



## **Research Update**

**Richard Bethell, EVP Discovery Research**

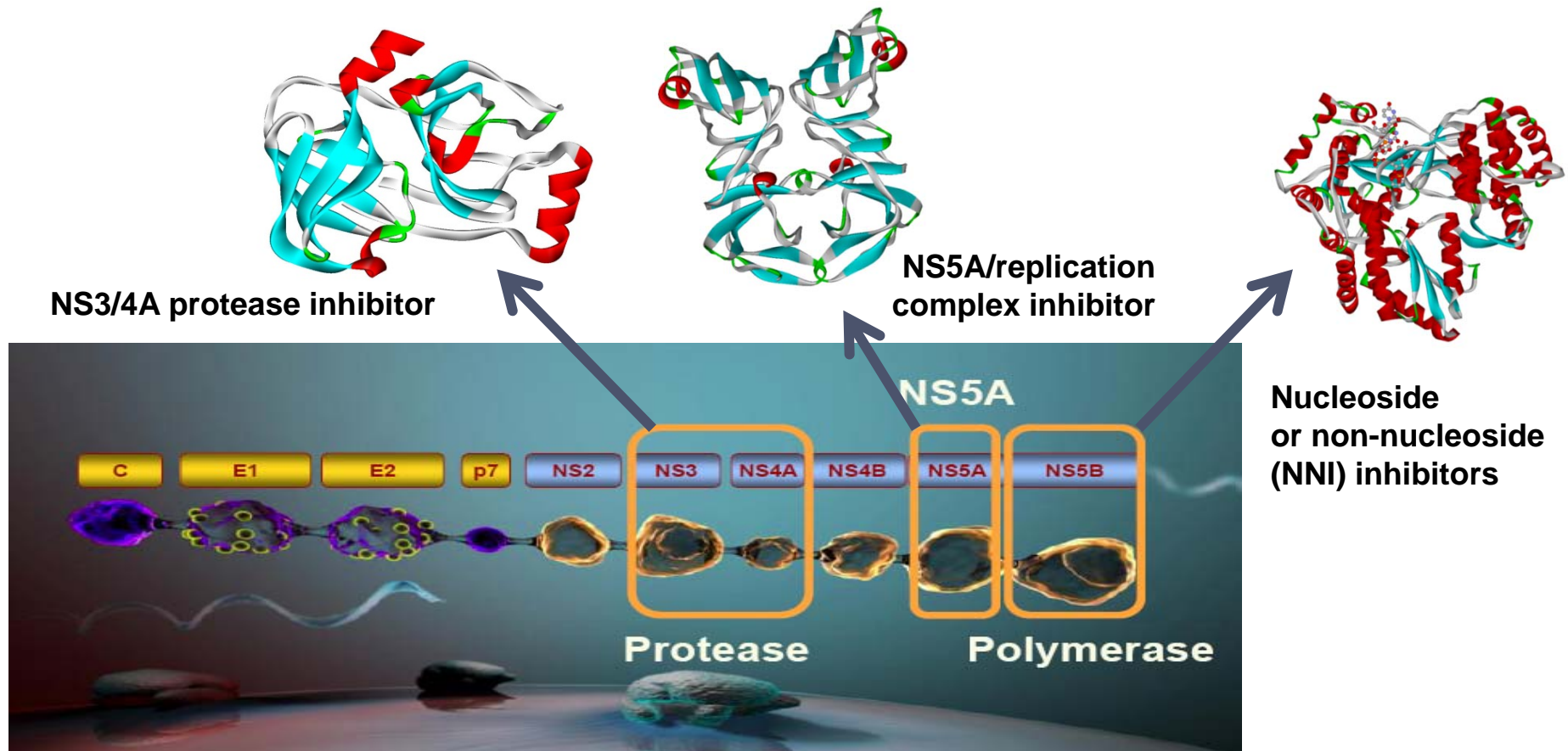
# R&D pipeline emphasizes focus in hepatitis C

Field	Project	Partner	Preclinical phase		Clinical phase				Market	
			Re- search	Deve- lopment	Phase I	Phase IIa	Phase IIb	Phase III		
<b>Antivirals</b>										
Labial herpes	Xerclear (Zovido, Zovirax Duo)	GlaxoSmithKline (GSK)	[Green bar spanning Re-search, Deve-lopment, Phase I, Phase IIa, Phase IIb, Phase III]							
Hepatitis C	Simeprevir (TMC435), NS3 protease inhibitor	Janssen Pharmaceuticals	[Green bar spanning Re-search, Deve-lopment, Phase I, Phase IIa, Phase IIb, Phase III]							Approved in Japan
Hepatitis C	NS5B nucleotide-based polymerase inhibitor	Janssen Pharmaceuticals	[Green bar spanning Re-search, Deve-lopment]							
Hepatitis C	NS5B nucleotide-based polymerase inhibitor	Unpartnered	[Green bar in Re-search]							
HIV	Protease inhibitor	Janssen Pharmaceuticals	[Green bar in Re-search]							

