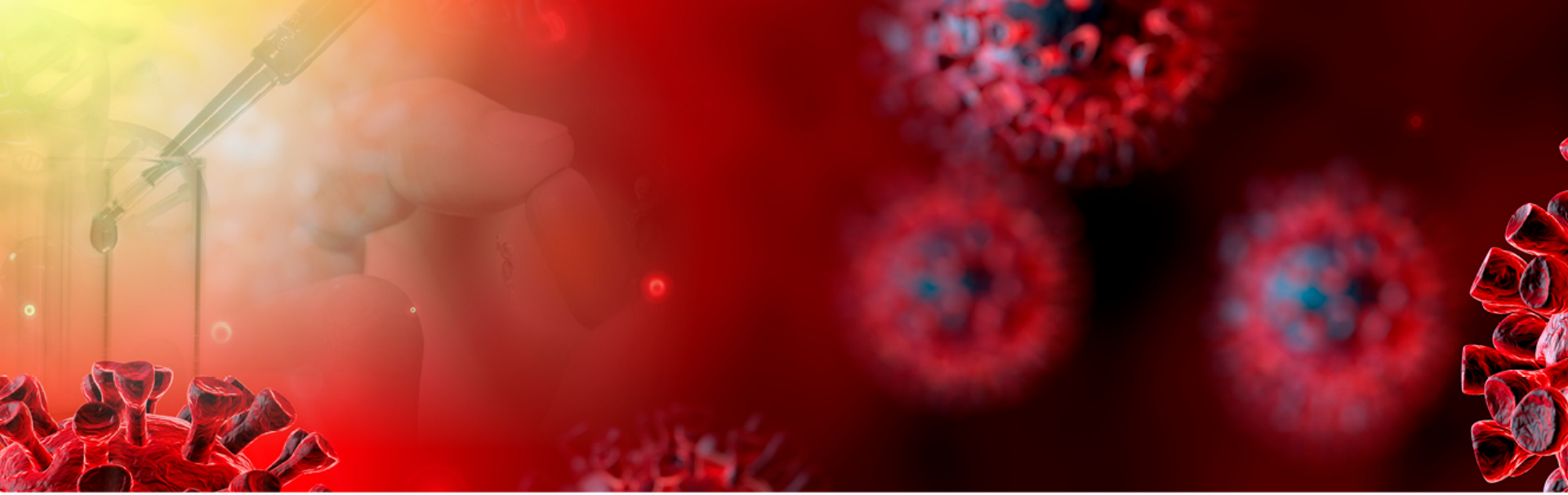

Presentation by Joan Mannick, MD

WEBINAR: *COVID-19: Can the Science of Aging move us Forward?*

March 24,2020

afar american federation for aging research

resTORbio™

Forward-looking statements

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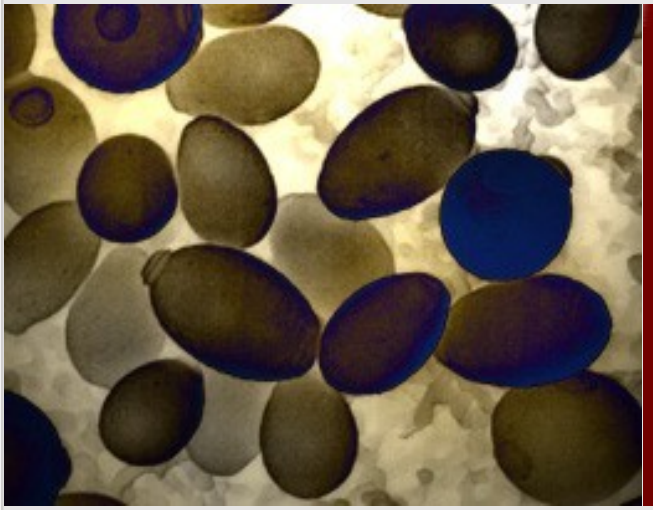
TORC1 is an evolutionarily conserved pathway that regulates aging



Yeast

Worms

Flies

Mice

TORC1 inhibition has extended lifespan and healthspan in multiple preclinical species

