

resTORbio™

August 2018



# 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. 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 into, and successfully complete, clinical studies, 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.

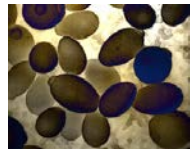
These statements are also subject to a number of material risks and uncertainties that are discussed in the section entitled "Risk Factors" in resTORbio’s annual report on Form 10-K for the fiscal year ended December 31, 2017, as well as discussions of potential risks, uncertainties, and other important 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.

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The biology of aging is regulated by TORC1

# TORC1 is an evolutionarily conserved pathway that regulates aging



Yeast



Worms



Flies



Mice



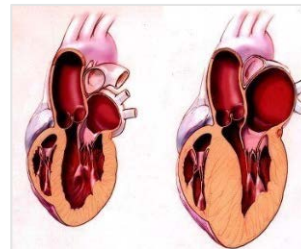
TORC1 inhibition extended lifespan and healthspan and improved the following aging-related conditions in preclinical studies:



Improved  
Immune Function



Ameliorate Heart  
Failure



Ameliorate  
Neurodegenerative  
Diseases





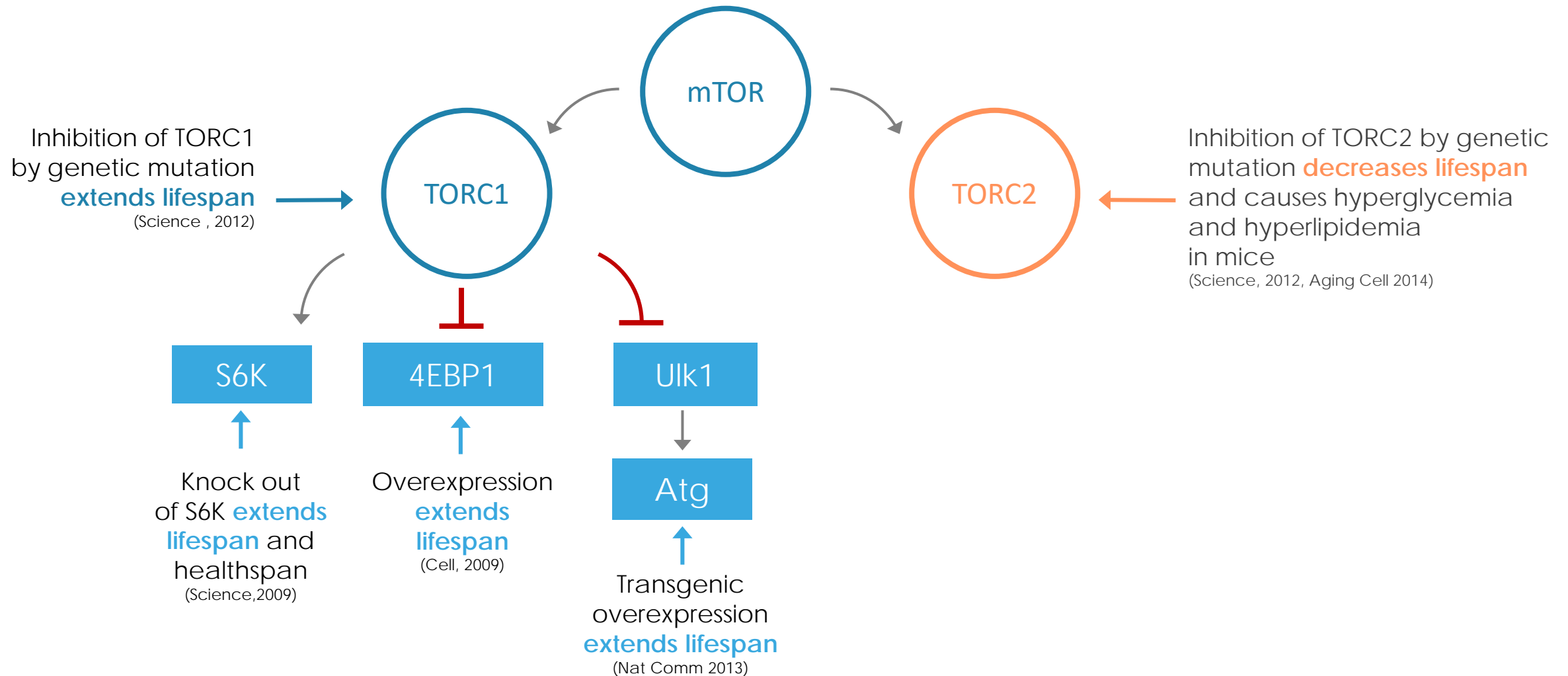
# resTORbio highlights

- **Developing first in class and most advanced selective TORC1 program**
