

A research based specialty pharmaceutical company focused on infectious diseases

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### 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



#### 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



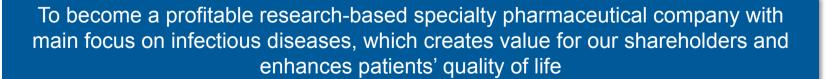
#### Xerclear® / Xerese® - global launch in 2011/2012

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



### **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





### FY 2011 Group level financial performance

- a strong year driven by substantial one-off-payments

CONSOLIDATED INCOME STATEMENT SUMMARY	2011	2010	2011	2010
(SEK m)	Oct-Dec	Oct-Dec	Jan-Dec	Jan-Dec
Net sales	131.8	1.3	698.6	54.9
Cost of goods sold	-96.7	-0.1	-240.6	-0.8
Gross profit/loss	35.1	1.2	458.0	54.1
Selling expenses	-18.4	-2.4	-95.2	-9.5
Administrative expenses	-13.9	-9.0	-47.2	-29.5
Research and development costs	-48.0	-48.2	-184.1	-153.4
Other operating income/expenses	1.2	1.5	-19.7	1.6
Operating profit/loss	-44.0	-56.9	111.9	-136.7
Net financial income/expense	-3.4	0.4	-0.7	2.5
Profit/loss after financial items	-47.4	-56.5	111.2	-134.2
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Tax	-5.7	0.0	2.5	0.0
Net profit/loss	-53.1	-56.5	113.8	-134.2



### FY 2011 financial performance at segment level

Net sales split		2011	2010	2011	2010
(SEK m)	(	Oct-Dec	Oct-Dec	Jan-Dec	Jan-Dec
Outlicensing and partnership agreements					
One-off payments		0.0	-	401.2	47.1
Pharmaceutical sales		47.5	-	111.2	0.1
Parallel imports		84.7	-	185.9	-
Other services		-0.4	1.3	0.3	7.7
Total		131.8	1.3	698.6	54.9
Pharmaceuticals segment		2011	2010	2011	2010
(SEK m)	0	ct-Dec	Oct-Dec	Jan-Dec	Jan-Dec
Net sales		47.1	1.3	512.7	54.9
EBITDA		-36.3	-55.3	137.6	-128.8
EBITDA %		-77.0%	-4253.8%	26.8%	-234.6%
Parallel Import segment		201	1 201		
(CEK ==)		Oct Do	- O-4 D-	Jan-	_
(SEK m)		Oct-De			
Net sales		84.		- 185.9	
EBITDA		0.	6	2.3	-

Solid financial position, cash and cash equivalents amounted to SEK 536 m at end of the period.





The Medivir Technology Platform and some selected Pipeline assets

# 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



# 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

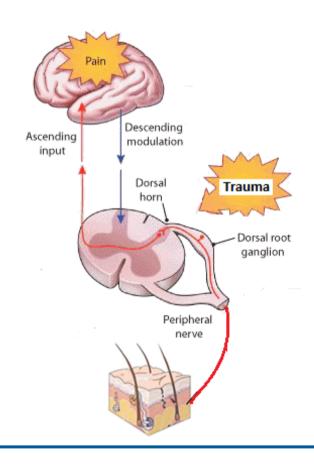
#### Cathepsin S inhibitor program

Potent, selective and orally bioavailable inhibitors developed by Medivir

#### Next decision point

Candidate drug selection potentially in Q4 2012

#### Principle for neuropathic pain







# Hepatitis C A rapidly evolving treatment landscape

### We are building a leadership position in hepatitis C

- development activities vs all three major HCV targets

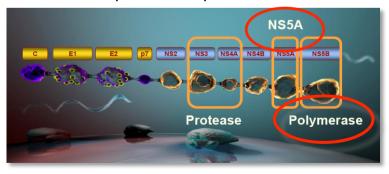
#### Two major internal HCV programs, both un-partnered

#### **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





### 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



### We are building a leadership position in hepatitis C

- development activities vs all three major HCV targets

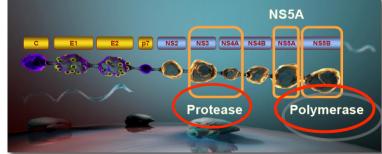
#### Two major HCV programs partnered with Janssen Pharmaceutica

#### 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



### TMC 435 - summary

#### **Best-in-class properties in triple combination SoC treatment**

- Documented safe and well tolerated
  - o 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



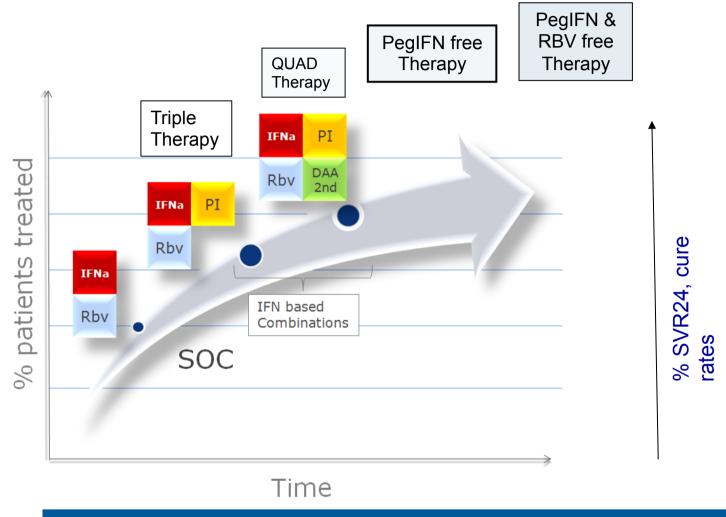


### **Hepatitis C – Treatment evolution**

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



### **Evolution of HCV therapy in HCV genotype 1 infection**



There are multiple paths leading to a PegIFN & RBV free therapy!



### **Treatment responses**

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

Most difficult to treat	Highest treatment responses
G1a G1b G4/6	G3 G2
F4 F3	Non-cirrhotic ( F0-F2)
Blacks Hispanic	Caucasian
тт ст	CC
null responder partial responde	er 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



### 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 AASI D
- Q4-12 Top line results from phase III trials with TMC435 (Quest 1+2 & Promise)

