UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d)
of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): January 7, 2019

RESTORBIO, INC.
(Exact name of registrant as specified in its charter)

Delaware	**001-38359**	**81-3305277**
(State or other jurisdiction of incorporation)	**(Commission File Number)**	**(I.R.S. Employer Identification No.)**

500 Boylston Street, 12th Floor
Boston, MA 02116
(Address of principal executive offices, including zip code)

(857) 315-5521
(Registrant's telephone number, including area code)

Not Applicable
(Former Name or Former Address, if Changed Since Last Report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§ 230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§ 240.12b-2 of this chapter).

Emerging growth company ☒

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 7.01. Regulation FD Disclosure.

resTORbio, Inc. (the "Company") from time to time presents and/or distributes to the investment community at various industry and other conferences slide presentations to provide updates and summaries of its business. A copy of its current corporate slide presentation (the "Presentation") is attached to this Current Report on Form 8-K as Exhibit 99.1. The Company undertakes no obligation to update, supplement or amend the materials attached hereto as Exhibit 99.1.

The information in Item 7.01 of this Form 8-K, including Exhibit 99.1 attached hereto, shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act") or otherwise subject to the liabilities of that section, nor shall it be deemed incorporated by reference in any filing under the Securities Act of 1933, as amended, or the Exchange Act, except as expressly set forth by specific reference in such a filing.

Item 9.01. Financial Statements and Exhibits.

(d) Exhibits

Exhibit No.	Description
99.1	Corporate slide presentation of resTORbio, Inc., dated January 7, 2019.

* * *

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

resTORbio, Inc.

Date: January 7, 2019

By: /s/ Chen Schor
Chen Schor
President and Chief Executive Officer

Exhibit 99.1

resTORbio™

Targeting the Biology of Aging to Restore Health

January 2019

Forward-looking statements

This presentation may contain “forward-looking statements” within the meaning of the Private Securities Litigation Reform Act of 1995, including, but not limited to, statements regarding the safety, efficacy and regulatory and clinical progress of our product candidates, including RTB101 alone and in combination with everolimus or sirolimus. All such forward-looking statements are based on management’s current expectations of future events and are subject to a number of risks and uncertainties that could cause actual results to differ materially and adversely from those set forth in or implied by such forward-looking statements. The use of words such as “may,” “might,” “will,” “should,” “expect,” “plan,” “anticipate,” “believe,” “estimate,” “project,” “intend,” “future,” “potential,” or “continue,” and other similar expressions are intended to identify forward-looking statements. Forward-looking statements are neither historical facts nor assurances of future performance. Instead, they are based on our current beliefs, expectations and assumptions regarding the future of our business, future plans and strategies, our clinical results and other future conditions. All statements other than statements of historical facts contained in this presentation, including statements regarding future results of operations and financial position, business strategy, current and prospective product candidates, planned clinical trials and preclinical activities, including the initiation, timing, progress and results of our preclinical and clinical studies and our research and development programs, product approvals, research and development costs, current and prospective collaborations, timing and likelihood of success, including our ability to advance RTB101 alone and in combination with everolimus or siroliumus into, and successfully complete, clinical studies, timing of the end-of-Phase 2 meeting with the U.S. Food and Drug Administration, and the timing or likelihood of regulatory filings and approvals, expectations regarding market acceptance and size, plans for launch and commercialization, plans and objectives of management for future operations, and future results of anticipated product candidates, are forward-looking statements. New risks and uncertainties may emerge from time to time, and it is not possible to predict all risks and uncertainties. No representations or warranties (expressed or implied) are made about the accuracy of any such forward-looking statements.

These statements are also subject to a number of material risks and uncertainties that are discussed in the section entitled "Risk Factors" in resTORbio’s annual report on Form 10-K for the fiscal year ended December 31, 2017, as well as discussions of potential risks, uncertainties, and other important factors in resTORbio's subsequent filings with the Securities and Exchange Commission. Any forward-looking statement speaks only as of the date on which it was made. Neither we, nor our affiliates, advisors, or representatives, undertake any obligation to publicly update or revise any forward-looking statement, whether as a result of new information, future events or otherwise, except as required by law.

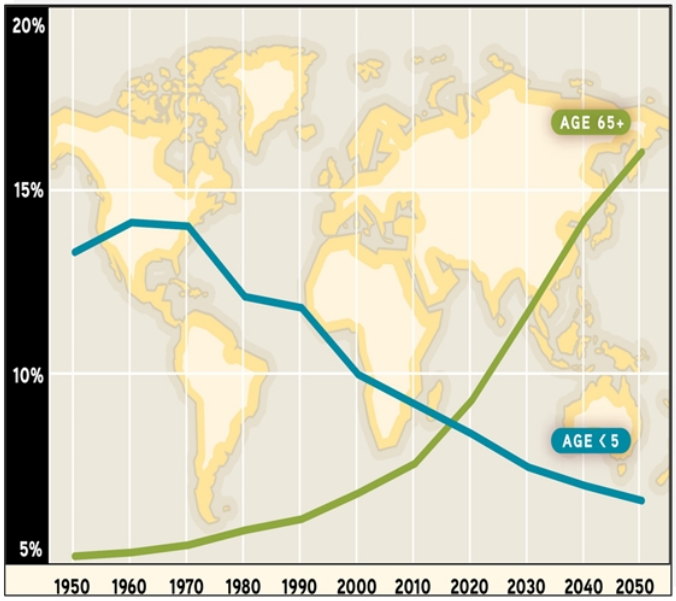
Certain information contained in this presentation relates to or is based on studies, publications, surveys and other data obtained from third-party sources and the Company’s own internal estimates and research. While we believe these third-party sources to be reliable as of the date of this presentation, we have not independently verified, and we make no representation as to the adequacy, fairness, accuracy or completeness of, any information obtained from third-party sources. In addition, all of the market data included in this presentation involves a number of assumptions and limitations, and there can be no guarantee as to the accuracy or reliability of such assumptions. Finally, while we believe our own internal research is reliable, such research has not been verified by any independent source.

resTORbio highlights

- **Targeting the biology of aging**
  - Lead clinical candidate, RTB101, is the most advanced selective TORC1 inhibitor
  - TORC1 inhibition improves the function of aging organ systems including the immune, neurologic, and cardiovascular systems
- **Positive results in Phase 2b to improve immune function and reduce the incidence of RTIs**
  - 30.6% reduction in the percentage of patients with laboratory-confirmed RTIs (p=0.025)
  - 52.1% reduction in percentage of patients with severe laboratory-confirmed RTI symptoms (p=0.034)
  - Successfully defined dose and patient population for Phase 3 program
  - End-of-Phase 2 meeting with the FDA expected in 1Q19; Plan to initiate Phase 3 program in 1H19
  - RTIs are the 4th most common cause of hospitalization in people 65+; 2nd in 85+ (US)
- **Data-driven approach to expand into additional aging-related indications**
  - Improving neurologic function: Plan to initiate Phase 2a study in GBA Parkinson's disease in 1Q19
  - Building a pipeline targeting multiple mechanisms underlying aging

RTI = respiratory tract infection

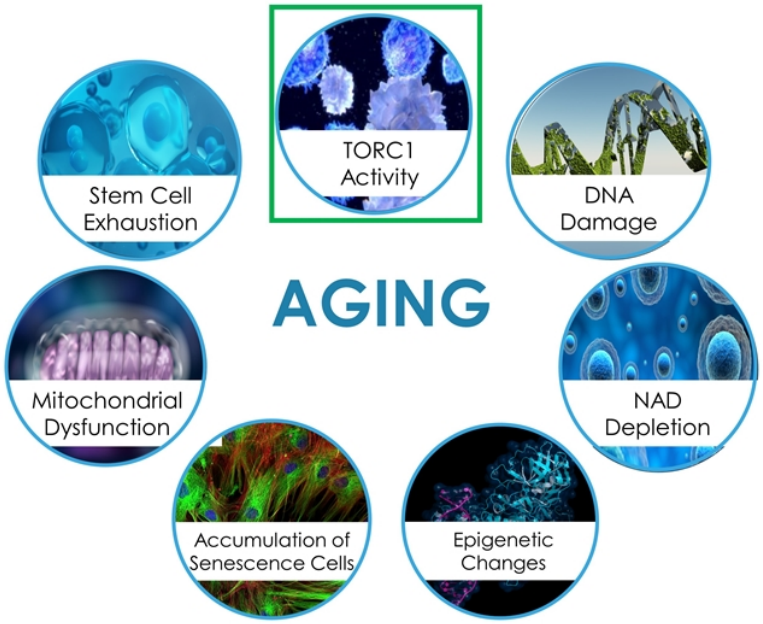
People age 65 and older are the fastest growing population globally and an increasing burden on healthcare systems[1]



