The front runner, TMC435 Considered "best in class PI" hepatitis C drug
- Global phase III trials fully recruited in G1 patients for TMC435, H1-2013 expected filing date
- Interferon-free combination trials is the next major development step



Bio

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, annual sales of ~75 MUSD with an EBITDA of ~15 MUSD
 - Established commercial platform ready for TMC435 launch in the Nordics

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	Xer W-et	clear 59	

– a Medivir company

Xerclear[®] / Xerese[®] - global launch in 2011/2012

• Cold sore drug with an unique, differentiated profile and blue-chip marketing partners. First in-house developed product on the market.





The Medivir Technology Platform and Project Pipeline

Strong pipeline with multiple paths to value creation

			Preclinio	al phase		Clinica	l phase	
Project	Therapy area	Partner	Research	Develop- ment	Phase 1	Phase 2a	Phase 2b	Phase 3
INFECTIOUS DISEASES								
Hepatitis								
TMC435	Hepatitis C	Tibotec Pharmaceuticals/J&J						
HCV POL	Hepatitis C	Tibotec Pharmaceuticals/J&J						
Nucleotide inhibitor	Hepatitis C							
NS5A inhibitor	Hepatitis C							
Lagociclovir valactate (MIV-210)	Hepatitis B	Daewoong						
HIV/AIDS								
MIV-410 (PPI-801/802)	HIV	Presidio						
HIV-PI	HIV	Tibotec Pharmaceuticals/J&J						
Herpes virus								
Valomaciclovir (MIV-606)	Shingles	Epiphany		1				
Dengue virus								
NS3 protease inhibitor	Dengue fever	Janssen Pharmaceutica						
OTHER INDICATIONS								
Cathepsin K inhibitor	Bone disorders							
Cathepsin S inhibitor	Neuropathic pain							
	Project INFECTIOUS DISEASES Hepatitis TMC435 HCV POL Nucleotide inhibitor NS5A inhibitor Lagociclovir valactate (MIV-210) HIV/AIDS MIV-410 (PPI-801/802) HIV-PI Herpes virus Valomaciclovir (MIV-606) Dengue virus NS3 protease inhibitor CTHER INDICATIONS Cathepsin K inhibitor Cathepsin S inhibitor	ProjectInterapyareaINFECTIOUS DISEASESHepatitisTMC435Hepatitis CTMC435Hepatitis CNucleotide inhibitorHepatitis CHuyAIDSHepatitis CMIV-410 (PPI-801/802)HIVHIV-PIHIVValomaciclovir (MIV-606)ShinglesDengue virusJengue feverNS3 protease inhibitorDengue feverCathepsin K inhibitorBone disordersCathepsin S inhibitorMeuropathic pain	ProjectTherapy areaPartnerINFECTIOUS DISEASESHepatitisTMC435Hepatitis CTMC435Hepatitis CHepatitis CTibotec Pharmaceuticals/J&JNucleotide inhibitorHepatitis CNS5A inhibitorHepatitis CLagociclovir valactate (MIV-210)Hepatitis BMIV-410 (PPI-801/802)HIVMIV-410 (PPI-801/802)HIVHIVTibotec Pharmaceuticals/J&JHU/PIHIVValomaciclovir (MIV-606)ShinglesParse virusShinglesNS3 protease 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PartnerImage: PartnerCathepsin K InhibitorBone disordersImage: PartnerImage: PartnerIma	Project Therapy area Partner Development Phase 1 Phase 2 Phase 2 INFECTIOUS DISEASES Image: Image

Projects targeting infectious diseases Projects targeting other indications *Mode of Action



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 antiresorptives

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



Preclincal support for beneficial effects of cathepsin K inhibition in both osteoarthritis and osteporosis



MIV-711 – Partial medial mensicectomy; an experimental <u>osteoarthritis</u> model in dog



MIV-711 dosed at 30 µmol/kg (p.o.) once daily for 28 days, n=15

MIV-711 reduced bone and cartilage degradation biomarkers in dog osteoarthritis model



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 fraktalkine activation

Cathepsin S inhibitor program

• Potent, selective and orally bioavailable inhibitors developed by Medivir

Next decision point

• Candidate drug selection

Descending Ascending modulation input Dorsal Trauma horn Dorsal root ganglion Peripheral nerve

Principle for neuropathic pain



Cathepsin S inhibition and 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 risk¹

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

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





Hepatitis C -A rapidly evolving treatment landscape

Building a leadership position in hepatitis C - development activities vs all three major HCV targets

Two major internal HCV programs, both un-partnered

Nucleotide NS5B inhibitor: in preclinical optimization phase

- A new class of nucleoside-core structures identified
- Highly potent molecules with characteristics comparable to the most advanced stage clinical nucleotides
- No observed cytotoxicity
- Patent applications filed
- Aiming for Candidate Drug selection Q4 2012

