Interim Phase II Results Webcast & Conference Call

RG-101, a Novel microRNA Therapeutic to Target the Host Factor of HCV

REGULUS THERAPEUTICS

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miR-122 Biology and HCV

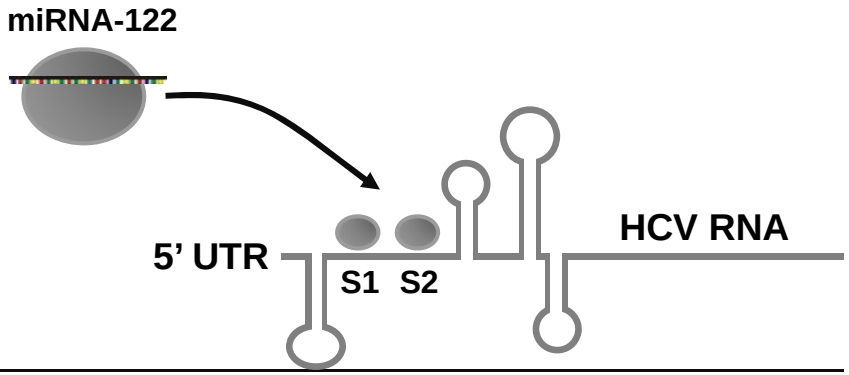
miR-122

- Highly conserved liver-specific miRNA
- Key regulator of cholesterol and fatty-acid synthesis [1,2]
- Important host factor for hepatitis C virus replication

miR-122 and HCV RNA

- 5' UTR contains two highly conserved miR-122 binding sites (S1 and S2) [3,4]
- miR-122 binding promotes HCV RNA stability and accumulation [3,5],

protects the HCV genome from degradation [6,7,8]

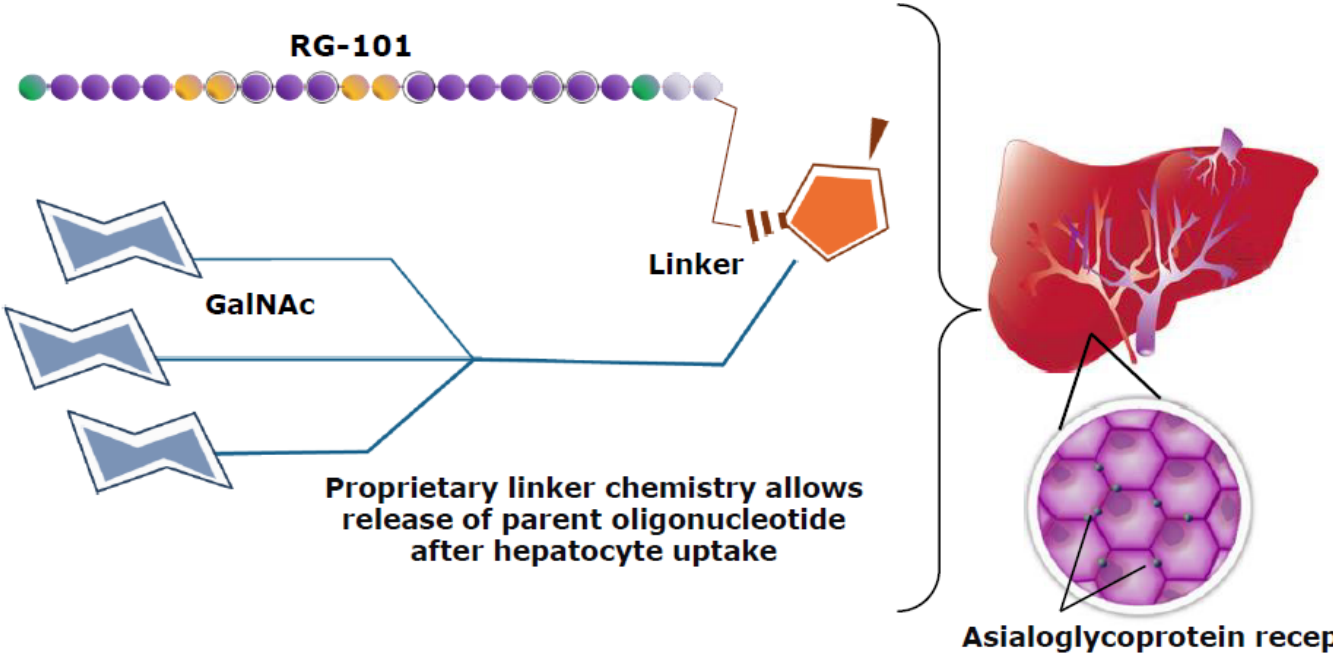


1. Krützfeldt et al, *Nature* 2005
2. Esau et al, *Cell Metab* 2006
3. Jopling et al, *Science* 2005
4. Jopling et al, *Cell Host Microbe* 2008
5. Lanford et al, *Science* 2010
6. Machlin et al, *PNAS* 2011
7. Sedano et al, *Cell Host Microbe* 2014
8. Li et al, *J. Virol* 2015

