REGULUS

*micro*RNA Therapeutics



RG101 Phase 2 “Closed-Face Sandwich” Results

Topline Primary Endpoint Data

7 June 2016

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Phase 2 Program Objectives

- Evaluate combination therapeutic approaches with commercial direct acting antivirals (DAAs) in shortened regimens of four weeks or less
- Evaluate RG-101 in combination with GSK-175 for potential for single-visit cure
- Evaluate RG-101 in underserved patient populations
- Pursue additional non-exclusive collaborations to evaluate RG-101 in combination with other investigational DAAs

Phase 2 program designed to demonstrate RG-101 potential in order to guide partnering and commercialization objectives

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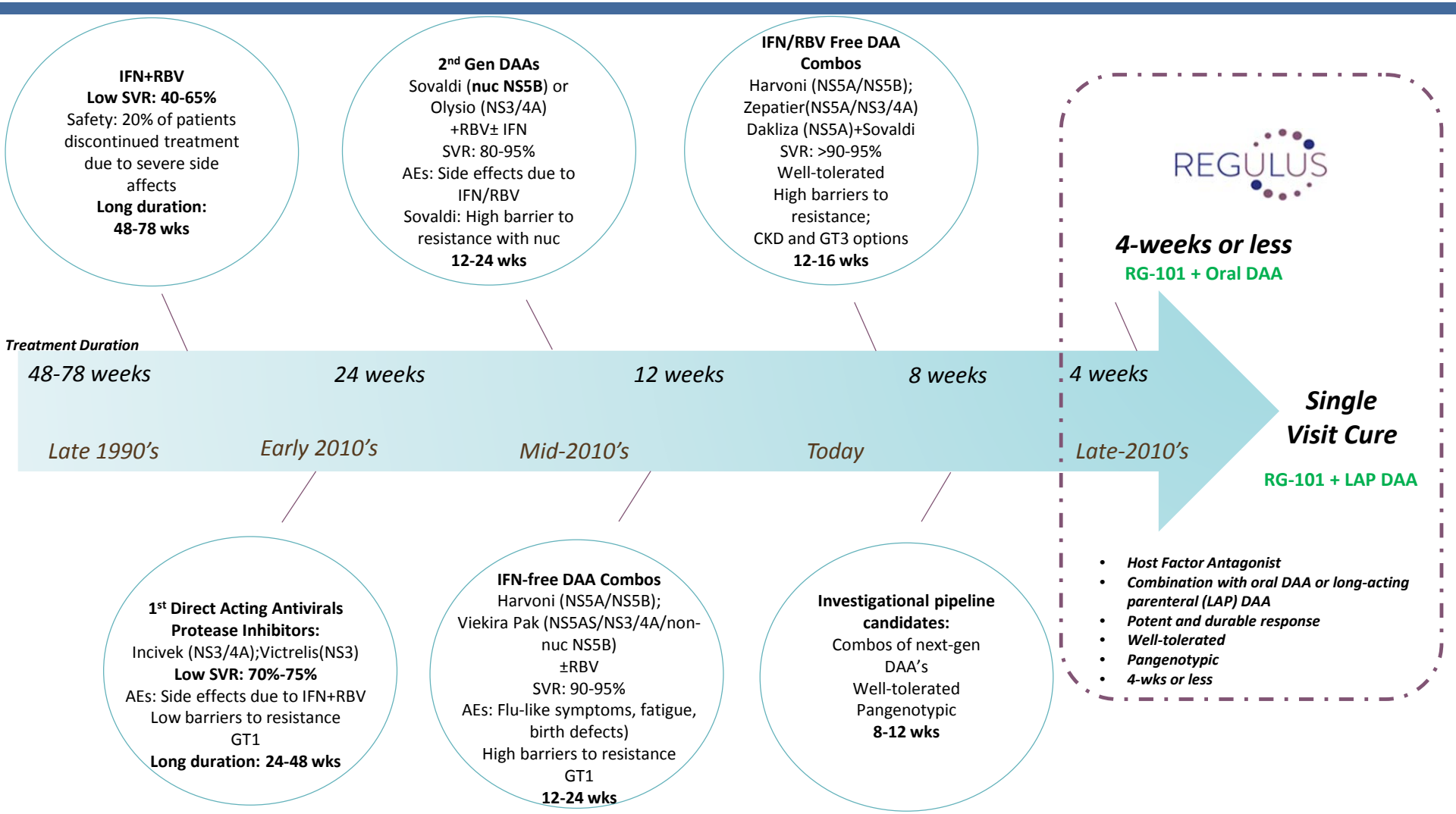
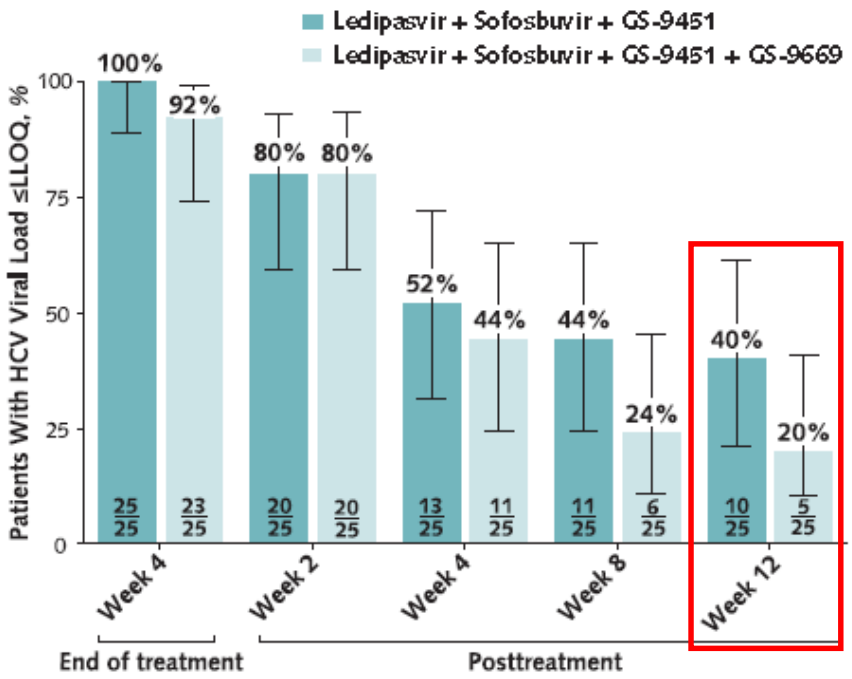
Evolution of HCV Therapies