NS5A replication complex inhibitor: in preclinical optimization phase

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





Building a leadership position in hepatitis C - development activities vs all three major HCV targets

Two major HCV programs partnered with Janssen Pharmaceutica

Protease inhibitor - TMC435

- A potent, once-daily, safe and efficacious protease inhibitor with broad genotypic coverage (1,2,4,5 and 6)
- Broad global phase III development program in genotype 1 infected patients
- Phase II IFN and ribavirin free combination studies

Polymerase inhibitor – nucleotide NS5B inhibitor

- A next generation, liver targeted nucleotide polymerase inhibitor program as part of ongoing partnership.
- Clinical Drug candidate selected
- Approaching clinical development





TMC435 in triple combination therapy with INF/RBV

• Best-in-class potential based on Phase II data

- A safe and efficacious drug with excellent tolerability
- Highly potent with advantageous low pill burden, 1 pill once daily

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

• Applicable in broad HCV patient populations

- G1 population, the most prevalent and difficult-to-treat
 - o Treatment naïve and treatment experienced patients
 - o Cirrhotic and non-cirrhotic patients

Robust clinical data with approximately 2000 patients exposed today



TMC435

- Broad clinical development program in HCV genotype 1 infected patients

Phase III

QUEST1 treatment-naïve patients; n=375

QUEST2 treatment-naïve patients; n=375

PROMISE (C3007) prior relapsed patients; n=375

Japan phase III program naïve and experienced patients; n=417 (four studies)

C3001 prior partial and null responders; n=744

Screening has started

IFN free combinations in Phase II development

TMC435 and GS-7977, a nucleotide NS5B inhibitor. A 12 or 24 weeks, +/- ribavirin PoC in prior null responders. n=180

Screening has started

TMC435 and daclatasvir (BMS-790052), an NS5A inhibitor. A 12 and 24 weeks, +/- ribavirin PoC in G1 patients

Trial will start Q2-2012

Regulatory filings H1-2013 in US, EU and Japan





Hepatitis C – Treatment evolution

A frantic race for the first INF-free combination delivers early promise but notably also sobering setbacks



Treatment responses

- Genotype/subtype
- Liver disease, F0-F4
- Population
- IL28B at baseline
- Patient characteristics
 - Treatament experienced
 - Treatment naives

N	Nost di	fficult to t	reat	Highest treatment responses
•	G1a	G1b	G4/6	G3 G2
	F4	F3		Non-cirrhotic (F0-F2)
	Black	(S	Hispanic	Caucasian
	TT		СТ	CC
	null	responder	partial responder	relapser
				treatment naive



Next generation therapy – Both INF and RBV free

Combinations of two DAAs being explored in experimental trials

- Early proof of concept achieved
- Combinations would meet cost and reimbursement challenges of the future
- Less risk of DDI interactions and time consuming trial explorations compared with three or more DAAs

New standard treatments should provide

- 12 weeks full treatment duration
- FDC and once daily
- Compelling efficacy, strong safety and minimal side effects

Ribavirin will be eliminated from future HCV combinations

- Ribavirin has severe side effects and safety issues on its own
- Can cause severe adverse events in patients, e.g. hemolytic anemia, teratogenicity, cough, dyspnea, rash, pruritus, insomnia and anorexia. It is a powerful mutagenic agent and is contraindicated in pregnant women and patients with hemoglobinopathies

Future HCV therapies will not contain interferon and ribavirin



IFN and RBV-free combinations – Proof-of-concept achieved in G1 patients

HCV protease inhibitor + NS5A replication complex inhibitor

- BMS daclatasvir + asunaprevir
 100% SVR24, 24 weeks in G1b null responders (Japan), no cirrhotics, n=10
- BMS daclatasvir + asunaprevir
 36% SVR12, 24 weeks in G1 null responders (64% RVR), n=11

A protease inhibitor in both combinations



IFN-free combinations with RBV -Proof-of-concept achieved in G1 patients

Combination: Two DAAs + ribavirin

- BI-201335(QD) + BI-207127(TID) + RBV, 63% SVR12, 76% cEVR, 16 weeks in G1 treatment naïve patients (SOUND-C2)
- ABT-458 + ritonavir + ABT-072 or ABT-333 + ribavirin, **90% SVR**, 12 weeks in G1 treatment naïve patients

A protease inhibitor in both combinations

Combination: One DAA + ribavirin

• GS-7977 + RBV

SVR12 still pending (primary endpoint defined as cure), **25% SVR4**, 100% RVR,12 weeks in 10 G1 null responders, (8/10 analyzed, 6 relapsed), ELECTRON trial, no cirrhotics