RG-101 Targets miR-122

RG-101

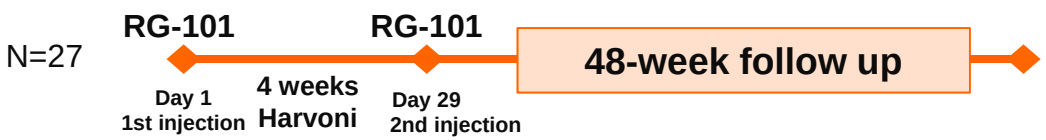
- Oligonucleotide inhibitor of miR-122 that is linked to GalNAc carbohydrate
- GalNAc binds the asialoglycoprotein receptor expressed by hepatocytes
- Increased potency (~20-fold) compared to non-conjugated oligonucleotide



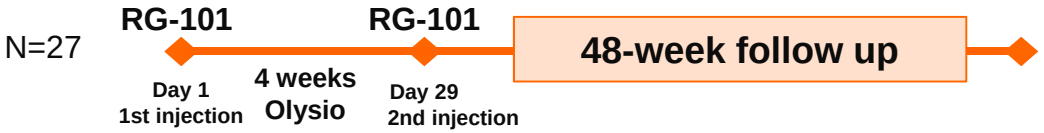
van der Ree, AASLD 2015 - 5

Closed Faced “Sandwich” Designed to Test Safety and Efficacy with Marketed Oral DAAs

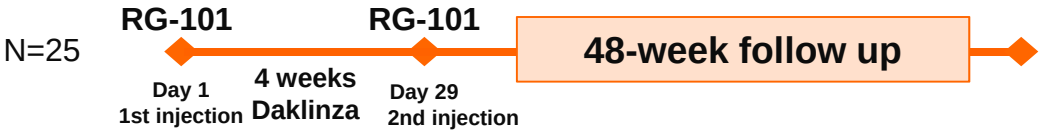
- GT1 and GT4, treatment naïve, non-cirrhotic patients
- Treated with: 2 mg/kg subcutaneous injection of RG-101 on Days 1 and 29 and a 4-week DAA treatment



Harvoni ®
Ledipasvir: NS5A Inhibitor 90mg
Sofosbuvir: NS5B nuc 400 mg



Olysio ®
Simeprevir: NS3/4A protease inhibitor 150 mg



Daklinza™
Daclatasvir: NS5A inhibitor 60 mg

Baseline Characteristics

	RG-101 + Harvoni (N=27)	RG-101 + Olysio (N=27)	RG-101 + Daklinza (N=25)	Overall (N=79)
Mean Age (years)	41.5	45.6	48.1	45.0
Female Gender (%)	40.7%	59.3%	64.0%	54.4%
White Race (%)	100%	100%	96.0%	98.7%
Mean Baseline Viral Load (Log_{10})	5.845	5.768	5.801	5.805
Genotype				
Genotype 1 (%)	77.8%	77.8%	76.0%	77.2%
Genotype 4 (%)	22.2%	22.2%	24.0%	22.8%
Fibroscan Stage				
Stage 0-1 (%)	88.9%	77.8%	92.0%	86.1%
Stage 2 (%)	3.7%	3.7%	0	2.5%
Stage 3 (%)	7.4%	18.5%	8.0%	11.4%
Stage 4 (%)	0	0	0	0

High Virologic Response Rates* in all Treatment Groups

	RG-101 + Harvoni	RG-101 + Olysio	RG-101 + Daklinza	Overall
Patients Responding at Follow-up Week 8	12/12	14/14	11/12	37/38 (97.4%)
Patients Responding at Follow-up Week 12	5/5	4/4	5/5	14/14 (100%)

**Response defined as HCV RNA viral load below LLOQ using RealTime HCV Assay (Abbott) with LLOQ < 12 IU/mL*

RG-101 Well Tolerated when Administered in Combination with Oral DAAs

Safety Findings to Date

- Multiple injections of RG-101 in combination with oral agents were well tolerated in HCV patients
- AE's were mostly mild to moderate in intensity
- Most common AE's were fatigue and headache (~11% each)
- Majority of AE's not considered by investigators to be study drug related
- 2 SAE's reported during follow-up period
- No study discontinuations

Pharmacodynamic Findings to Date

- No clinically significant changes in hematological and renal laboratory values
- Decrease in mean ALT and AST levels to a normal range
- 1.5x increase in mean ALP and ~25% decrease in cholesterol – PD markers of miR-122 inhibition

Summary of RG-101 Data Catalysts in 2016

- ✓Interim data mid-February for closed-face sandwich
- Additional data potentially presented at EASL in mid-April (pending abstract acceptance)
- Primary endpoint analysis (12 week follow-up) for all patients in late Q2
- Safety and PK in US Phase 1 CKD+HCV population in 2H2016
- Interim data from open-faced sandwich with GSK-175 by YE2016

RG-101 Positioned as Potential Backbone HCV Therapy

DATA SEEN TO DATE

- Compelling interim efficacy data in combination with Harvoni®, Olysio®, Daklinza™
- Safe and well tolerated to date
- Potent, durable and pan-genotypic
- Proprietary targeting of host factor microRNA-122 with RG-101 alone and in combination demonstrates significant anti-viral activity

PROMISING PRODUCT PROFILE

- RG-101 combination holds potential to shorten treatment regimen to four-weeks
- Improved potential compliance benefits

Regulus to accelerate development of RG-101

Thank You

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