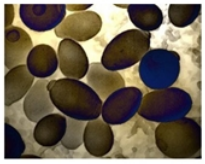
- 62% of people age 65 and older have 2 or more chronic diseases which represent the **greatest challenge for healthcare systems** in the 21st century[2]
- Healthcare expenditures for the elderly are 3-5x higher than for younger individuals (per capita; U.S.)[3]
- Aging is the biggest risk factor for most chronic diseases
- Increasing preclinical data demonstrate that aging is a modifiable risk factor regulated by biological pathways including the TORC1 pathway
- Medicines that target the biology of aging may represent a new class of medicine for treating and preventing diseases in the elderly

[1]United Nation Department of Economic and Social Affairs, Population Division. *World Population Prospects. The 2004 Revision.* New York: United Nations, 2005 in *Why Population Aging Matters: A Global Perspective;* [2]*Salive ME. Epidemiol Rev. 2013;35:75-83;* [3]*CMS.gov(2018), https://www.cms.gov/research-statistics-data-and-systems/statistics-trends-and-reports/nationalhealthexpenddata/nhe-fact-sheet.html*

Targeting the biology of aging



TORC1 is an evolutionarily conserved pathway that regulates aging


Yeast


Worms


Flies


Mice

TORC1 inhibition extended lifespan and healthspan in multiple species

Source: Lamming, Dudley W., et al. (2013) *Journal of Clinical Investigation*123 (3): 980–989.

Extensive genetic validation that TORC1 inhibition extends lifespan across species

Species	Genetic Manipulation to Inhibit mTOR
Yeast	*SCH9* (*Akt/S6K* homolog) insertional mutant [1]
	SCH9 (*Akt/S6K* homolog) deletion [1]
	SCH9 (*Akt/S6K* homolog) insertional mutant [2]
	SCH9 (*Akt/S6K* homolog) deletion [2]
	TOR1 deletion [3]
	TOR1 deletion [4]
C. elegans	TOR (*let-363*) RNAi [5]
	Raptor (*daf-15*) heterozygous [6]
	S6K (*rsks-1*) RNAi [7]
	S6K (*rsks-1*) deletion mutant [7]
	TOR (*let-363*) RNAi [7]
	S6K (*rsks-1*) RNAi [8]
	S6K (*rsks-1*) deletion mutant [8]
	TOR (*let-363*) RNAi [8]
	Raptor (*daf-15*) RNAi [9]
	RagGTPase (*raga-1*) RNAi [9]
	RagGTPase (*raga-1*) RNAi [9]
	Rheb (*rheb-1*) RNAi [9]
D. melanogaster	*dTSC1* overexpression [10]
	dTSC2 overexpression [10]
	dTOR FRB domain (dominant negative) [10]
	dS6K dominant negative [10]
	DTOR mutant (hypomorph) [11]
	d4E-BP overexpression [12]
	d4E-BP weak activated [12]
	d4E-BP strong activated [12]
M. musculus	Loss of S6K1 [13]
	Mtor$^{+/-}$*Mlst8*$^{+/-}$ genotype [14]

Science AAAS

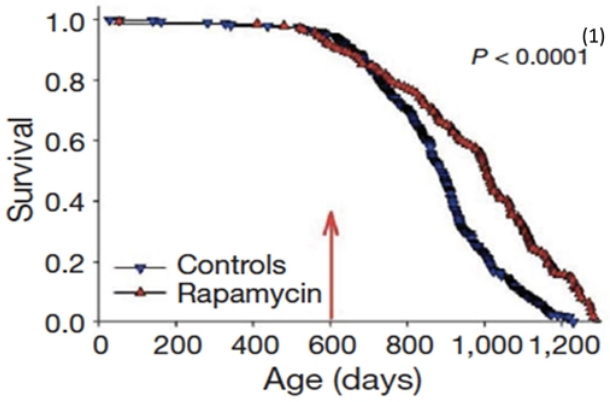
nature

Cell

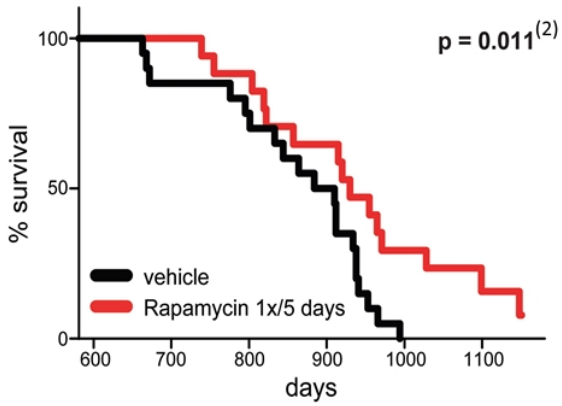
Cell Metabolism

Corresponding citations can be found on slide 43

TORC1 inhibitors extend lifespan in mice even when started late in life and given intermittently



Daily Dosing

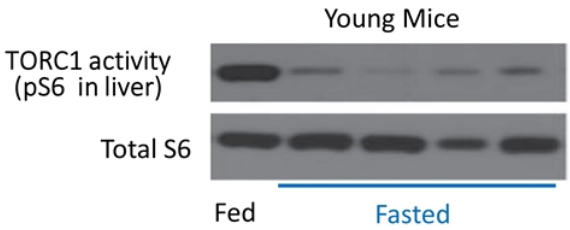


Intermittent Dosing
Once Every 5 Days

Harrison et al. (2009) *Nature*, 460:392-396

Arriola Apelo et al. (2016) *Gerontol A Biol Sci Med Sci*, 71: 876–88

TORC1 may become dysregulated and overactive in some aging organ systems



- Feeding activates TORC1 leading to increased protein and lipid synthesis
- Fasting inhibits TORC1 leading to upregulation of protective pathways

- TORC1 activity remains aberrantly elevated during fasting , preventing upregulation of protective pathways

Sengupta et al., *Nature* 2010

Decreasing TORC1 activity may upregulate protective pathways and may have benefits in aging-related diseases

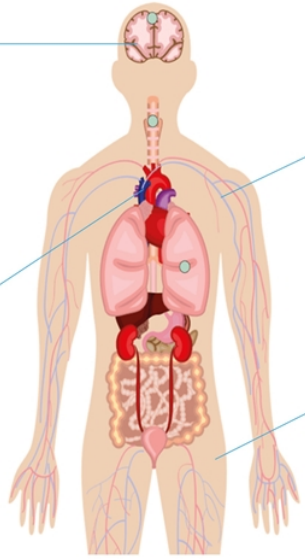
TORC1 inhibition may improve the function of multiple aging organ systems

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



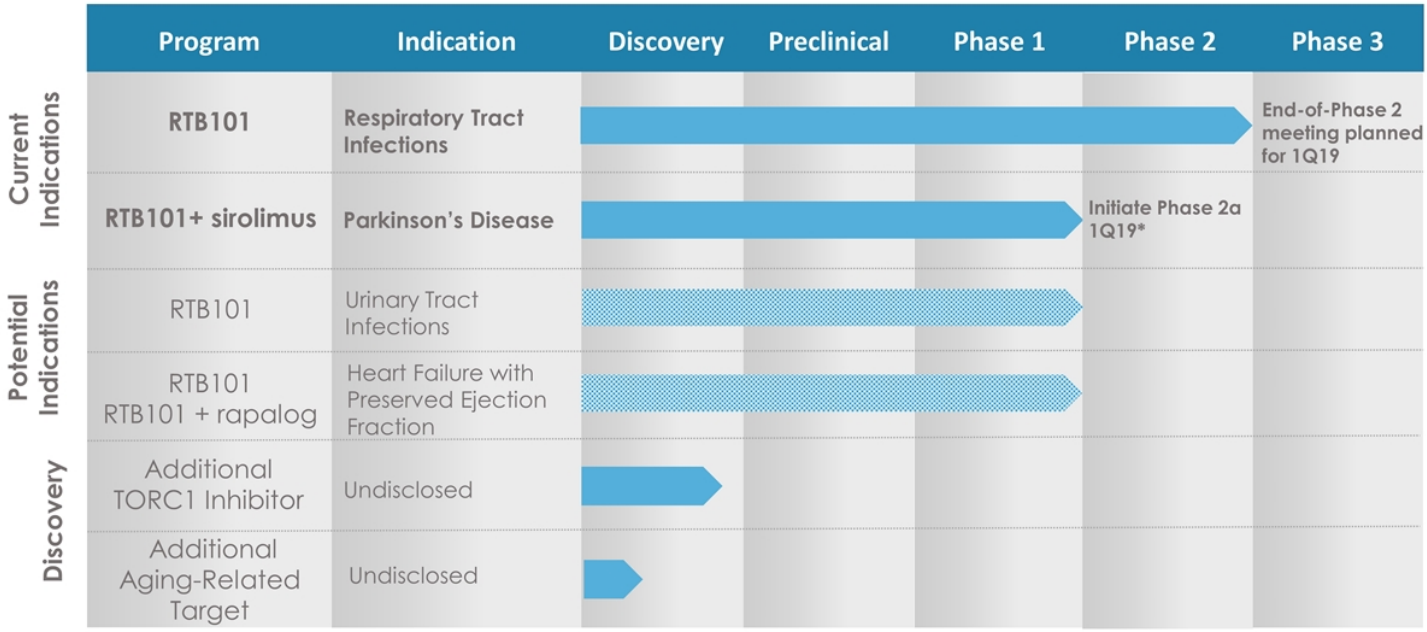
Reversal of aging-related immune dysregulation