Prior Attempts to Shorten Therapy to 4 Weeks Have Proven Unsuccessful



Triple and quadruple DAA combination regimens with LDV+SOF have achieved only **20-40% SVR12**

	Treatment Naïve, Non-cirrhotic
SVR 4/8 Rates	12/31 (38.7%)
Virologic Failures	19*

*All patients who did not achieve SVR were virologic failures

C-SWIFT regimen with triple therapy (grazeprevir, elbasvir, and sofosbuvir) x 4 weeks have achieved only **38.7% SVR4/8**

Kohli et al., Ann Intern Med. Doi 10.7326/M15-0642
Merck Newsroom Home (http://www.mercknewsroom.com) on 11/9/14 6:53 pm EST

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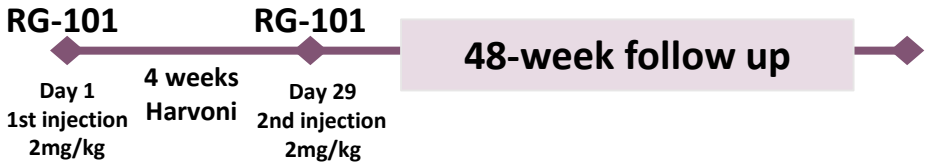
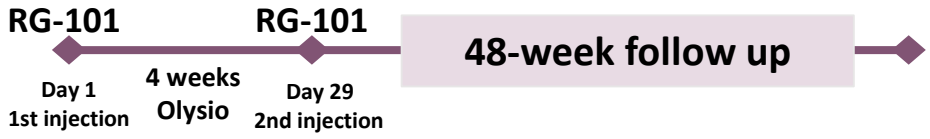
Phase 2 “Closed-Face Sandwich” Study Designed to Test Four-Week Treatment Course

N=27



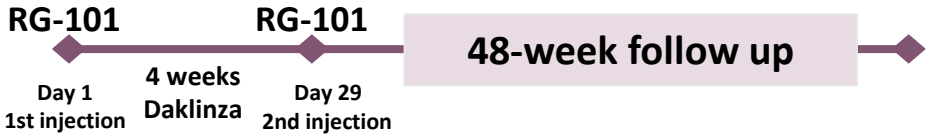
Harvoni ®
Ledipasvir: NS5A Inhibitor 90mg
Sofosbuvir: NS5B nuc 400 mg

