

Medivir at

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Medivir - Key achievements 2008



- Strong phase IIa data presented for TMC435 (hepatitis C protease inhibitor)
- Our biggest deal ever signed in May with JNJ/Tibotec for hepatitis C polymerase inhibitors (>USD 190m). CD selected yesterday triggered a milestone payment of USD4m
- Applications for approval of Lipsovir (labial herpes) filed and validated in the US and Europe. Approval target date Q3 2009
- Co-promotion deal for GSK products in the Nordic countries
- Strong cash position by end of Q3 (USD 38m)



~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 December 2008

Prioritized	projects										app	roval	
Project	Indication(s)	Partners/ Date of agreement	Terms	Medivir's markets	Explora- tive phase	Optimiza- tion	Preclinical dev.*	Phase I	Phase II	Phase III			
Lipsovir® (ME-609)	Labial herpes	In-house											-
TMC435350 (HCV-PI)	Hepatitis C	Tibotec / 2004	EUR 80,5 m + royalties and FTE funding	Nordic region							P	hase II	b
MIV-701 (Cath K)	Osteoporosis, osteoarthritis, bone metastases	In-house									ir	to be	d
Cathepsin K	Osteoporosis, osteoarthritis, bone metastases	In-house										Incluce	G
HIV PI	HIV	Tibotec / 2006	EUR 64 m + royalties and FTE funding	Nordic region									
HCV POL	Hepatitis C	Tibotec / 2008	EUR 142-272 m + royalties and FTE funding	Nordic region					CD se	elect	ed		
HCV POL	Hepatitis C	Roche/2003/ inhouse	Undisclosed	Nordic region					yest	erda	ıy		
COPD PI	COPD	In-house (Hengrui)		World exc. China									
Renin	Hypertension	In-house											
BACE	Alzheimer's	In-house						Dr	ioriti	cod			
Cathepsin S	Rheumatoid arthritis, multiple sclerosis	In-house						pr	eclin	ical			
Protease ir * The regulated	nhibitor 📕 Poly I preclinical developmer	merase inhibito 1t phase.	r 🧧 Polymeras	e inhibition/hyd	rocortisone			р	rogra	am			





Filed for

Pipeline (continued)

Medivir HIV Franchise AB

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

• Polymerase inhibition/hydrocortisone

Protease inhibitor

Polymerase inhibitor

¹⁾ The regulated preclinical development phase.





Two active phase II trials

Commercial focus in the coming 6-12 months

LIPSOVIR	• Secure optimal partnership structure for both US & EU			
HEPATITIS C	 TMC435: start phase IIb trials HCV-Polymerase inhibitors: Potential start of phase I 			
CATHEPSIN K	 Select follow-on candidate drug Start partnering process 			
HIV PI	Candidate drug selection			
Other preclinical	 Initiate partner discussions for at least one program 			
PHARMA SALES	 Continue selling GSK products in Sweden Secure new co-promotion deals and potential own product(s) 			











Lipsovir[®] 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. Approval target date Q3 2009
- First product to prevent cold sores
 - Currently marketed products reduce healing time modestly without preventive effect on emerging lesions





Phase III results: Lipsovir prevents cold sores and shortens episodes

- Primary endpoint = prevention
 - Lipsovir[®] prevents cold sores in 42% of subjects with an emerging lesion
- Proportion of subjects with non-ulcerative recurrences

- Lipsovir[®] > vehicle (p<0.0001)
- Lipsovir[®] > acyclovir in our vehicle (p<0.014)
- Secondary endpoint = episode duration
 - Lipsovir[®] > vehicle on episode duration (p<0.05)
 - Lipsovir[®] 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 *nonulcerative* recurrence





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



Hepatitis C protease - Medivir/Tibotec - J&J program

Status

- Planning for phase IIb ongoing
- Phase IIa ongoing
 - Data from 25 and 75 mg dose groups presented in November

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

NS3/4A: Key protease for virus replication



Enzyme inhibiting compound



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



TMC435: Data presented at AASLD November 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 completed
 - 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-naive patients.



PegIFN α -2a (180 µg 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 4weeks 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 log₁₀ 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 ₁₀ , 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 🗲	RVR of 89%
HCV RNA levels were assesse 25 IU/mL and an LLD of ~10 imputed with 24 IU/mL and v	d with Roche IU/mL. To calc alues below LI	COBAS Taq Man HCV/H ulate mean HCV RNA v LD with 9 IU/mL.	PS assay v2 with alues, results bel	an LLQ of ow LLQ are	



Opera-1 (cohort 1): Conclusions

- TMC435 25 and 75 mg once daily in combination with SoC (PegINFα-2a / RBV) demonstrated dose-dependent potent antiviral efficacy and a favorable safety profile when dosed up to 28 days in treatment naïve HCV genotype 1 patients
- 4 weeks of triple therapy with 75 mg TMC435 once daily resulted in a viral load reduction of -5.5 log₁₀ IU/mL and 8 of 9 (89%) patients with undetectable virus
- There were no Tx discontinuations during 28 days of TMC435 dosing



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_{50} values below 13 nM for all except genotype 3A (37 nM)



HCV PI Competitive landscape



Medivir 19



In collaboration with Tibotec Pharmaceuticals

HCV Polymerase

Existing HCV polymerase compounds



Hepatitis C Polymerase - Medivir/J&J program

Status

- CD selected yesterday, triggered a milestone of € 2.6m
- 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
- The hepatitis C polymerase collaboration with JNJ/Tibotec in preclinical development phase towards clinical trials
- Applications for approval of Lipsovir® (labial herpes) filed and validated in the US and Europe. Approval target date Q3 2009