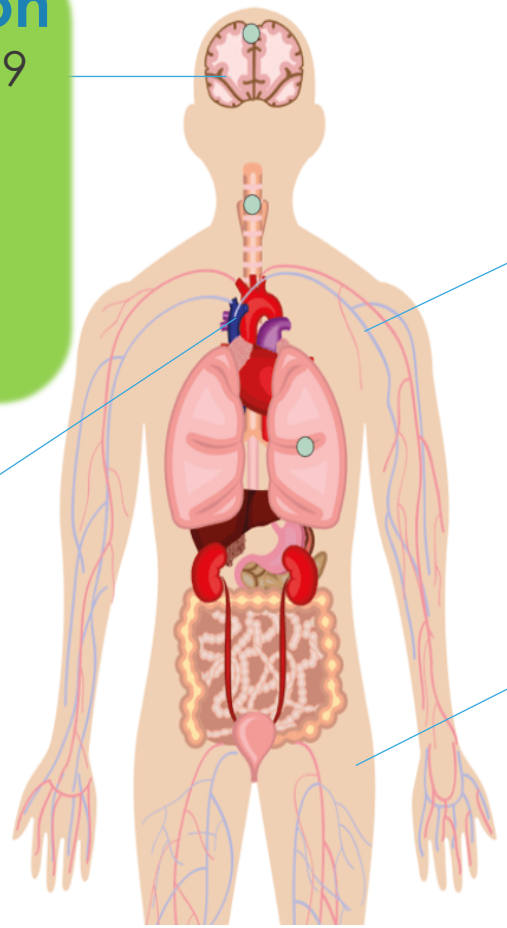
Inhibition of TORC1 has the potential to improve the function of multiple aging organ systems

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 immune dysregulation

Chen et al., *Science Sig*, 2009
Selman et al., *Science*, 2011
Neff et al., *JCI*, 2013
Hurez et al., *Aging Cell*, 2015



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

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)

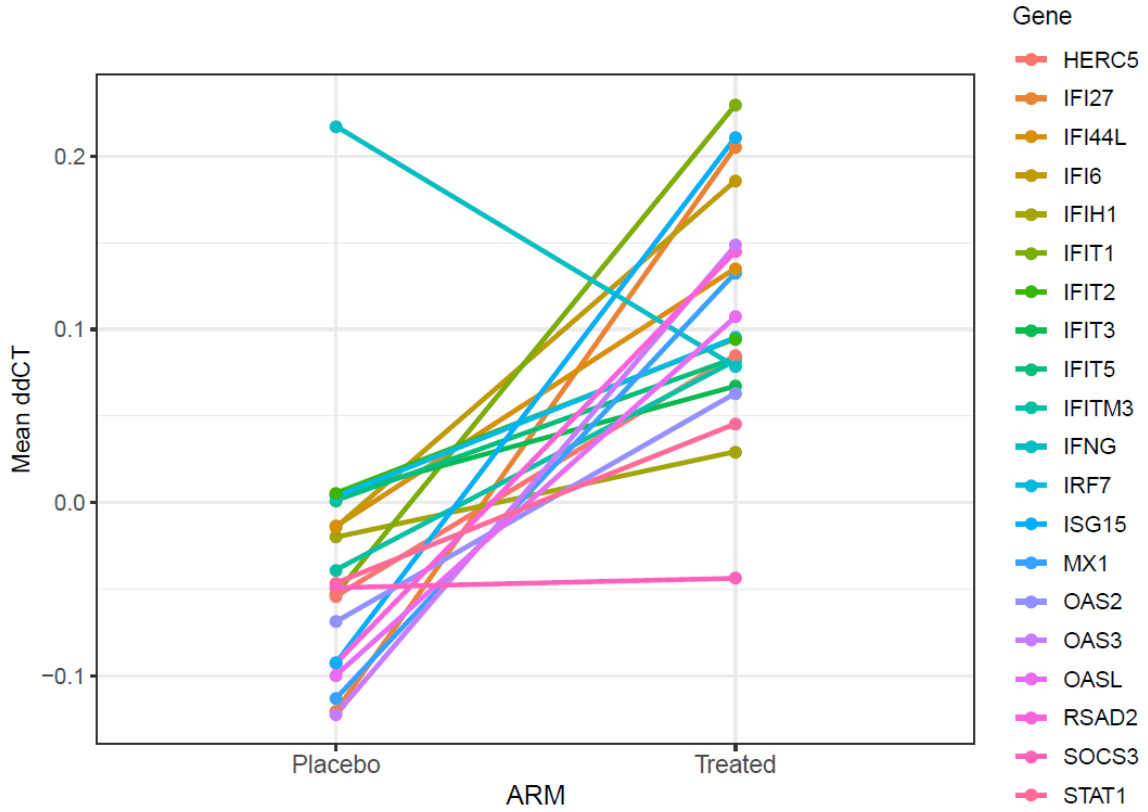
52.1% reduction in percentage of subjects with severe laboratory-confirmed respiratory tract infection symptoms (p=0.034)