N=27



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

N=25



Daklinza™
Daclatasvir: NS5A inhibitor 60 mg

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Key Eligibility Criteria

Inclusion Criteria

- Male or female, 18-65 years of age
- Chronic HCV infection, genotype 1 or 4 (viral load ≥75,000 IU/mL)
- Treatment-naïve, non-cirrhotic

Exclusion Criteria

- HBV or HIV co-infection
- Cirrhosis Child-Pugh B or C
- Other causes of liver disease
- History of hepatocellular carcinoma

Baseline Characteristics

	RG-101 + Harvoni (N=27)	RG-101 + Olysio (N=27)	RG-101 + Daklinza (N=25)	Overall (N=79)
Mean Age (years)	41.6	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})	5.85	5.77	5.80	5.81
Genotype				
Genotype 1 (%)	77.8%	77.8%	76.0%	77.2%
Genotype 1a (%)	29.6%	11.1%	20.0%	20.3%
Genotype 1b (%)	48.1%	66.7%	44.0%	53.2%
Genotype 4 (%)	22.2%	22.2%	24.0%	22.8%
Fibroscan Grade				
Grade 0-1 (%)	88.9%	77.8%	92.0%	86.1%
Grade 2 (%)	3.7%	3.7%	0	2.5%
Grade 3 (%)	7.4%	18.5%	8.0%	11.4%

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Topline Efficacy Data from Week 12 Interim Analysis
Virologic Response by Treatment Group

Number and Percentage of Patients with Virologic Response

Week of Follow-up	RG-101 + Harvoni	RG-101 + Olysio	RG-101 + Daklinza
Week 12	27/27 (100%)	26/27 (96.3%)	22/24* (91.7%)
Week 16	21/21 (100%)	19/20 (95.0%)	20/22 (90.9%)
Week 20	14/14 (100%)	13/15 (86.7%)	13/13 (100%)
Week 24	10/10 (100%)	8/10 (80.0%)	8/9 (88.9%)

**Twenty-five patients were enrolled in the Daklinza arm. One patient missed the Week 12 visit. Viral load results for this patient at Week 8 and 16 were collected and indicate that the patient was a responder at both time points.*