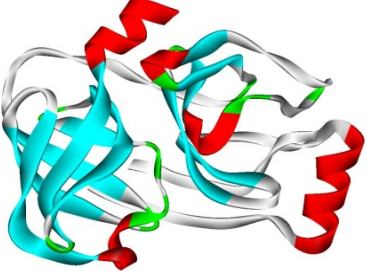
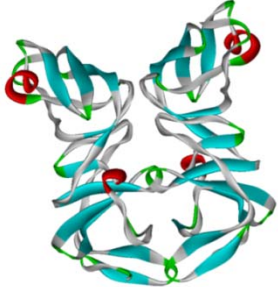

## Other indications

Bone related disorders	Cathepsin K inhibitor	Unpartnered	[Blue bar spanning Re-search, Deve-lopment, Phase I]				Phase I data			
Neuropathic pain	Cathepsin S inhibitor	Unpartnered	[Blue bar spanning Re-search, Deve-lopment]		CD nominated					

# Three major hepatitis C targets

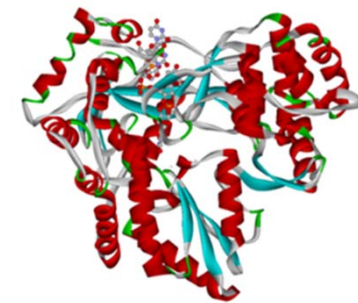


# Direct Acting Antivirals (DAAs) to transform HCV treatment through interferon-free combinations

	<p><b>NS3/4A protease</b></p> <ul style="list-style-type: none"><li>• Highly active molecules</li><li>• Potent molecules target some other GT in addition to GT1</li><li>• Relatively low barrier to resistance in monotherapy</li><li>• Simeprevir appears best-in-class (efficacy:safety)</li></ul>
	<p><b>NS5A replication complex</b></p> <ul style="list-style-type: none"><li>• Exceptionally potent in vitro replication inhibitors</li><li>• Polymorphisms compromise clinical response in some genotypes (e.g. in GT1a)</li><li>• Use in a 2 DAA combo in such genotypes means the other DAA must have high potency and barrier to resistance</li></ul>
	<p><b>NS5B RNA-dependent RNA polymerase</b></p> <ul style="list-style-type: none"><li>• Nucleotide inhibitors have superior clinical antiviral efficacy to nucleosides and non-nucleosides</li><li>• Nucleosides and Nucleotides<ul style="list-style-type: none"><li>• High barrier to resistance and pan-genotype activity</li><li>• High attrition (preclinical/clinical safety)</li></ul></li></ul>

# Wholly owned HCV nucleotide program is an important strategic asset

- Medivir has leveraged nucleoside experience to pursue high value nucleotide compounds
- Current Medivir effort focused on novel uridine-based series
- Medivir's compounds are structurally distinct from existing nucleoside starting points
- Initial protide series features include:
  - EC50 values <100nM
  - High in vitro selectivity indices
  - Attractive early pharmacokinetic profile