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

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

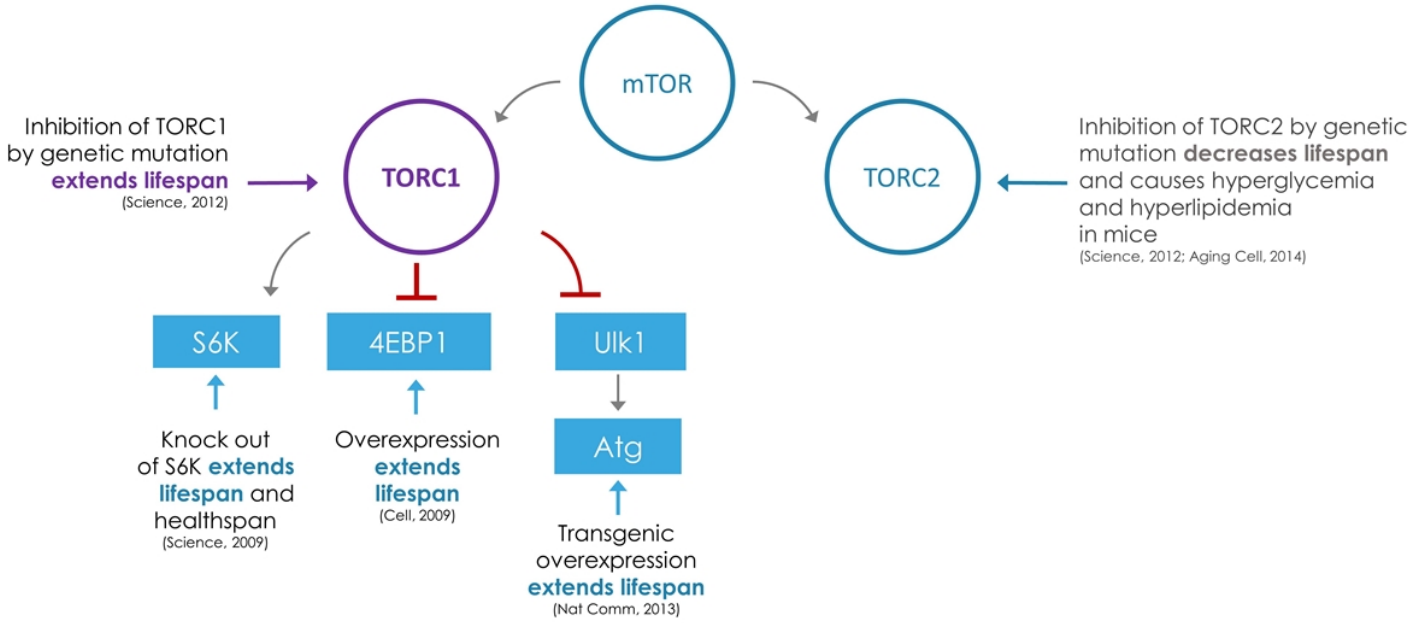
Most advanced pipeline targeting aging-related diseases



For heart failure with preserved ejection fraction, Parkinson's Disease and certain other infections, we may be required to file an investigational new drug application, or IND, prior to initiating Phase 2 clinical trials. We expect to have the ability to initiate these Phase 2 clinical trials without the need to conduct prior Phase 1 trials.

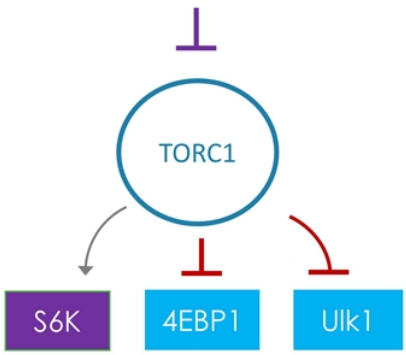
TORC1 Pathway

Selective inhibition of TORC1 may have therapeutic benefit for the treatment of aging-related diseases



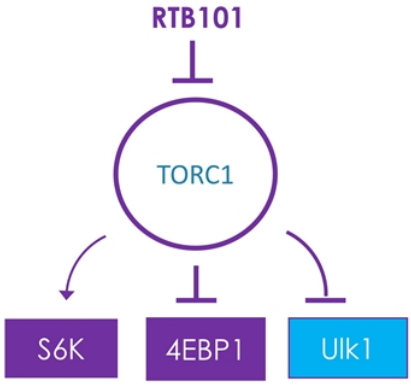
Spectrum of TORC1 inhibition with RTB101 and rapalog

everolimus or sirolimus



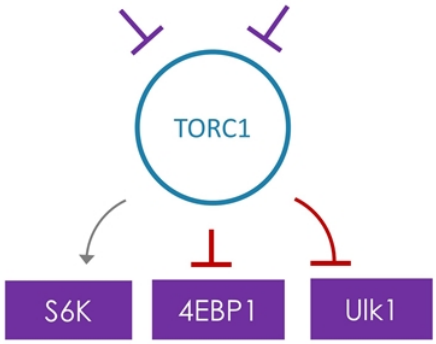
Inhibiting the phosphorylation of 1 target of TORC1

RTB101



Inhibiting the phosphorylation of 2 targets of TORC1

RTB101 + everolimus or sirolimus



Inhibiting the phosphorylation of 3 targets of TORC1

= indicates phosphorylation is inhibited

RTB101: First-in-class immunotherapy targeting TORC1

Best validated target for aging-related diseases	• Extensive body of literature that TORC1 pathway regulates aging • RTB101 is a potent inhibitor of TORC1 • Potential to treat multiple diseases of aging
Robust safety profile	• Over 1,000 patients dosed • Dose for improving immune function is 1/120th of the maximum tolerated dose in humans
Positive Phase 2a and Phase 2b clinical trial results	• Phase 2a and 2b clinical trials in 900 elderly subjects demonstrated that RTB101 10mg once daily improved immune function and reduced the incidence of respiratory tract infections
Convenient administration	• Orally administered, small molecule • Half-life of approximately 4-6 hours • Potential to transiently reduce TORC1 activity

Improving Immune Function
Respiratory Tract Infections (RTIs)

Improving immune function to reduce the incidence of RTIs in the elderly

Fastest Growing Population[1]

The elderly is the fastest growing population across the globe

1.4 Episodes/Year[2]

Elderly subjects have an average of 1.4 episodes of RTIs per person per year

4th Most Common Cause of Hospitalization[3]

RTIs are the 4th most common cause of hospitalization in people age 65+ (US); 2nd in 85+ (US)

8th Leading Cause of Death[4]

RTIs are the 8th leading cause of death in people age 65+ (US); 7th in 85+ (US)

Antibiotics Ineffective[5]

Antibiotics are often prescribed indiscriminately to treat RTIs, leading to potential side effects and contributing to growing antibiotic resistance

No Approved Therapies[6]

Viruses for which there are no approved therapies cause the majority of RTIs including community-acquired pneumonia in subjects ≥80 years

Sources: [1]The Older Population 2010 US Census Briefs, National Center for Health Statistics Data Brief 2015; [2]JAMA, August 14, 2002 – Vol 288, No 6; BMJ 1997; 315:1060-4; [3]Pfunter, A (2013) HCUP Statistical Brief #162; [4] National Vital Statistics Report (2018), Deaths, Final Data for 2016; [5]JAMA. 2016; 315(17): 1864-1873; [6]Jain, S., et al., NEJM (2015) 373: 415-427.