  - TORC1 inhibition improves immune, cardiac and neurologic function in aging preclinical species
  - Proprietary TORC1 inhibitor, RTB101, in clinical development
- **Positive topline results in Phase 2b study of RTRB101** to improve immune function and decrease the incidence of respiratory tract infections (RTIs) in high risk elderly patients
  - Successfully **identified dose (RTB101 10 mg once daily) and high-responding patient populations** to move forward into pivotal trials
  - RTB101 10 mg also significantly decreased the incidence of RTIs in a prior Phase 2a
  - All doses of RTB101 observed to be well-tolerated
  - Potential to treat **high unmet need**; RTIs are the 4<sup>th</sup> leading cause for hospitalization in the 65+; 2<sup>nd</sup> in 85+ (US)
- **Data-driven approach to expand into additional indications in 2018**
  - Detecting signals in the Phase 2b trial for two additional aging-related diseases in 2H 2018
  - Initiate at least one Phase 2 trial in an additional indication(s) in Q4 2018/Q1 2019
- **Well financed through 2020 with over \$125 million as of June 30, 2018**

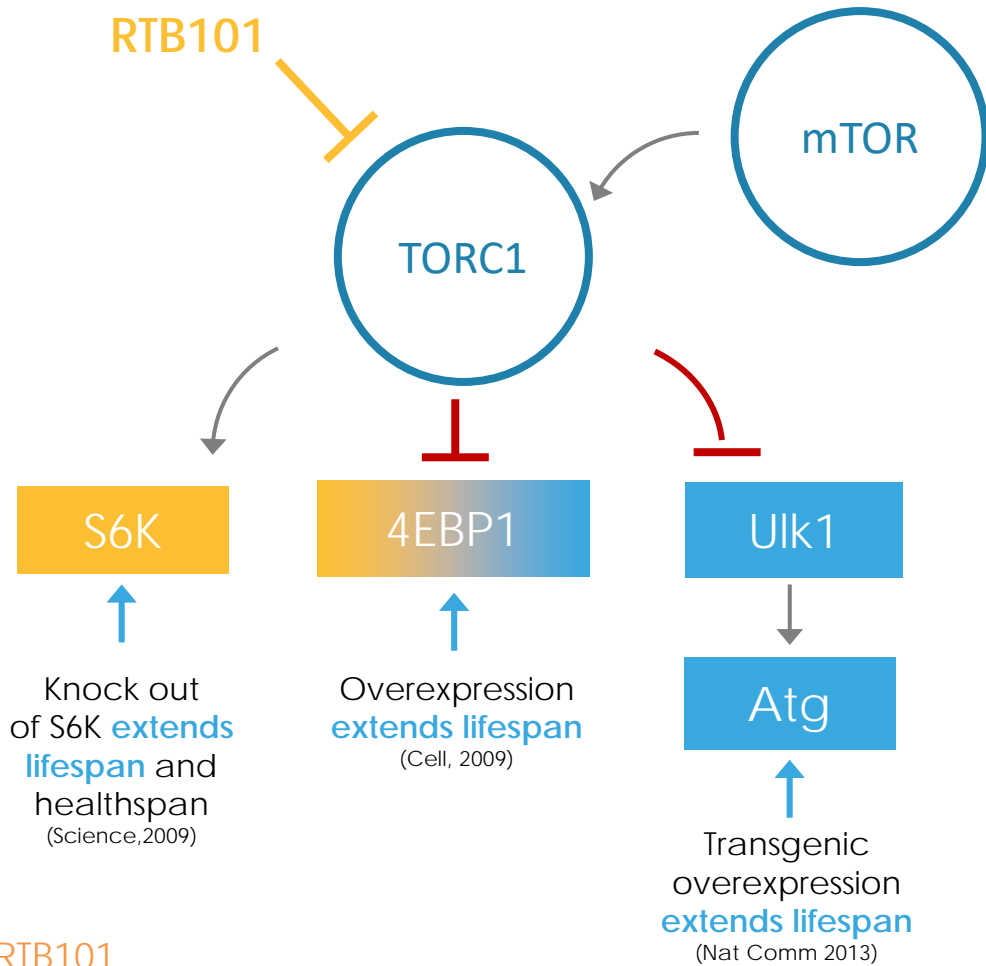
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# TORC1 Pathway

