Phase 1 Study of Intranasal Fusion Inhibitor RQ-01 for the Treatment of COVID-19

Control Number 5689/ Poster Number AAR-SUNDAY-521

S. Kottilil[1], K. Kenaston[2], P. Da Silva Jardine[3], M. Mitchnick[2], K. Cameron[4], L. R. Smith[2], S. Recchio[2], H. Herce[2], R.B. Moss[2, 9], L. Rojas[5], R. J. Garcia[6], C. Crystal[7], B. Torkan[8], and P, Eisenberg[3] for the RQ-01 Study Team

[1] Institute of Virology; University of Maryland School of Medicine, [2]Red Queen Therapeutics, [3]Apple Tree Partners, [4]KOC Consulting, [5]INCSD LLC, [6]Florida International Medical Research, [7]Eastside Research Associates, [8]LA Universal Research Center, Inc., [9]Former Red Queen Employee

BACKGROUND

- COVID-19 continues to be a public health problem with emergence of new variants that evade prior immunity.
- RQ-01 is a novel stapled lipopeptide designed to target the conserved heptad-repeat 1 domain of the spike protein to inhibit the six-helical domain fusion mechanism
- RQ-01 has potent *in vitro* antiviral activity against numerous SARS-COV-2 variants, as well SARS-CoV-1 and other pathogenic human seasonal coronaviruses.
- Preclinical efficacy was also demonstrated against SARS-CoV-2 in the Syrian hamster model of COVID-19

METHODS

- A first-in-human Phase 1, multicenter, randomized, double-blind, placebo-controlled study was conducted to evaluate the safety of RQ-01 in SARS-CoV-2 infected subjects
- COVID patients (18 – 64 years old, n=66) who had a positive rapid antigen test (RAT; Abbott BinaxNOW™) and mild COVID-19 symptoms < four days of the onset of symptoms
- Subjects were randomized in a 1:1:1 ratio (22 per arm, stratified by age <50 or 50 – 64 years) to either RQ-01 5 mg, RQ-01 10 mg, or matching placebo administered by a nasal inhaler device on Days 1, 2, and 3.
- Primary endpoint was safety and tolerability parameters were monitored until Day 33
- Nasal swabs for RAT were obtained on Days 1 and 5, NP swabs for RT-qPCR on Days 1, 2, 3, 5, 7, 14, 21 and 33, and Days 1, 3 and 5 for TCID50.
- Nasopharyngeal (NP) viral shedding as measured by RT-qPCR and viral culture ($TCID_{50}$) assays
- Secondary endpoints included assessment of inhibition of viral shedding by RQ-01 vs placebo
- Statistics: Kaplan-Meier Analysis of RT-PCR and $TCID_{50}$. GraphPad Prism for comparative analysis

RESULTS

Table 1 – Baseline Characteristics

Category	Placebo (n=21)	RQ-01 5 mg (n=24)	RQ-01 10 mg (n=22)
Age (mean ,SD)	43.1,12.2	41.3, 12.6	41.5 ,11.9
Age >= 50 years (n, %)	7, 33%	8, 33%	7, 32%
Female Sex (n, %)	13, 62%	13, 54%	20,91%
Race (n, %)			
White	17, 81%	20, 83%	22, 100%
Black or African American	4, 19%	3, 12.5%	0
Asian	0	1, 4%	0
Ethnicity (n, %)			
Hispanic	17, 81%	15, 63%	18, 82%
Not Hispanic or Latino	4, 19%	9, 37%	4, 18%
Fertility Status (n, %)			
Potentially child bearing	7, 54%	10, 77%	14, 70%
COVID-19			
Time since current COVID-19 symptoms onset (Mean, SD)	1.85 ,0.7	1.79, 0.89	1.95, 0.65
COVID-19 Vaccination in the past (n, %)	16, 76%	21, 88%	20, 91%
COVID-19 Infection in the past (n, %)	14, 67%	13, 54%	17, 77%
COVID-19 Variant at Baseline			
Omicron (n, %)	19, 90%	23, 96%	20, 91%

None of the baseline characteristics were statistically different between the three groups

