Forward-looking statements

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TORC1 is an evolutionarily conserved pathway that regulates aging.

TORC1 inhibition has extended lifespan and healthspan in multiple preclinical species.
Inhibition of TORC1 has the potential to improve the function of multiple aging organ systems

**Improved Neurologic Function**
- Tain et al., *Nature Neuroscience*, 2009
- Malagelada et al., *J Neurosci*, 2010
- Spilman et al., *PLoS ONE*, 2010
- Halloran et al., *Neuroscience*, 2012
- Majumder et al., *Aging Cell*, 2012
- Neff et al., *JCI*, 2013

**Reversal of aging-related cardiac dysfunction**
- Flynn et al., *Aging Cell*, 2013
- Dai et al., *Aging Cell*, 2014
- Chiao et al., *Aging*, 2016

**Improvement in physical activity**
- Selman et al., *Science*, 2011
- Harrison et al., *Nature*, 2009
- Wilkinson et al., *Aging Cell*, 2014
- Flynn et al., *Aging Cell*, 2013

**Reversal of aging-related immune dysregulation**
- Chen et al., *Science Sig*, 2009
- Selman et al., *Science*, 2011
- Neff et al., *JCI*, 2013
- Hurez et al., *Aging Cell*, 2015
In Phase 2 clinical trials enrolling > 900 people 65 years of age and older, RTB101 was observed to decrease the incidence and/or severity of respiratory tract infections.

**Phase 2a trial**
- 264 healthy elderly
- RTB101 10 mg QD

**42% reduction** in the rate of RTIs (p=0.006)

Antiviral defense systems were upregulated in whole blood

RTB101 was well-tolerated (Mannick et al, *Sci Transl Med*, 2018)

**Phase 2b trial**
- 652 high-risk elderly
- RTB101 10 mg QD

**30.6% reduction** in the percent of patients with laboratory-confirmed respiratory tract infections (p=0.025)

**52.1% reduction** in percentage of subjects with severe laboratory-confirmed respiratory tract infection symptoms (p=0.034)

5 day reduction in the time to alleviation of moderate to severe symptoms due to laboratory-confirmed RTIs (p=0.025)

RTB101 was well-tolerated
Phase 2b: RTB101 10mg QD was observed to increase expression of innate antiviral genes

<table>
<thead>
<tr>
<th>ISGs upregulated (mean ddCT ≤0)</th>
<th>Placebo n (%)</th>
<th>RTB101 10mg QD n (%)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>5 (25%)</td>
<td>19 (95%)</td>
<td>0.00001</td>
<td></td>
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<table>
<thead>
<tr>
<th>ISGs not upregulated (mean ddCT &gt;0)</th>
<th>Placebo n (%)</th>
<th>RTB101 10mg QD n (%)</th>
<th>p-value</th>
</tr>
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<tr>
<td>15 (75%)</td>
<td>1 (5%)</td>
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Antiviral genes observed to be upregulated in subjects treated with RTB101 encode proteins that inhibit multiple steps in viral replication

Adapted from Schneider et al. Annu Rev Immunol, 2014
Phase 2b: RTB101 reduces the incidence of respiratory tract infections caused by multiple viruses including coronavirus.
RTB101 was well-tolerated in high-risk elderly patients through Week 24

- Adverse events (AEs) were balanced between the RTB101 10 mg QD and placebo cohorts
- 1 unrelated death occurred in the RTB101 10mg QD cohort (patient was hit by car while riding a bicycle), 1 unrelated death occurred in the RTB101 10mg BID cohort and 1 unrelated death occurred in the placebo cohort (both from unknown causes)

<table>
<thead>
<tr>
<th>% of patients in treatment group</th>
<th>RTB101 10mg QD</th>
<th>Placebo</th>
</tr>
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<tbody>
<tr>
<td><strong>Mild AEs</strong></td>
<td>74.4%</td>
<td>71.7%</td>
</tr>
<tr>
<td><strong>Moderate AEs</strong></td>
<td>38.1%</td>
<td>40.6%</td>
</tr>
<tr>
<td><strong>Severe AEs</strong></td>
<td>5.7%</td>
<td>7.8%</td>
</tr>
<tr>
<td><strong>Serious AEs</strong></td>
<td>4.5%</td>
<td>7.8%</td>
</tr>
<tr>
<td><strong>Discontinued study drug due to an AE</strong></td>
<td>5.1%</td>
<td>5.6%</td>
</tr>
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QD = once daily; BID = twice daily
Conclusions

- In preclinical species, TORC1 inhibition has been shown to improve the function of multiple aging organ systems including the immune system.

- Randomized, double-blind placebo-controlled clinical trials in almost 2,000 older adults have been completed to determine if TORC1 inhibition with RTB101 improves immune function in older adults.

- In a phase 2b trial, RTB101 10 mg once daily was observed to be well tolerated, upregulate innate antiviral gene expression, and reduce the incidence of laboratory-confirmed respiratory tract infections caused by multiple viruses including coronavirus in older adults age ≥65 years.

- RTB101 has the potential to decrease the severity of COVID-19 infections in adults age >65 years.