A nucleotide DAA plus RBV likely suboptimal in G1 non-responder populations



IFN and RBV free combination studies – TMC435 in first half of 2012

Combination of two DAAs

TMC435 + GS-7977 in G1 null responders

- GS-7977, clinically most advanced nucleotide
- 12 and 24 Week duration arm included
- INF and RBV free arms

TMC435 + daclatasvir in G1 patients

- Daclatasvir, clinically most advanced NS5A inhibitor:
- 12 Week duration arm included
- INF and RBV free arms

Further developments on TMC435 to be anticipated in 2012

TMC435, a best in class PI strongly positioned to become the principal component of future IFN-free therapies



Medivir committed to deliver new and innovative HCV treatments – Compelling opportunities in a rapidly evolving HCV field

New regulatory guidelines, novel treatment regimes and shorter trial designs have radically transformed the process towards drug registration in the HCV space

Shorter development timelines

- Interferon-free therapies will have shorter treatment duration than SoC today
- Primary endpoint has shifted from SVR24 to now SVR12, results in shorter pivotal trials
- Phase III dose selection can now be made from SVR4 interim phase IIb data
- Phase III trials may be allowed without an active comparator arm under certain circumstances
- Available data from a large number combo trials evaluating different DDAs will facilitate selection of the right combo design early in development

New and innovative drug candidates could file for market approval in less than 4 years from start of Phase I and at substantially lower costs



Medivir focused on delivering new HCV nucleotides

General features of nucleotides:

Promising clinical efficacy demonstrated

- Pan-genotypic coverage
- High barrier to resistance development
- Rapid onset of antiviral effects

Mechanism-of-action

• Nucleotides are converted in the liver to their corresponding active triphosphates which inhibits the NS5B polymerase activity and prevents viral replication to take place

Potential limitations

- Triphosphates may also be substrates for endogenous polymerases, notable e.g. mitochondrial DNA polymerase, resulting in side effects/toxicity
- The nucletides/nucleosides rely on the activity of several enzymes in the liver (e.g. kinases, esterases) to become activated (release of prodrug moiety and transformation to triphosphate form). The clinical consequences of this has yet to be fully determined
- Liver targeting principle may limit impact on extra hepatic viral replication

High need for efficacious and safe nucleotides Will likely be an important component of future combo treatments



TMC 435 - summary

Best-in-class properties in triple combination SoC treatment

- Documented safe and well tolerated
 - Close to 1800 patients have completed TMC435 treatments showing it to be safe and well tolerated
 - o Approx.1000 additional patients are being recruited in upcoming trials in 2012
- Highly efficacious in both G1a and G1b patients, in both cirrhotics and non-cirrhotics, and high response rates regardless of IP-10 level or *IL28B* genotype, CC, CT or TT, as demonstrated in three large phase 2b trials (PILLAR, ASPIRE and DRAGON)
- · Low dose and one tablet once daily
- Pan genotypic coverage G1-6, with the exception of G3
- Directly active on its HCV protease target, *i.e.* does not require serial steps for activation in the liver as for e.g. nucleotides
- High liver to plasma ratio (~40) and high plasma exposure at trough
 - Allow inhibition of extra hepatic HCV replication
- Can restore endogenous IFN signaling, ablated by the action of the HCV protease

Currently advancing in two, all oral, IFN-free combination trials



Expected key news flow highlights during 2012

- ✓ Q4 Agreement signed to evaluate TMC435 and daclatasvir (BMS-790052) in DAA combination trials
- ✓ Q1-12 DAA phase II combination study with TMC435 and GS-7977 started
- ✓ Q1-12 OTC launch of Xerclear® in Europe by GSK
- ✓ Q1-12 FY report and update on projects and financials
- Q1-12 Start of Phase III trials with TMC435 + SoC in prior null and partial responder patients (C3001) vs. Telaprevir. Screening has started.
- Q2-12 EASL ASPIRE full SVR24 data
- Q2-12 Start of DAA phase II combination study with TMC435 and daclatasvir
- Q2-12 Aim to start Phase I trials with MIV-711
- Q4-12 Potential CD selection in our internal Nucleotide NS5B inhibitor program
- Q4-12 EoT-data from Cohort 1 with TMC435 and GS7977 DAA phase II study
- Q4-12 Potential CD selection in cathepsin S (Neuropathic pain) program
- Q4-12 Aim to start phase 1 trials with Medivir / Janssen Nucleotide NS5B inhibitor
- Q4-12 AASLD
- Q4-12 Top line results from phase III trials with TMC435 (Quest 1+2 & Promise)