Results of Phase 2a trial

- 264 mostly healthy elderly people randomized to the following TORC1 inhibitor treatment arms (all doses were QD):

  - Everolimus 0.1mg + RTB101 10mg
  - RTB101 10mg
  - Everolimus 0.5mg
  - Everolimus 0.1mg
  - Placebo

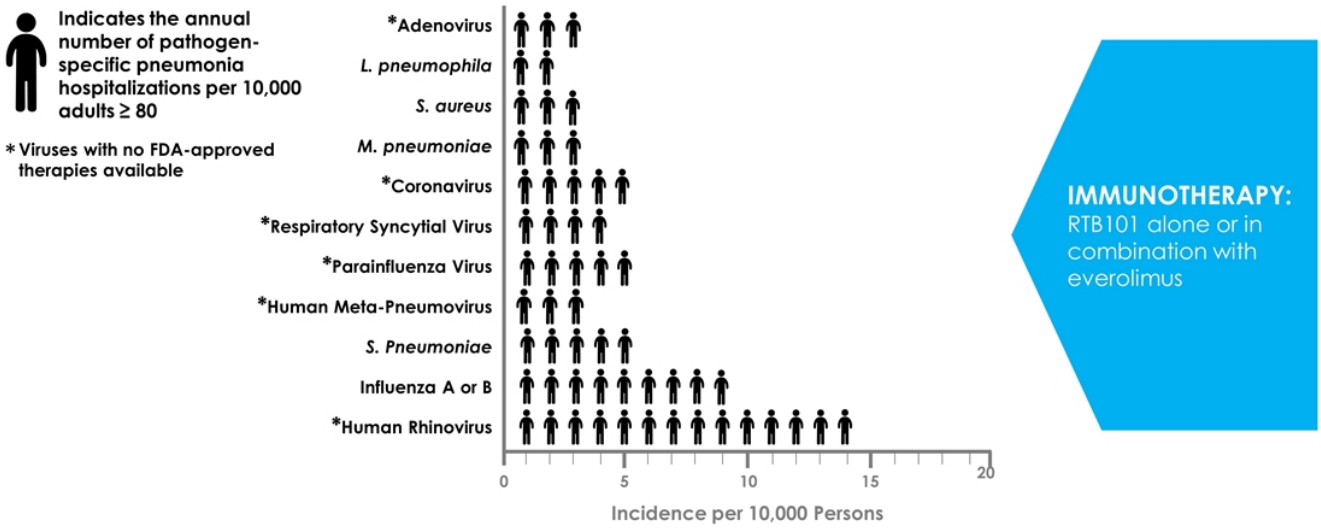
- Both RTB101 10mg QD and RTB101 10mg + everolimus 0.1mg QD significantly reduced the incidence of all infections as well as respiratory tract infections (RTIs)
  - Reduction in RTIs:
    - RTB101 10mg: 42% reduction (p=0.006)
    - RTB101 10mg + everolimus 0.1mg: 36% reduction (p=0.01)

- Both RTB101 10mg and RTB101 10mg + everolimus 0.1mg upregulated antiviral gene expression in whole blood

QD = once daily

RTB101 offers new approach to harnessing the immune system to target multiple pathogens

The majority of pathogens detected in elderly people hospitalized for pneumonia are viruses for which **NO APPROVED THERAPIES** are currently available



IMMUNOTHERAPY:
RTB101 alone or in combination with everolimus

Source: S. Jain et al., NEJM 2015

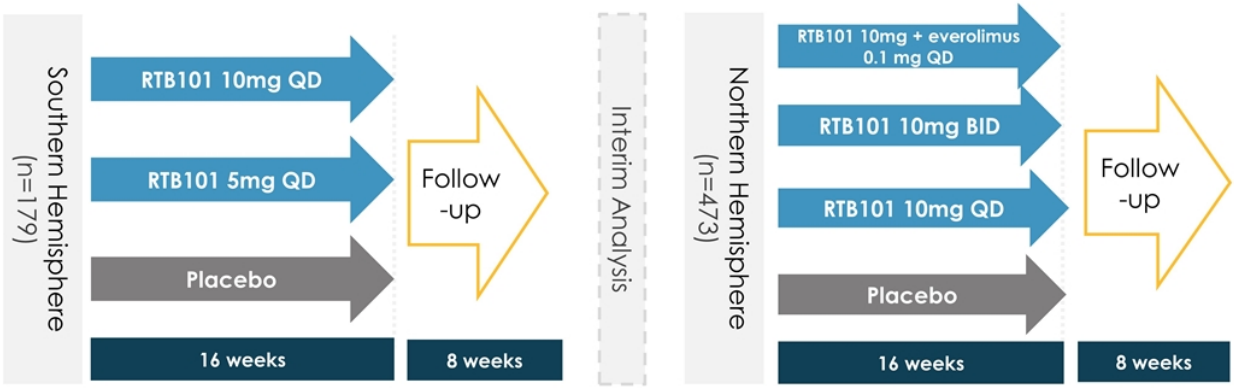
Phase 2a to Phase 2b: Population, primary endpoint and dosing duration were modified

	Phase 2a	Phase 2b
POPULATION:	 Healthy, 65 and older	 85 and older  65 and older w/ asthma  65 and older w/ diabetes  65 and older w/ COPD  65 and older, smokers
PRIMARY ENDPOINT:	Self-reported RTIs	Laboratory-Confirmed RTIs
DOSING DURATION:	6 weeks	16 weeks

Goal: Define patient population for Phase 3 program

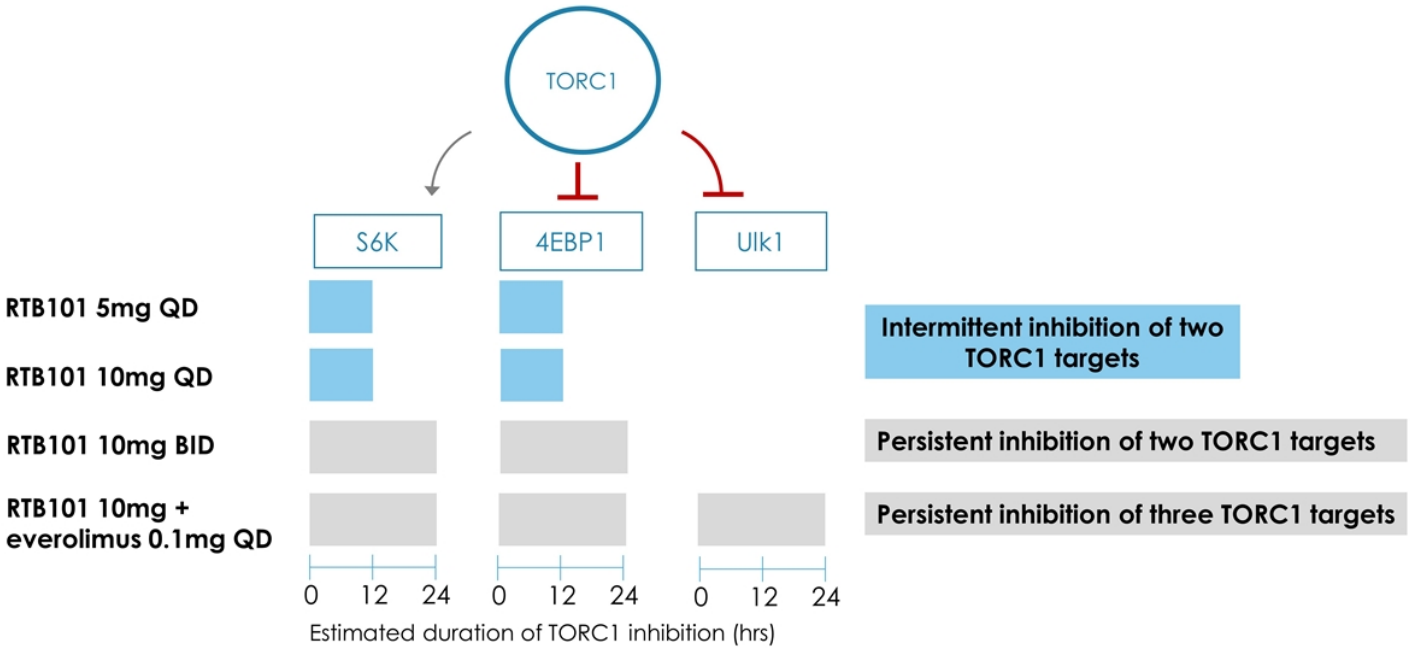
Phase 2b design

- **Primary Endpoint**: Reduction in the percentage of patients with laboratory-confirmed RTIs through week 16
- **Population**: Elderly subjects at increased risk of RTI-associated morbidity and mortality, defined as:
  - ≥ 85 years of age
  - 65-84 years of age with one or more comorbidities including:
    - Asthma
    - Chronic obstructive pulmonary disease (COPD)
    - Type 2 diabetes mellitus (T2DM)
    - Current smoker