Table 2- Safety Parameters

Category (n, %)	Placebo (n=21)	RQ-01 5 mg (n=24)	RQ-01 10 mg (n=22)
Atleast one TEAE	4, 20%	0,0%	3, 14%
Serious TEAE			
Total	0, 0%	0, 0%	0, 0%
Grade 3 or above	0, 0%	0, 0%	0, 0%
Death	0, 0%	0, 0%	0, 0%
Neutropenia	1, 5%	0, 0%	0, 0%
Leukopenia	1, 5%	0, 0%	0, 0%
Abdominal pain RUQ	0, 0%	0, 0%	1, 5%
Pain in extrmity	1, 5%	0, 0%	0, 0%
Nasal discomfort	0, 0%	0, 0%	1, 5%
Oropharyngeal pain	0, 0%	0, 0%	1, 5%
TEAEs leading to permanent discontinuation of Study drug	0, 0%	0, 0%	0, 0%
TEAEs leading to temporary discontinuation of Study drug	0, 0%	0, 0%	0, 0%

TEAE: treatment emergent adverse events

Figure 1 – Time to undetectable SARS-CoV-2 levels by RT-PCR

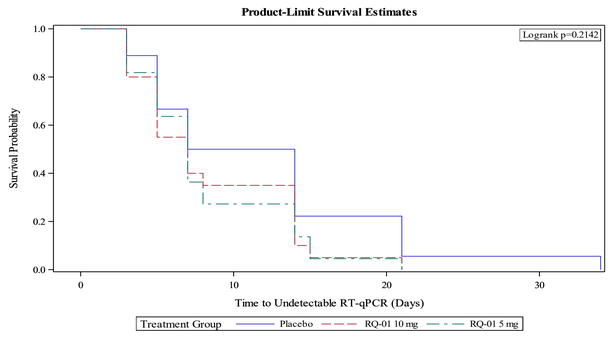

Figure 2– Time to undetectable SARS-CoV-2 Levels $TCID_{50}$

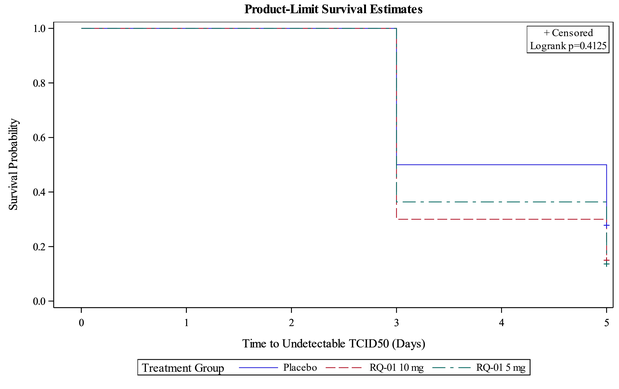

Table 3– Comparative efficacy of RQ-01 for viral clearance on Day 5

Treatment Arm	Day 5 $TCID_{50}$/mL Pos/Neg	Number of Subjects
Placebo	Positive	7
	Negative	11
RQ-01 5 mg	Positive	5
	Negative	17
RQ-01 10 mg	Positive	4
	Negative	16

RESULTS

- Both doses of RQ-01 were well tolerated without any serious TEAEs or laboratory abnormalities requiring study discontinuation Table 2.
- Systemic levels of RQ-01 were below the lower limit of quantification (<20ng/mL) for all subjects in the PK substudy (n=18).
- Numerically, more patients on RQ-01 achieved viral levels in NP swabs below LOD by RT-PCR. 91% in 5mg dose group and 85% on 10mg dose group achieved SARS-CoV-2 levels below LOD by Day 14 compared to 72% on placebo (p=ns).
- Similarly, 80% on 5mg dose group and 77% on 10mg dose group achieved viral level below LOD by $TCID_{50}$ by Day 5 compared to 61% in the placebo group (p=ns) Table 3.

CONCLUSION

- RQ-01 is a novel fusion inhibitor that was safe and well-tolerated when administered nasally to subjects with mild COVID-19.
- Intranasal administration of RQ-01 did not result in systemic absorption
- Numerically, low risk COVID-19 patients on RQ-01 achieved reduced viral shedding compared to those receiving placebo.
- This apparent antiviral activity needs to be further confirmed in high-risk population such as immunocompromised patients, who may benefit from rapid viral clearance leading to reduced complications and hospitalizations or mortality.

Disclosures: Kottilil S. Advisory Board of Orsobio, DMC of Gilead Sciences,
Apple Tree Partners and Red Queen employees have stocks or stock options with Red Queen Therapeutics

Funding Statement: This research was funded by Red Queen Therapeutics