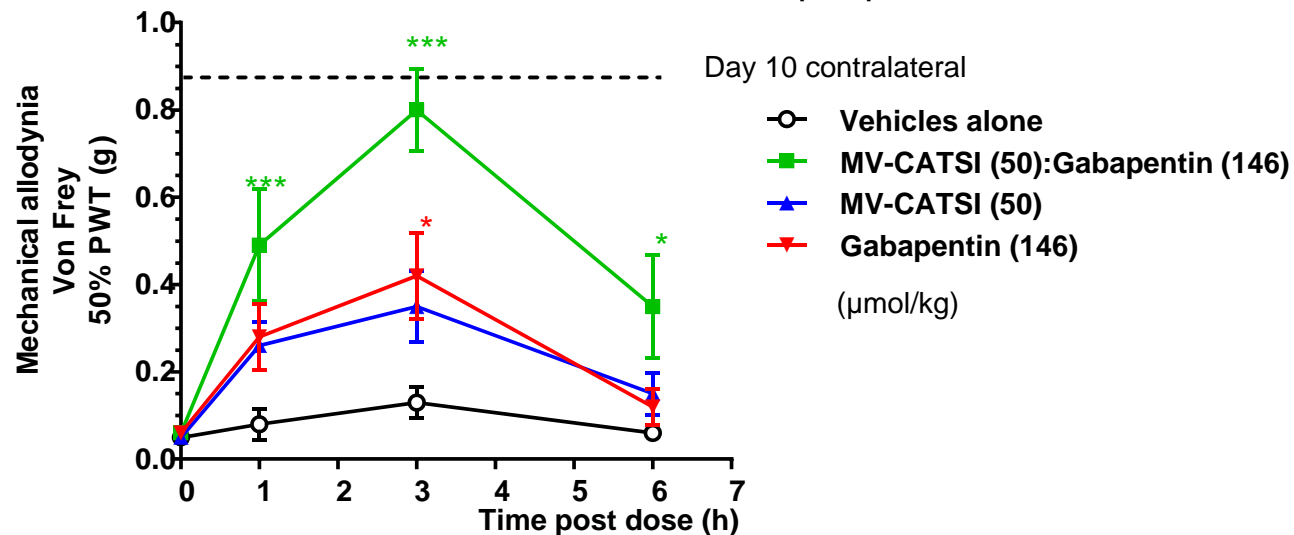
# Cathepsin S inhibitor to address unmet needs in treatment of neuropathic pain (NP)

## Neuropathic pain

- Associated with a lesion or disease affecting the somatosensory system
  - e.g. diabetic neuropathic pain, post-herpetic neuralgia & neuropathic lower back pain
- Inhibition of Cat S prevents inflammatory damage to the sensory system in the spinal cord by blocking fractalkine release

## Big market with high medical need

- Current treatments incl. anticonvulsants and antidepressants
- Pain persists in 75% patients with at best a 50% reduction in overall pain
- Significant side effects e.g. dizziness, somnolence
- 25M people in the 7 MM suffer from NP



# R&D pipeline bolstered by Cat S progress

Field	Project	Partner	Preclinical phase		Clinical phase				Market	
			Re-search	Deve-lopment	Phase I	Phase IIa	Phase IIb	Phase III		
<b>Antivirals</b>										
Labial herpes	Xerclear (Zoviduo, Zovirax Duo)	GlaxoSmithKline (GSK)	[Green bar spanning Re-search, Deve-lopment, Phase I, Phase IIa, Phase IIb, Phase III]							
Hepatitis C	Simeprevir (TMC435), NS3 protease inhibitor	Janssen Pharmaceuticals	[Green bar spanning Re-search, Deve-lopment, Phase I, Phase IIa, Phase IIb, Phase III]							Approved in Japan
Hepatitis C	NS5B nucleotide-based polymerase inhibitor	Janssen Pharmaceuticals	[Green bar spanning Re-search, Deve-lopment]							
Hepatitis C	NS5B nucleotide-based polymerase inhibitor	Unpartnered	[Green bar spanning Re-search]							
HIV	Protease inhibitor	Janssen Pharmaceuticals	[Green bar spanning Re-search]							

## Other indications

Bone related disorders	Cathepsin K inhibitor	Unpartnered	[Blue bar spanning Re-search, Deve-lopment, Phase I]				Phase I data		
Neuropathic pain	Cathepsin S inhibitor	Unpartnered	[Blue bar spanning Re-search, Deve-lopment]		CD nominated				

# Medivir has answers for key R&D challenges facing the pharma industry

## Industry R&D Challenges

## Medivir Answers

Finding good leads for high-quality targets

- Focus on protease inhibitor and nucleoside/nucleotide expertise

Gaining confidence in clinical outcomes early in development

- Utilize strength in medicinal and structural chemistry
- Leverage expertise in disease biology and translational science

Maximizing value from projects (licenses, post-approval pricing)

- Focus on well differentiated profiles for our CDs
- Advance to early development (proof of concept)

Maintaining cost-efficient productivity

- Maintain lean model through effective outsourcing, collaborations with centres of excellence