QD = once daily; BID = twice daily

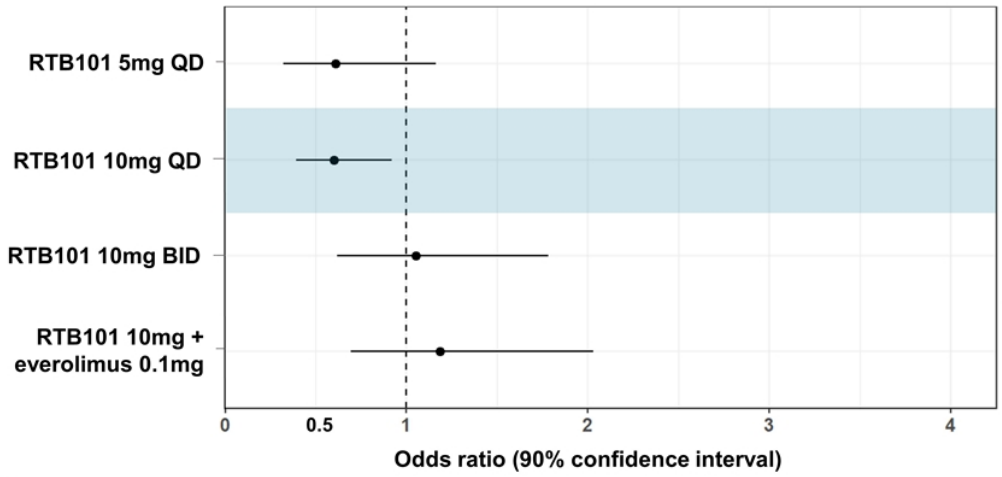
Dosing regimens in Phase 2b estimated to result in different duration and spectrum of TORC1 inhibition



QD = once daily; BID = twice daily

Odds ratio supports dose selection and potential efficacy of RTB101 10mg QD

Odds ratio of experiencing lab-confirmed RTIs through Week 16



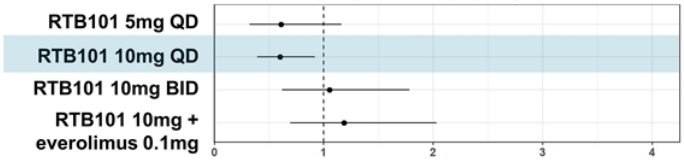
	Active rate[1]	Placebo rate[1]	Odds ratio[2]	p-value[3]
RTB101 5mg QD	21/61	26/60	0.618	0.109
RTB101 10mg QD	**34/176**	**50/180**	**0.601**	**0.025***
RTB101 10mg BID	25/120	24/120	1.050	0.560
RTB101 10mg + everolimus 0.1mg	25/115	24/120	1.187	0.700

RTB101 10mg QD demonstrated a 30.6% reduction in the percentage of patients with laboratory-confirmed RTIs compared to placebo

[1]No. of patients in cohort with one or more laboratory-confirmed RTIs/No. of patients in cohort; [2]Odds ratio represents the odds of experiencing one or more laboratory-confirmed RTIs in the active treatment group versus the placebo group; [3]One-sided p-value; *p<0.05; QD = once daily; BID = twice daily

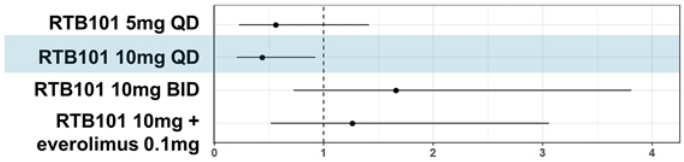
RTB101 10mg QD showed consistent benefit in multiple pre-specified analyses of lab-confirmed RTIs

Odds ratio of experiencing lab-confirmed RTIs through Week 16 – primary endpoint



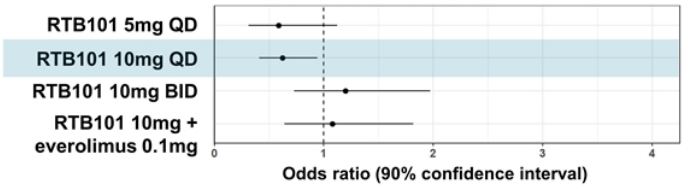
OR=0.601; p=0.025

Odds ratio of experiencing severe lab-confirmed RTI symptoms through Week 16



OR=0.437; p=0.034

Odds ratio of experiencing lab-confirmed RTIs through Week 24

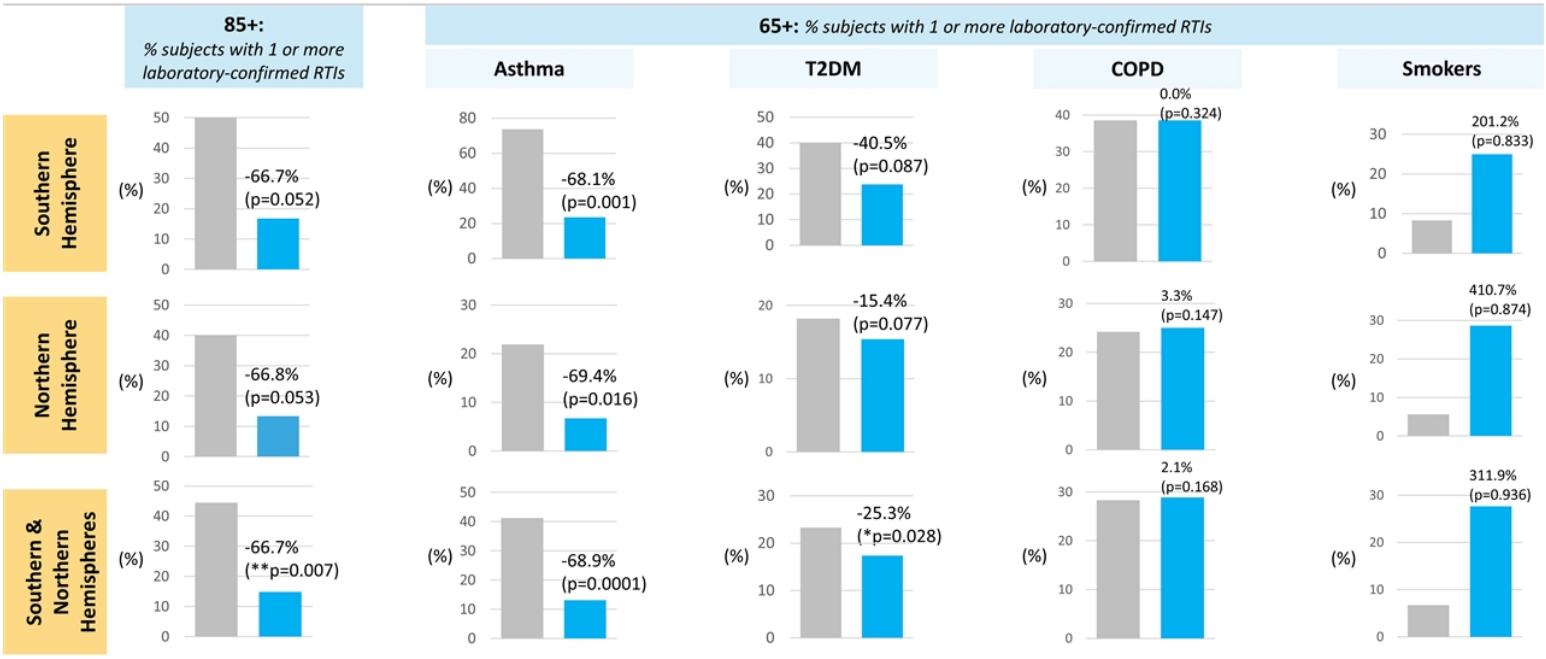


OR=0.623; p=0.030

RTB101 10mg QD associated with statistically significant reductions across three different analyses of laboratory-confirmed RTIs: Week 16, severe RTIs and Week 24

One-sided p-value; QD = once daily; BID = twice daily;
Odds ratio represents the odds of experiencing one or more event in the active treatment group versus the placebo group

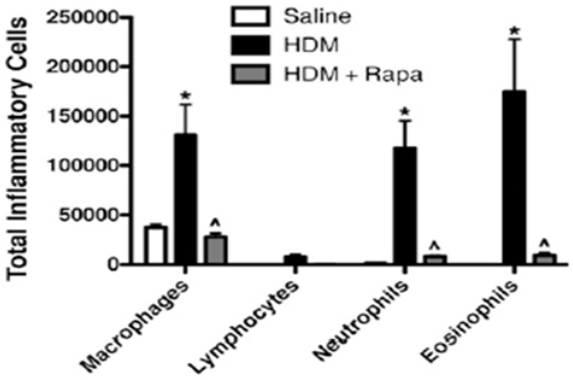
COPD and smokers were non-responding subgroups (pre-specified analyses)



= placebo cohort; = RTB101 10mg once daily cohort; One-sided p-value; QD = once daily; BID = twice daily