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

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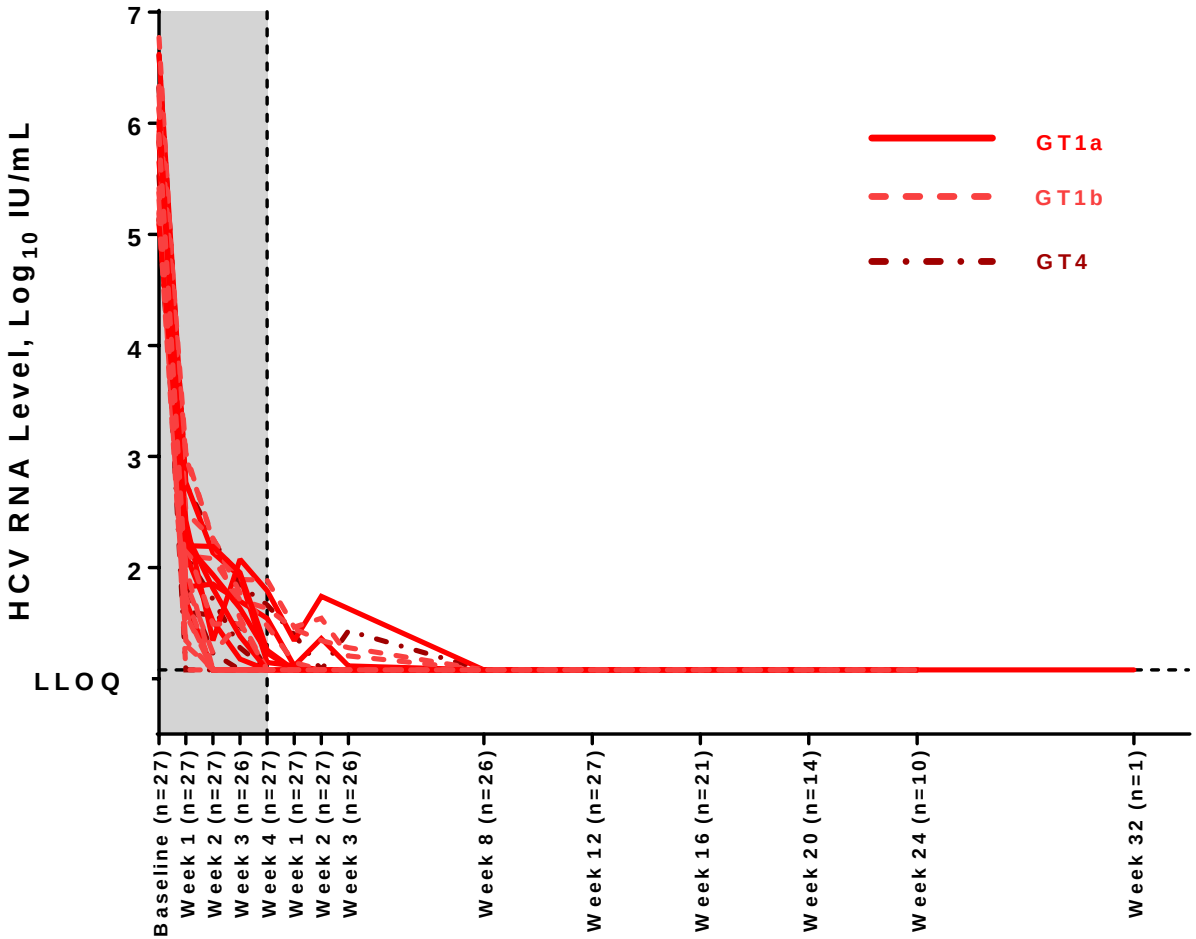