## Medivir's drug discovery efforts will continue to include high value virology programs

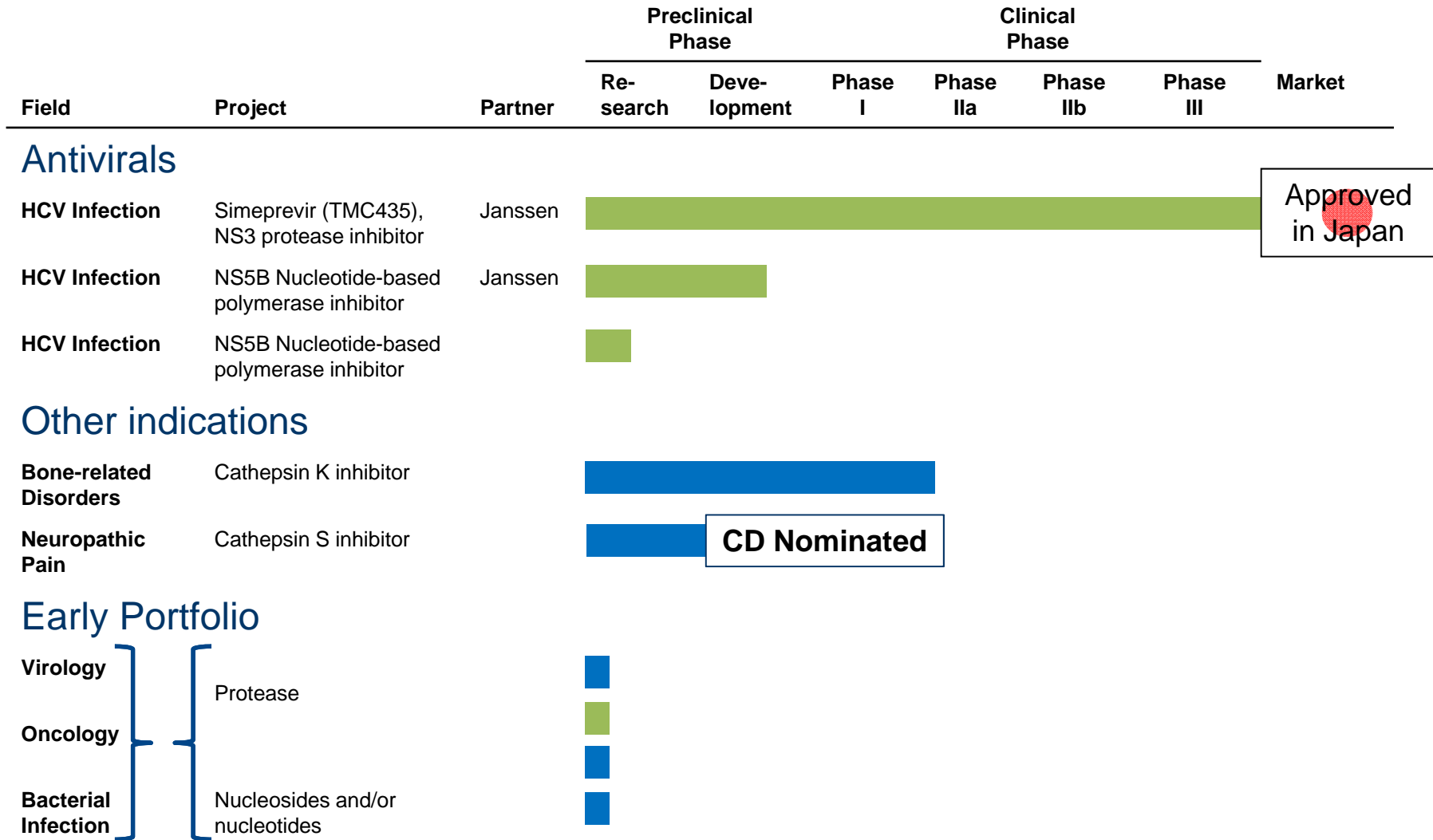
- Largest internal effort remains HCV – NS5B polymerase inhibitors
- Antivirals have been a focus since Medivir was founded
  - Limited time window for new drugs for HCV; very limited opportunities seen in HIV and HBV
  - Opportunities exist for best-in-class entrants in a number of indications (e.g. CMV, RSV, rhinovirus, dengue etc.)
- Medivir's expertise in protease and nucleoside/nucleotides can drive opportunities in multiple disease areas

# Medivir's drug discovery future will need to look beyond virology to differentiated products in new areas

## Early portfolio focused on:

- Technological strengths
  - Protease inhibitors
  - Nucleoside and Nucleotide analogues
- Indications with:
  - High unmet medical need
  - Opportunity to strengthen confidence in Phase 3 outcomes early in development
- Candidate areas currently being evaluated include:
  - Oncology and bacterial infections

# R&D pipeline with early portfolio emerging in new therapeutic areas





## Coffee Break