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

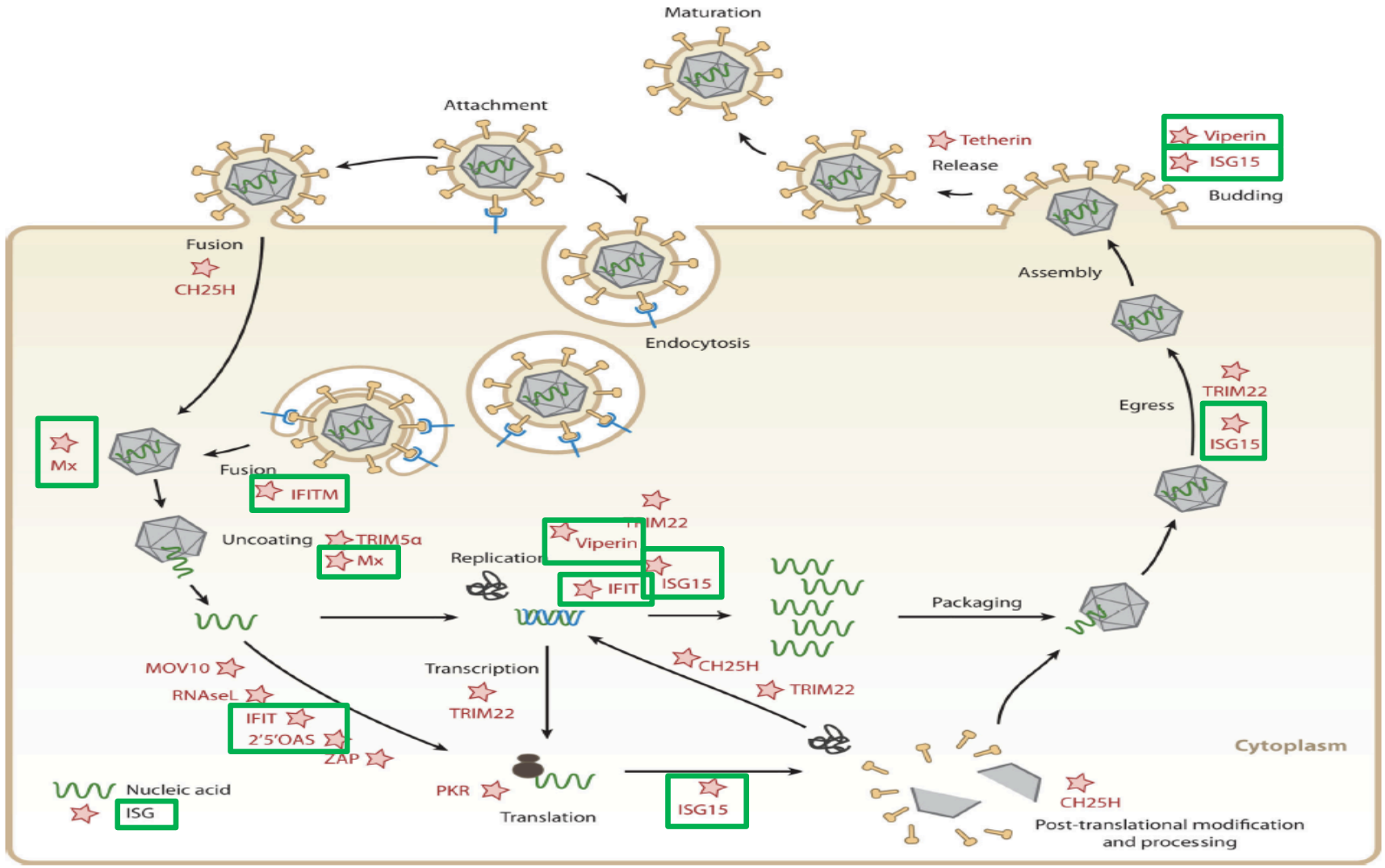
QD = once daily

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



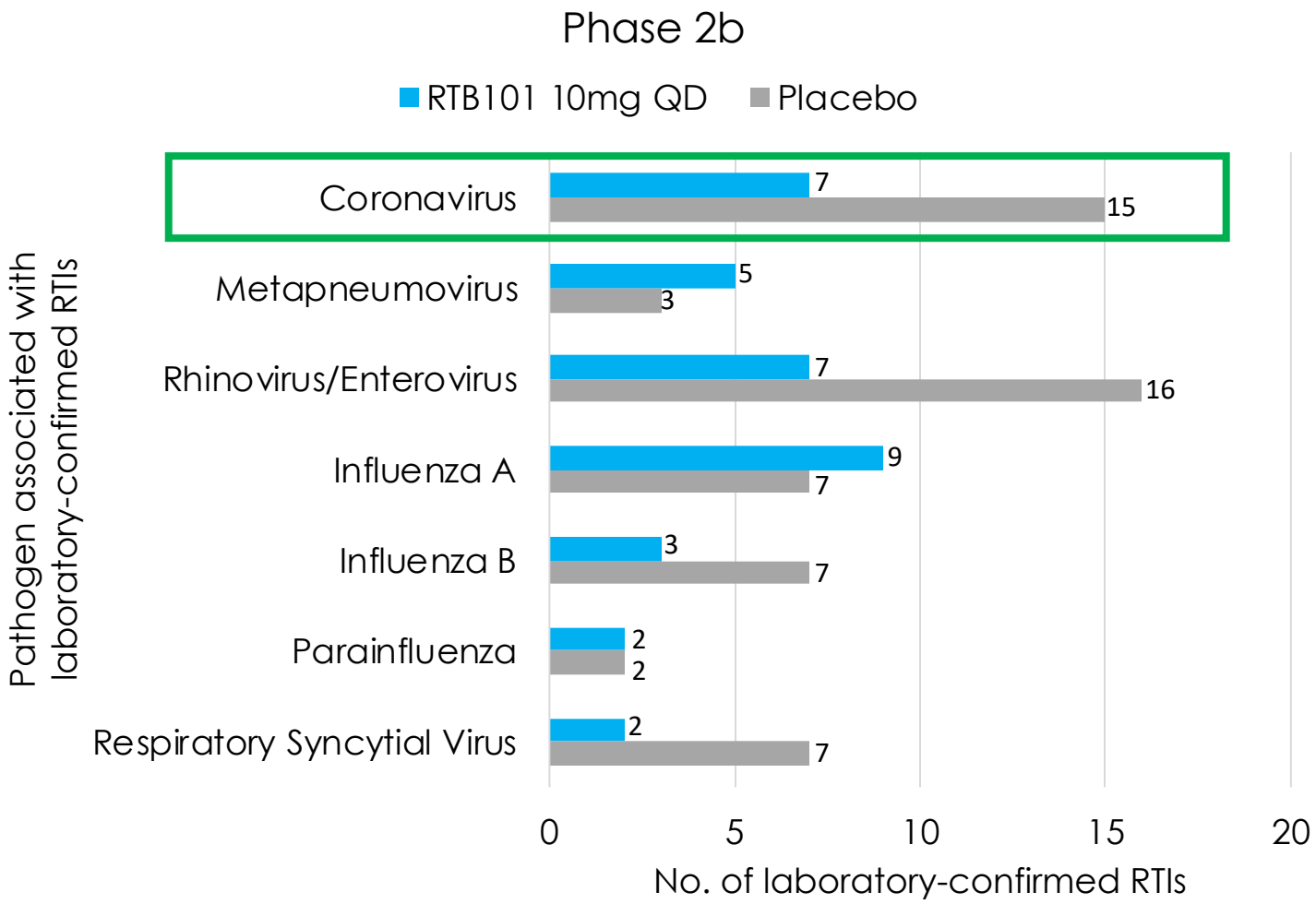
	Placebo n (%)	RTB101 10mg QD n (%)	*p*-value
ISGs upregulated (mean ddCT ≤0)	5 (25%)	19 (95%)	0.00001
ISGs not upregulated (mean ddCT >0)	15 (75%)	1 (5%)	-

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)

	% of patients in treatment group	
	RTB101 10mg QD	Placebo
Mild AEs	74.4%	71.7%
Moderate AEs	38.1%	40.6%
Severe AEs	5.7%	7.8%
Serious AEs	4.5%	7.8%
Discontinued study drug due to an AE	5.1%	5.6%

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.