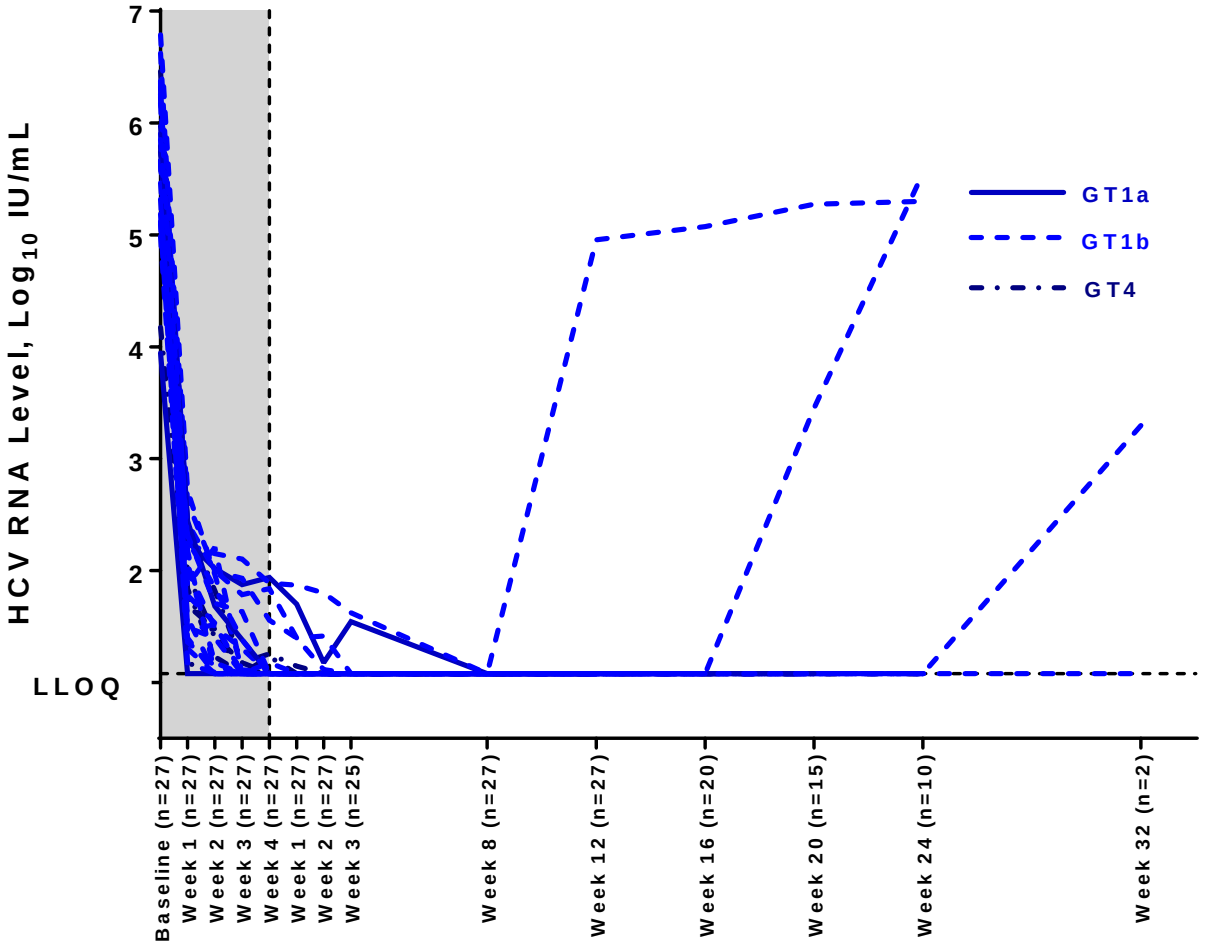
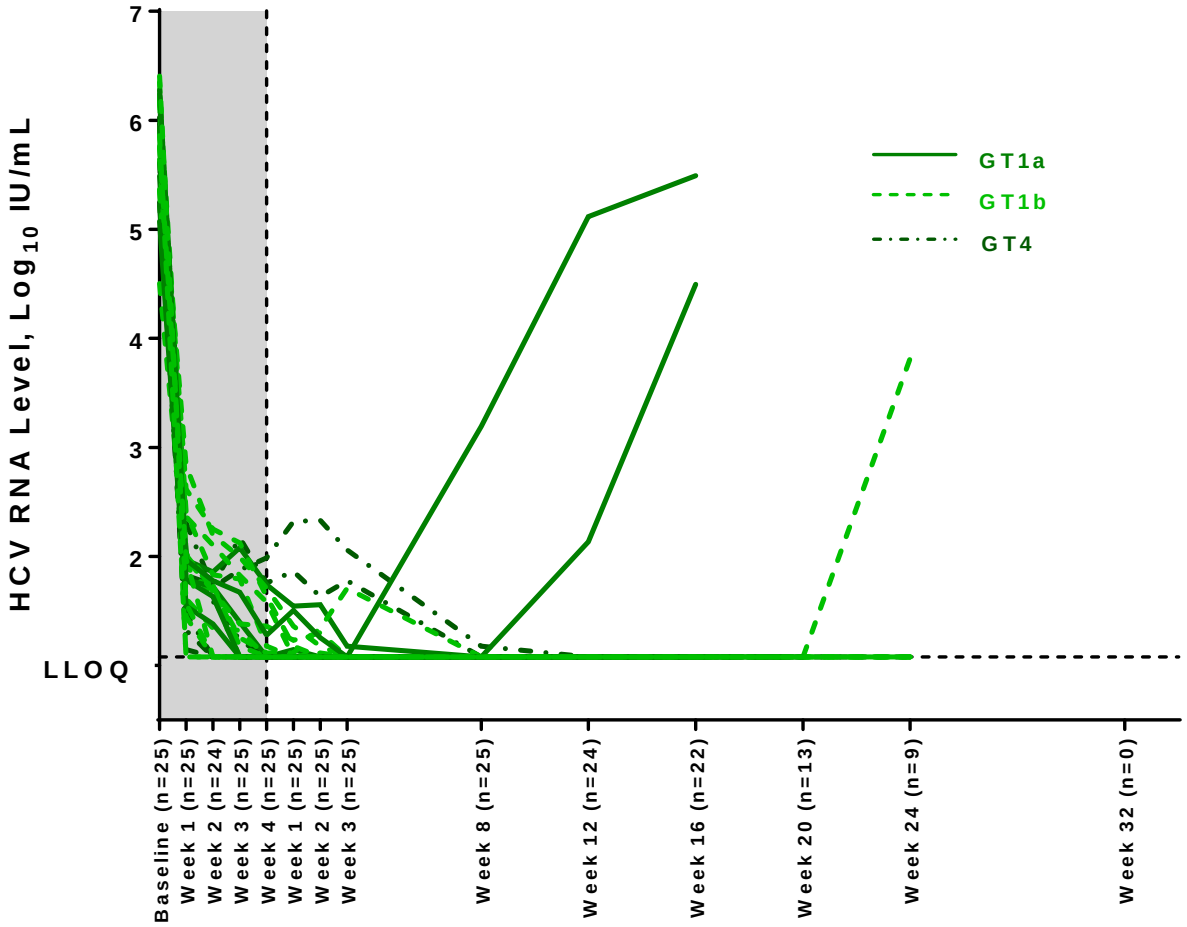
Viral Kinetics: RG-101 + Harvoni