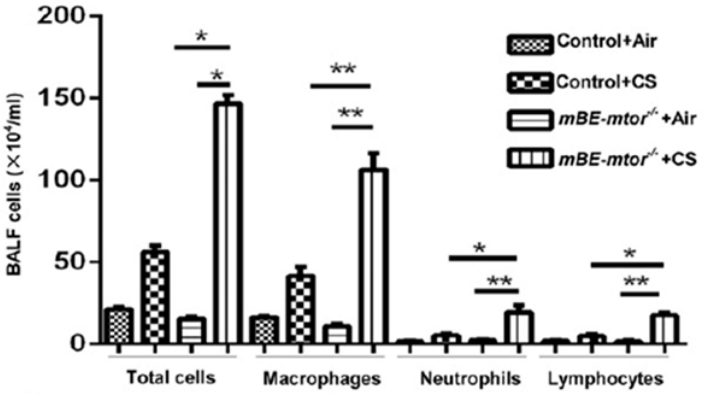
mTOR inhibition decreased airway inflammation in asthma and increased airway inflammation due to smoking

Asthma



mTOR inhibition with rapamycin (Rapa) significantly **decreased** airway inflammation in a preclinical asthma model in which mice were exposed to intranasal house dust mites (HDM)[1]

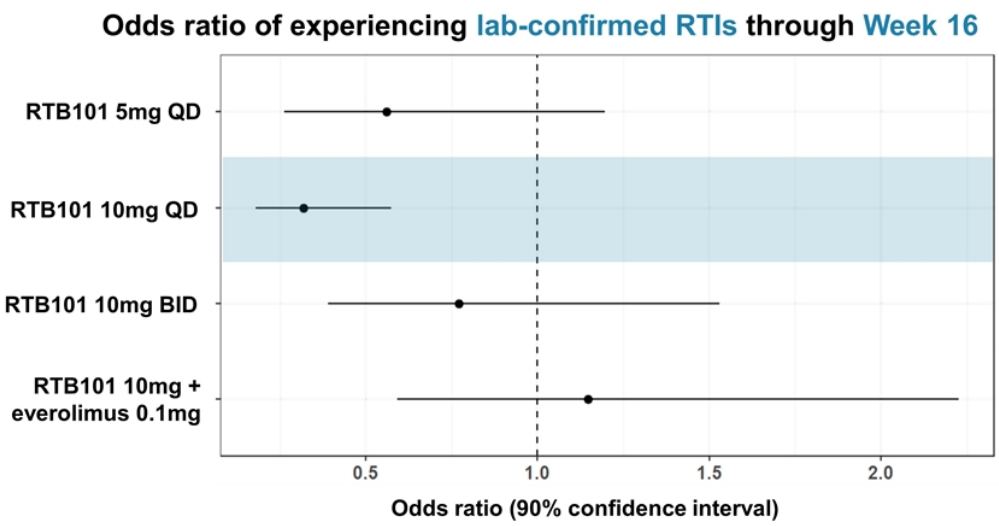
Smoking



Disruption of mTOR selectively in bronchial epithelial cells (mBE-mtor$^{-/-}$) significantly **increased** cigarette smoke (CS)-induced lung inflammation in a COPD model in which mice were exposed to cigarette smoke for 6 months[2]

[1]Mushaben E. M. *et al., J Immunol* 2011:187:5756-5763; [2] Wang Y *et al., J Immunol* 2018:200:2571-2580; *p<0.05, **p<0.01

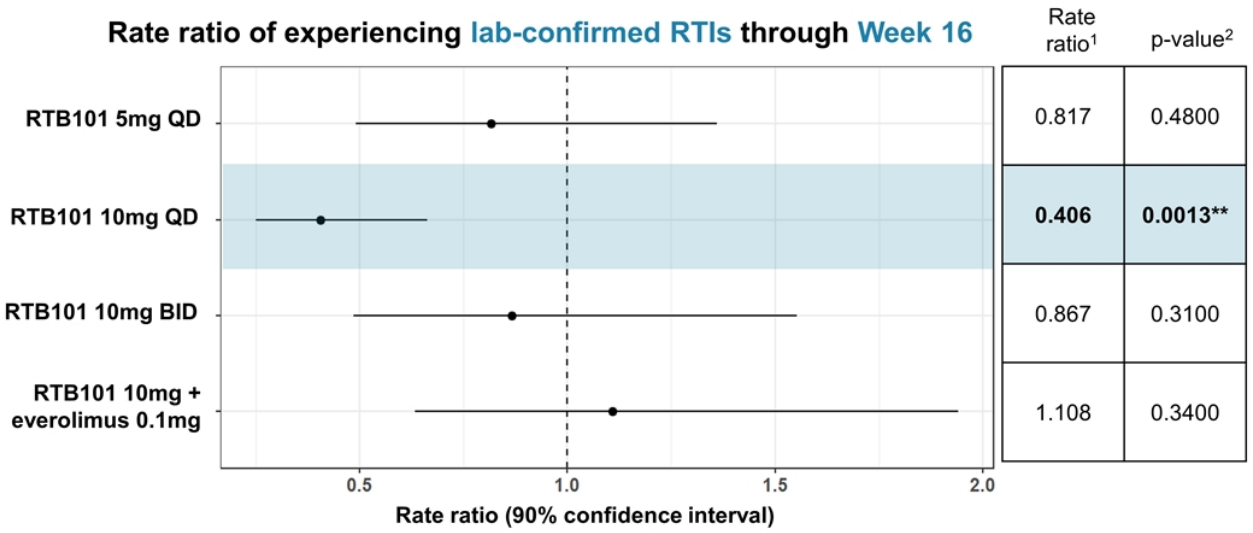
A significant reduction in the incidence of laboratory-confirmed RTIs was observed in subjects 65+ (excluding smokers/COPD patients)



	Active rate[1]	Placebo rate[1]	Odds ratio[2]	p-value[3]
RTB101 5mg QD	15/41	21/42	0.560	0.1000
RTB101 10mg QD	**15/113**	**36/117**	**0.319**	**0.0007*** **
RTB101 10mg BID	14/83	15/75	0.771	0.4700
RTB101 10mg + everolimus 0.1mg	18/78	15/75	1.147	0.2700

[1]No. of patients in cohort with one or more laboratory-confirmed RTIs/No. of patients in cohort; [2]Odds ratio represents the odds of experiencing one or more laboratory-confirmed RTIs in the active treatment group versus the placebo group; [3]One-sided p-value; ***p<0.0001; QD = once daily; BID = twice daily

A significant reduction in the rate of laboratory-confirmed RTIs was observed in subjects 65+ (excluding smokers/COPD patients)



	Rate ratio[1]	p-value[2]
RTB101 5mg QD	0.817	0.4800
RTB101 10mg QD	**0.406**	**0.0013****
RTB101 10mg BID	0.867	0.3100
RTB101 10mg + everolimus 0.1mg	1.108	0.3400

[1]Rate ratio represents the rate of experiencing one or more laboratory-confirmed RTIs in the active treatment group versus the placebo group; [2]One-sided p-value; **p<0.001; QD = once daily; BID = twice daily

Summary of RTB101 10mg QD data from two Phase 2 clinical studies enrolling > 900 elderly subjects

Phase 2a
264 healthy elderly
(23% with comorbidities)

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

Phase 2b
652 elderly
(100% with comorbidities)

- **30.6% reduction** in the percent of patients with laboratory-confirmed RTIs (p=0.025)
- **56.9% reduction** in the percent of patients with laboratory confirmed RTIs (excluding smokers/COPD patients; p=0.007)

Data from two Phase 2s enrolling >900 elderly subjects demonstrate RTB101 10 mg QD potential efficacy in subjects 65 and older (excluding smokers/COPD patients)

QD = once daily

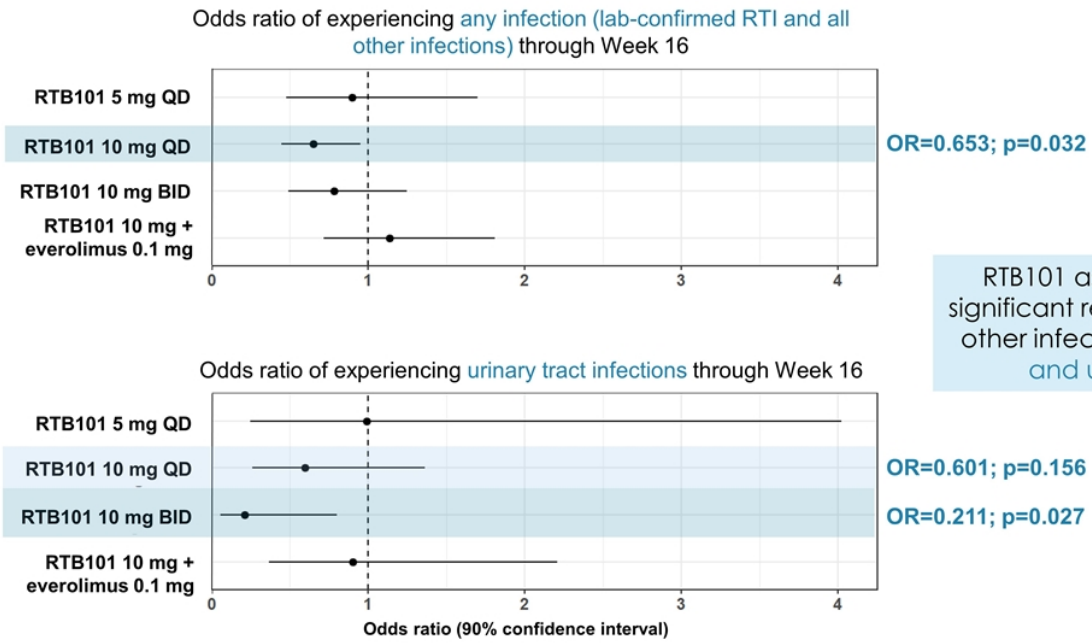
RTB101 was well-tolerated in high-risk elderly patients through Week 24