Viral Kinetics: RG-101 + Olysio



Viral Kinetics: RG-101 + Daklinza



RG-101 in Combination with Oral DAAs Generally Well Tolerated

Type of Adverse Event	RG-101 + Harvoni (N=27) n (%)	RG-101 + Olysio (N=27) n (%)	RG-101 + Daklinza (N=25) n (%)	Overall (N=79) n (%)
Any AE	24 (88.9%)	22 (81.5%)	21 (84.0%)	67 (84.8%)
AE Leading to Premature Withdrawal	0	0	0	0
AE Causing Death	0	0	0	0
Serious AE (SAE)*	0	2 (7.4%)	1 (4.0%)	3 (3.8%)
AEs by Severity				
Grade 1: Mild	15 (55.6%)	8 (29.6%)	9 (36.0%)	32 (40.5%)
Grade 2: Moderate	8 (29.6%)	13 (48.1%)	10 (40.0%)	31 (39.2%)
Grade 3: Severe†	1 (3.7%)	1 (3.7%)	2 (8.0%)	4 (5.1%)
Grade 4/5: Life threatening/Fatal	0	0	0	0

**SAEs of dyspnea and multiple sclerosis in Olysio arm and one SAE of jaundice in Daklinza arm*

†Severe AEs of headache in Harvoni arm, multiple sclerosis in Olysio arm (same as SAE above), and allergic reaction to insect bite and jaundice (same as SAE above) in Daklinza arm

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Summary of Preliminary Baseline Sequencing Data

- Baseline genomic sequencing available on 78 of 79 patients enrolled
- 22% of patients had baseline mutations at NS5A, NS5B, or NS3/4A regions which may confer resistance to DAAs
- No baseline mutations were detected in the 5' untranslated region (UTR), where RG-101 activity could be affected

	RG-101 + Harvoni	RG-101 + Olysio	RG-101 + Daklinza
Number (%) of Patients with Baseline RAVs	**6/26 (23%)** with either NS5A or NS5B mutation (2/26 [8%] with both)	**6/27 (22%)** with NS3/4A mutation	**5/25 (20%)** with NS5A mutation
SVR12 rates in Patients with Baseline RAVs	**100% (6/6)**	**83% (5/6)**	**100% (5/5)**
SVR12 rates in Patients without Baseline RAVS	**100% (20/20)**	**100% (21/21)**	**89% (17/19)**

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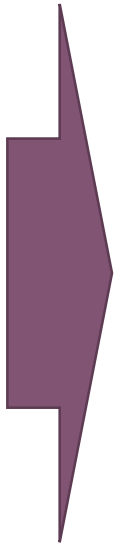
Phase 2 “Closed-Face Sandwich” Topline Data Conclusions

- RG-101 demonstrates significant virologic response rates
  - 100% in combination with 4-weeks of Harvoni
  - 88% in combination with monotherapies of Olysio or Daklinza
- RG-101 generally well-tolerated in combination with oral DAAs
  - Majority of AEs mild or moderate in severity; low incidence of SAEs
  - Similar safety profile to marketed DAAs
  - No AEs led to discontinuation



RG-101 first to demonstrate compelling SVR with four-week treatment course

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Key 2016 Catalysts

- RG-101
  - ✓Early Q1 2016 - report interim results from Phase II "closed-face sandwich" study
  - ✓Q1 2016 - initiate "open-face sandwich" Phase II study with GSK
  - ✓Q1 2016 - initiate IND-opening PK study in the US
  - ✓Oral presentation at EASL 2016
  - ✓Late Q2 2016 - report primary analysis data from Phase II “closed-face sandwich" study
  - Data presentations at AASLD (pending acceptance)
  - Year-end 2016 – interim results expected from the RG-101 GSK “open-face sandwich” study
- RG-012
  - ✓Expand enrollment of Alport syndrome patients in ATHENA
  - ✓Present interim results from ATHENA to medical meeting in Q2 2016
  - Mid 2016 – Initiation of Phase II study in Alport syndrome patients planned
- RG-125
  - ✓Collect $10M milestone payment for advancing RG-125 into Phase I
- Pre-clinical pipeline
  - Anticipate the nomination of 1 additional clinical candidate in 2016

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Thank You

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