- Adverse events (AEs) were balanced between the RTB101 10mg 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)

	RTB101 10mg QD	Placebo
Serious AEs (% of patients)	4.5%	7.8%
Discontinued study drug due to an AE (% of patients)	5.1%	5.6%
Number of severe AEs	12	25

QD = once daily; BID = twice daily

RTB101 may also reduce the incidence of total infections of any kind



RTB101 associated with statistically significant reductions across analyses of other infections: Infections of any kind and urinary tract infections

OR = Odds ratio represents the odds of experiencing one or more infections in the active treatment group versus the placebo group; One-sided p-value; QD = once daily; BID = twice daily

Market Opportunity in RTIs

RTIs in the elderly represent a significant healthcare burden

- Mortality from RTIs is higher than mortality from colorectal, pancreatic, breast or prostate cancer[1]
- RTIs are the 4th most common cause for hospitalization in 65+ (2nd in 85+)[2]
- RTIs cause the majority of asthma exacerbations in the elderly[3]
- The majority of RTIs are caused by viruses for which there are no approved therapies[4]
- Decreasing the incidence of RTIs in the elderly may significantly decrease health care costs

Sources: [1]2017, NCHS, National Vital Statistics System, Mortality; 2015, American Cancer Society, Inc, Surveillance Research; [2]Pfunter, A (2013) HCUP Statistical Brief #162; [3] BMJ, 1995, 310:1225-1228; BMJ, 1993, 307:982-986; [4] Am J Med. 2002. 112(6A):42S-49S

Estimated number of elderly that may benefit from RTB101 in key geographies

	US	EU5	JP	CN
# Elderly People without COPD and who are non-smokers*	40M	53M	29M	77M
Elderly (65-84 years old) with asthma:	3.2M	3.3M[1]	2.1M[2]	2.5M[3]
Very elderly (85+ years old):	6.5M	9.3M	5.5M	8.9M

**Based on references provided on slide 44;* [1]Based on estimated percentage of asthmatics in older adults in high-income countries. [2]Based on percentage of asthmatics in the Japanese adult population. [3]Based on percentage of adults age ≥60 on asthma medication in Jinan province; Likely underestimated due to low

Survey of 100 physicians to determine potential usage in the target patient populations

Physician survey*: Expected use in target populations

% Reduction in RTI	Estimated % prescribed in patients (patient-weighted means)		
	≥85	65-84 with asthma	65-84 with comorbidities
25%	33%	36%	36%
33%	41%	44%	47%
40%	**46%**	**48%**	**51%**

***Respondent background (n=100):**

Medical Specialty	
Geriatrics	25
Primary Care	50
Pulmonologist	25

Practice characteristics	
Years practicing medicine	Avg 19 *(median 19.5, range 6-33)*
# pts ≥ 65 seen/month	Avg 250 *(median 220, range 80-600)*
% services billed to Medicare	Avg 63% *(median 65%, range 30-100%)*

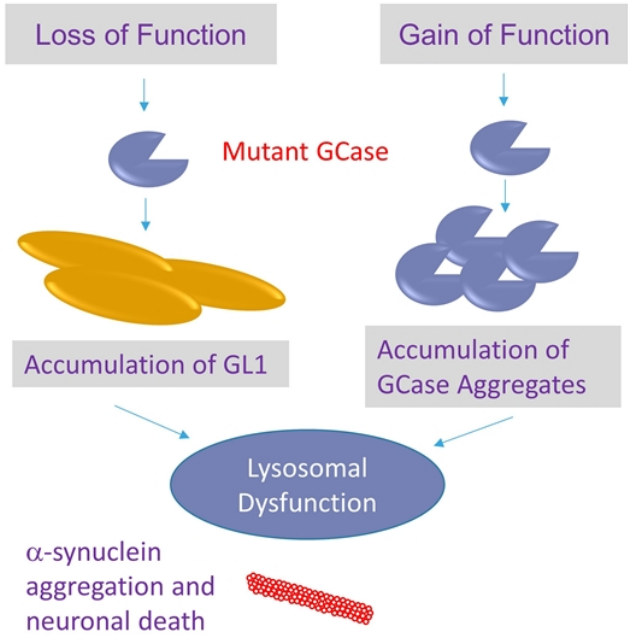
Ameliorating Neurodegenerative Diseases

GBA Parkinson's Disease

GBA mutation in Parkinson's disease (PD) leads to α-synuclein aggregation and neuronal cell death

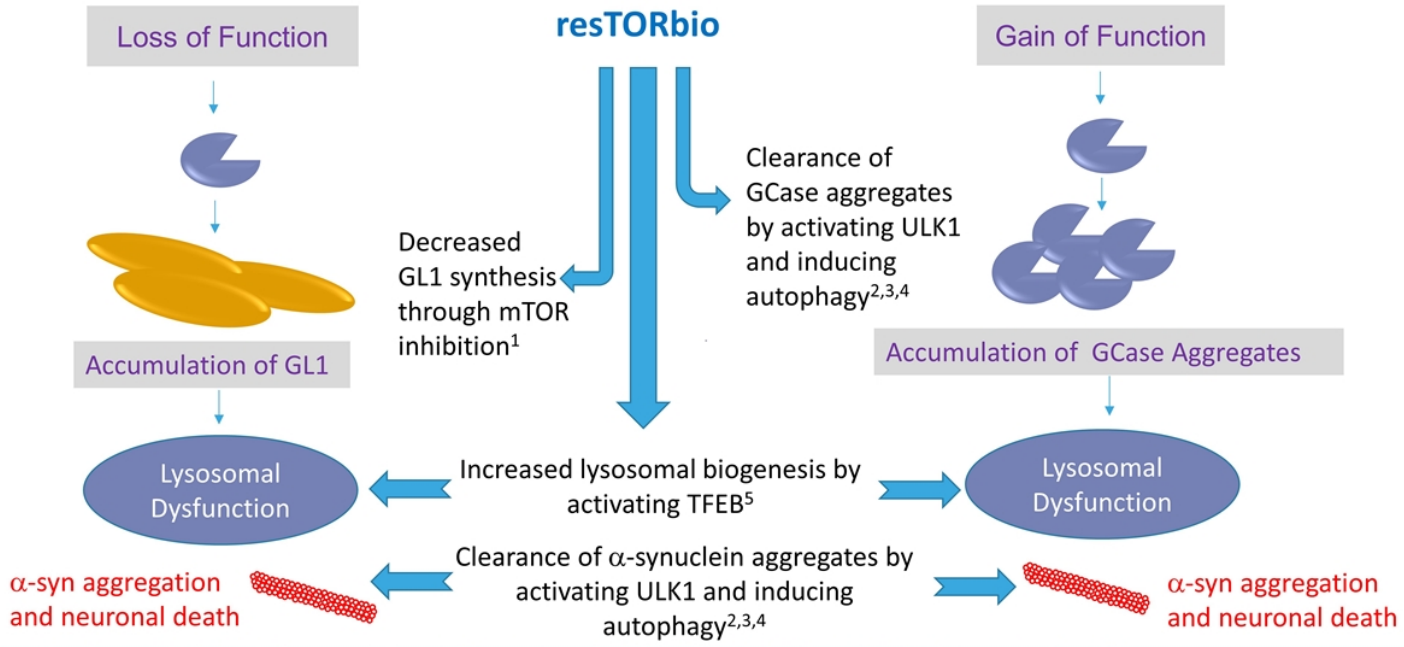
Disease cascade:

- GBA is a gene encoding the lysosomal enzyme glucocerebrosidase (GCase)
- Mutant GCase may contribute to PD pathogenesis through a loss or gain of function:
  - **Loss of function:** Decreased GCase activity leading to an accumulation of its lipid substrate glucosylceramide (GL1) that disrupts lysosomal function[1]
  - **Gain of function:** Accumulation of misfolded GCase aggregates that disrupt lysosomal function[2]
- Disruption of lysosomal function prevents clearance of aggregated a-synuclein and leads to neuronal death



[1]Mazzulli, J. R., et al. (2011). *Cell* 146(1): 37-52; [2]Cullen,V., et al. (2011). *Annals of Neurology* 69(6): 940-953.
GBA = glucocerebrosidase; α-syn = alpha-synuclein

resTORbio GBA PD program potential benefits to GBA PD patients (both loss or gain of function GBA mutations)



[1]Guri, Y., et al. (2017). *Cancer Cell* 32(6): 807-823; [2]Decressac, M., et al. (2013). *Proc Natl Acad Sci USA* 110(19): E1817-1826; [3]Cullen,V., et al. (2011). *Ann Neurol* 69(6): 940-953; [4]Kinghorn, K.J., et al. (2016). *J Neurosci* 36(46): 11654-11670; [5]Roczniak-Ferguson, A., et al. (2012). *Sci Signal* 5(228): ra42.

Phase 2a Parkinson's disease trial design

Design	**Randomized, Placebo-Controlled Phase 2a Study (12-week dosing)** • Mild-to-moderate PD patients (mH&Y I-III) with confirmed GBA mutation • On stable medication regimen of PD drugs • Once weekly dosing
Study Size	N=45
Key Endpoints	**Primary endpoint:** • Safety and tolerability **Secondary endpoint:** • Exposure in blood, plasma and CSF **Exploratory endpoints:** • Biomarkers in plasma and CSF • Tremor, sleep pattern, UPDRS, PDQ-39

Cohort	RTB 101 dose (mg)	Sirolimus dose (mg)
1	300	0
2	0	2
3	300	2
4	300	4
5	300	6

or matching placebo

Phase 2a initiation planned for 1Q19

Near term milestones and financials

Milestones

Q1 2019	End of Phase 2 meeting with the FDA
Q1 2019	Initiate Phase 2a study in Parkinson's disease
H1 2019	Initiate Phase 3 program for reducing the incidence of RTIs

Financials

Cash, cash equivalents and marketable securities were ~$115 million as of September 30, 2018

resTORbio highlights

- **Targeting the biology of aging**
  - Lead clinical candidate, RTB101, is the most advanced selective TORC1 inhibitor
  - TORC1 inhibition improves the function of aging organ systems including the immune, neurologic, and cardiovascular systems
- **Positive results in Phase 2b to improve immune function and reduce the incidence of RTIs**
  - 30.6% reduction in the percentage of patients with laboratory-confirmed RTIs (p=0.025)
  - 52.1% reduction in percentage of patients with severe laboratory-confirmed RTI symptoms (p=0.034)
  - Successfully defined dose and patient population for Phase 3 program
  - End-of-Phase 2 meeting with the FDA expected in 1Q19; Plan to initiate Phase 3 program in 1H19
  - RTIs are the 4th most common cause of hospitalization in people 65+; 2nd in 85+ (US)
- **Data-driven approach to expand into additional aging-related indications**
  - Improving neurologic function: Plan to initiate Phase 2a study in GBA Parkinson's disease in 1Q19
  - Building a pipeline targeting multiple mechanisms underlying aging

RTI = respiratory tract infection

resTORbio™

Targeting the Biology of Aging to Restore Health

January 2019

Extensive genetic validation that TORC1 Inhibition extends lifespan across species

1) Fabrizio P, Pozza F, Pletcher SD, Gendron CM, Longo VD. Regulation of longevity and stress resistance by Sch9 in yeast. *Science*. 2001;292(5515):288–290.
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3) Kaeberlein M, et al. Regulation of yeast replicative life span by TOR and Sch9 in response to nutrients. *Science*. 2005;310(5751):1193–1196.
4) Bonawitz ND, Chatenay-Lapointe M, Pan Y, Shadel GS. Reduced TOR signaling extends chronological life span via increased respiration and upregulation of mitochondrial gene expression. *Cell Metab*. 2007; 5(4):265–277.
5) Vellai T, Takacs-Vellai K, Zhang Y, Kovacs AL, Orosz L, Muller F. Genetics: influence of TOR kinase on lifespan in C. elegans. *Nature*. 2003;426(6967):620.
6) Jia K, Chen D, Riddle DL. The TOR pathway inter- acts with the insulin signaling pathway to regulate C. elegans larval development, metabolism and life span. *Development*. 2004;131(16):3897–3906.
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8) Pan KZ, et al. Inhibition of mRNA translation extends lifespan in Caenorhabditis elegans. *Aging Cell*. 2007;6(1):111–119.
9) Robida-Stubbs S, et al. TOR Signaling and rapamy- cin influence longevity by regulating SKN-1/Nrf and DAF-16/FoxO. *Cell Metab*. 2012;15(5):713–724.
10) Kapahi P, Zid BM, Harper T, Koslover D, Sapin V, Benzer S. Regulation of lifespan in Drosophila by modulation of genes in the TOR signaling pathway. *Curr Biol*. 2004;14(10):885–890.
11) Luong N, et al. Activated FOXO-mediated insulin resistance is blocked by reduction of TOR activity. *Cell Metab*. 2006;4(2):133–142.
12) Zid BM, et al. 4E-BP extends lifespan upon dietary restriction by enhancing mitochondrial activity in Drosophila. *Cell*. 2009;139(1):149–160.
13) Selman C, et al. Ribosomal protein S6 kinase 1 signaling regulates mammalian life span. *Science*. 2009;326(5949):140–144.
14) Lamming DW, et al. Rapamycin-induced insulin resistance is mediated by mTORC2 loss and uncoupled from longevity. *Science*. 2012; 335(6076):1638–1643.

References for number of elderly people without COPD and who are non-smokers

US:

1. 4,038,000 elderly people estimated to be smokers in the US. U.S. NHIS 2017, https://www.cdc.gov/nchs/nhis/SHS/tables.htm (accessed Jan 5, 2019), Table A-12b.
2. Prevalence of COPD in the elderly estimated at 14.2%. Hanania, N. et al, 2010 "COPD in the Elderly Patient" https://www.medscape.com/viewarticle/730813_2 (accessed Jan 5, 2019)
3. 14.1% of current smokers were assumed to have COPD. Cunningham, T.J., et al., COPD, 2015. 12(3): p. 276-86.
4. Size of U.S. elderly population estimated at 50,858,679 in 2017. U.S. Census Bureau. https://factfinder.census.gov/faces/nav/jsf/pages/index.xhtml? (accessed Jan 5, 2019)

Europe:

1. Smoking prevalence in the elderly in each European country. Eurostat database, http://appsso.eurostat.ec.europa.eu/nui/show.do?dataset=hlth_ehis_sk3e&lang=en (accessed Jan 5, 2019)
2. COPD prevalence in the elderly estimated at 14.2%. Raherison, C. and P.O. Girodet, Epidemiology of COPD. Eur Respir Rev, 2009. 18(114): p. 213-21.
3. 29.6% & 16.1% of COPD patients aged 65-75 & 75 and over, respectively estimated to be current smokers. Worth, H., et al., The 'real-life' COPD patient in Germany: The DACCORD study. Respir Med, 2016. 111: p. 64-71.
4. Size of elderly population in each European country. UN Data, United Nations Statistics Division, http://data.un.org/Data.aspx?d=POP&f=tableCode%3A22 (accessed Jan 5, 2019)

Japan:

1. Smoking prevalence in people aged 60 and over in Japan (21.2% in men, 5.6% in women). Japan Tobacco Inc., JT's Annual Survey Finds 18.2 % of Japanese Adults Are Smokers. 2017. https://www.jt.com/media/news/2017/pdf/20170727_E02.pdf (accessed Jan 5, 2019)
2. COPD prevalence in people aged 60 and over in Japan (11.5% of men, 5.8% of women); 17% & 0% of male and female current smokers, respectively, estimated to have COPD. Takemura, H., et al., *Prevalence of COPD in Japanese People on Medical Check-Up.* Journal of Experimental Medicine, 2005. **207**: p. 41-50.
3. Size of elderly population estimated at 35,228,000 (15,294,000 men, 19,933,000 women). E-Stat, Portal Site of Official Statistics of Japan. https://www.e-stat.go.jp/en/stat-search/files?page=1&layout=datalist&toukei=00200524&tstat=000000090001&cycle=1&year=20180&month=12040606&tclass1=000001011678 (accessed Jan 5, 2019)China:

China:

1. Smoking prevalence in the elderly in China estimated at 22.7%. Li, Q., J. Hsia, and G. Yang, *Prevalence of Smoking in China in 2010.* New England Journal of Medicine, 2011. **364**(25): p. 2469-2470.
2. COPD prevalence in the elderly: COPD prevalence among current smokers. Fang, L., et al., Chronic obstructive pulmonary disease in China: a nationwide prevalence study. The Lancet Respiratory Medicine, 2018. 6(6): p. 421-430.
3. Size of elderly population in China by age. https://www.populationpyramid.net/china/2016/ (accessed Jan 5, 2019)