# Selective and more complete inhibition of TORC1 may have therapeutic benefit for the treatment of aging-related diseases

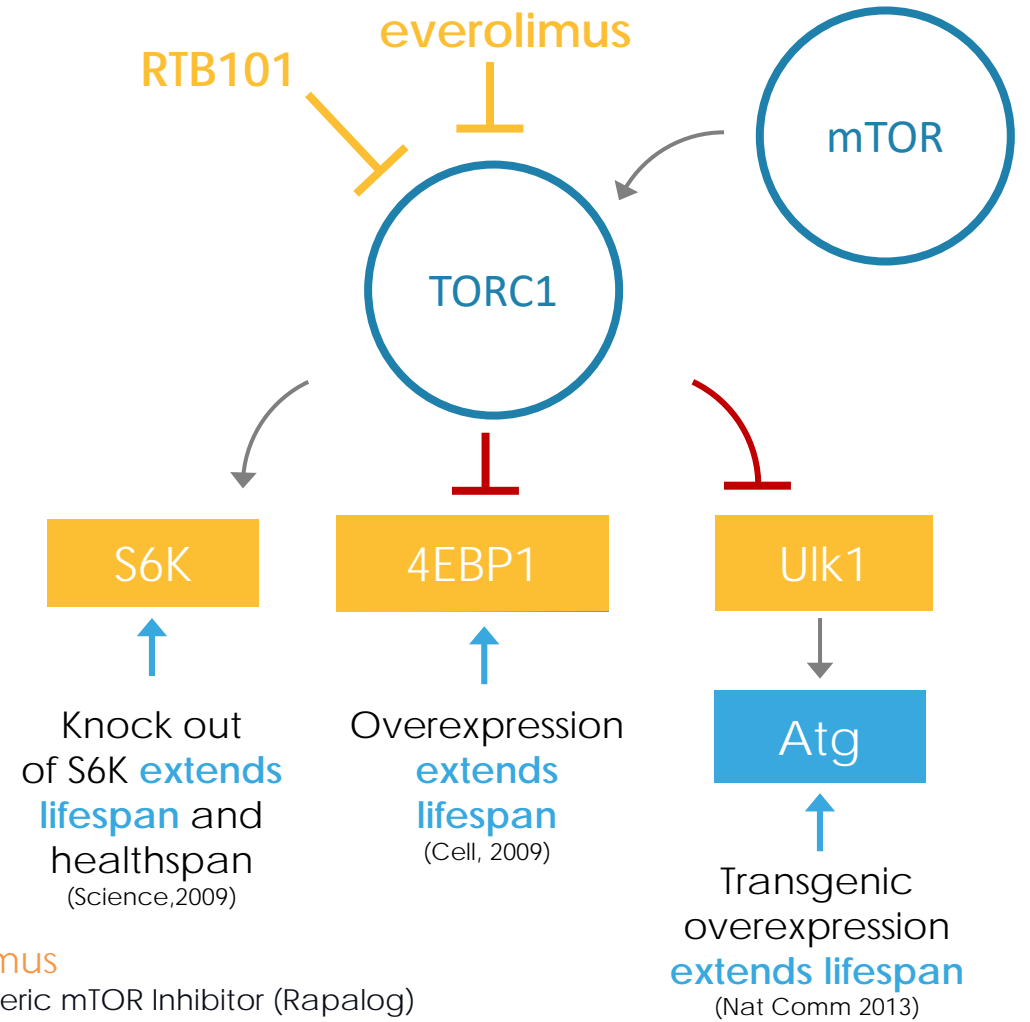


# RTB101 and RTB101+everolimus target multiple nodes downstream of TORC1



## RTB101

- Catalytic mTOR>PI3K inhibitor
- Over 1,000 patients exposed



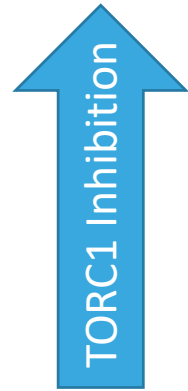
## everolimus

- Allosteric mTOR Inhibitor (Rapalog)
- Approved for oncology and organ transplant indications



# Results of Phase 2a trial


- 264 mostly healthy elderly people randomized to the following TORC1 inhibitor treatment arms:



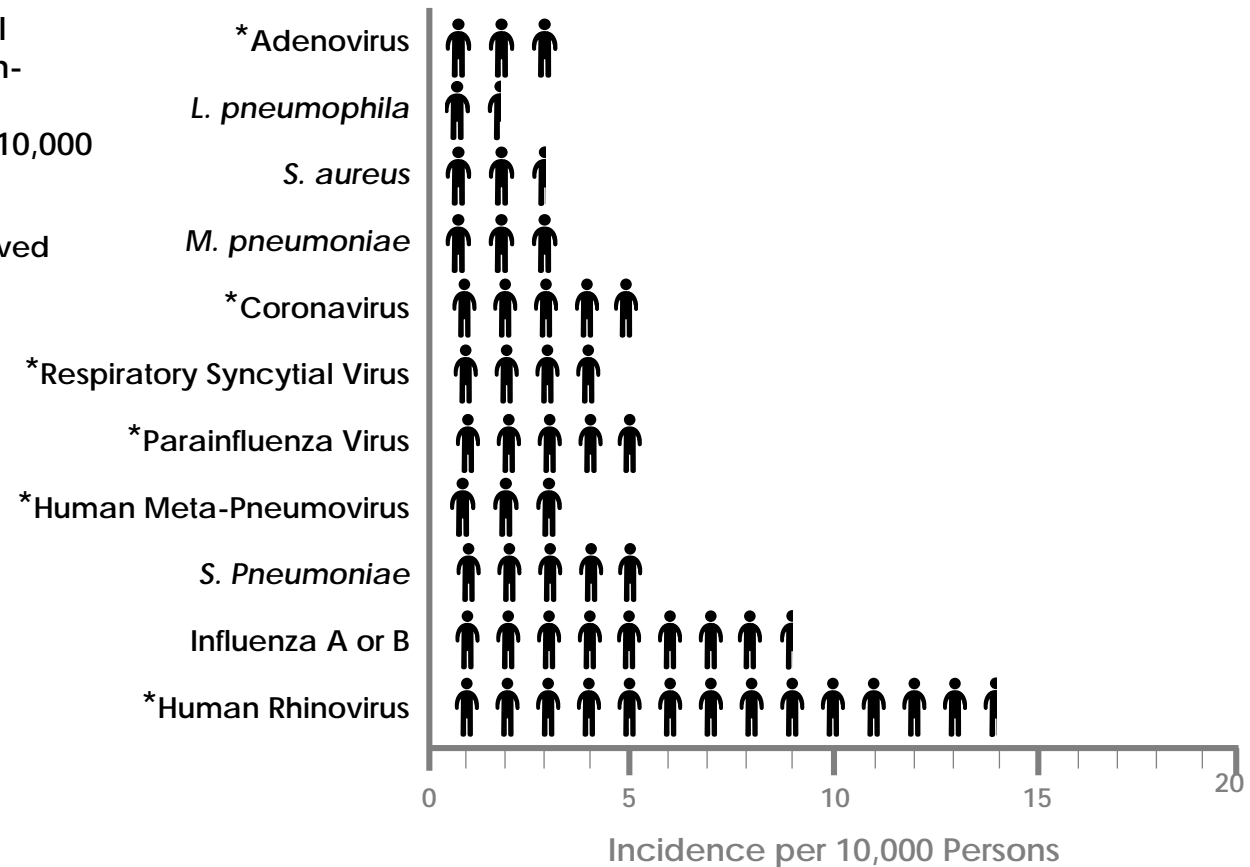
- Everolimus 0.1 mg + RTB101 10 mg
  - RTB101 10 mg
  - Everolimus 0.5 mg
  - Everolimus 0.1 mg
  - Placebo
- Both RTB101 10 mg once daily and RTB101 10 mg + everolimus 0.1 mg once daily significantly reduced the incidence of all infections as well as respiratory tract infections (RTIs)
    - Reduction in RTIs;
      - RTB101 10 mg : 42% reduction (p=0.006)
      - RTB101 10 mg + everolimus 0.1 mg : 36% reduction (p=0.01)
  - Both RTB101 10 mg and RTB101 10 mg + everolimus 0.1 mg upregulated antiviral gene expression in whole blood

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

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

 Indicates the annual number of pathogen-specific pneumonia hospitalizations per 10,000 adults ≥ 80

\* Viruses with no FDA-approved therapies available



**IMMUNOTHERAPY:**  
RTB101 alone or in combination with everolimus

# Phase 2a to Phase 2b



Phase 2a: 65 and older,  
23% with comorbidities



Phase 2b



85 and older



65 and older w/ asthma



65 and older w/  
diabetes



65 and older w/  
COPD



65 and older, smokers

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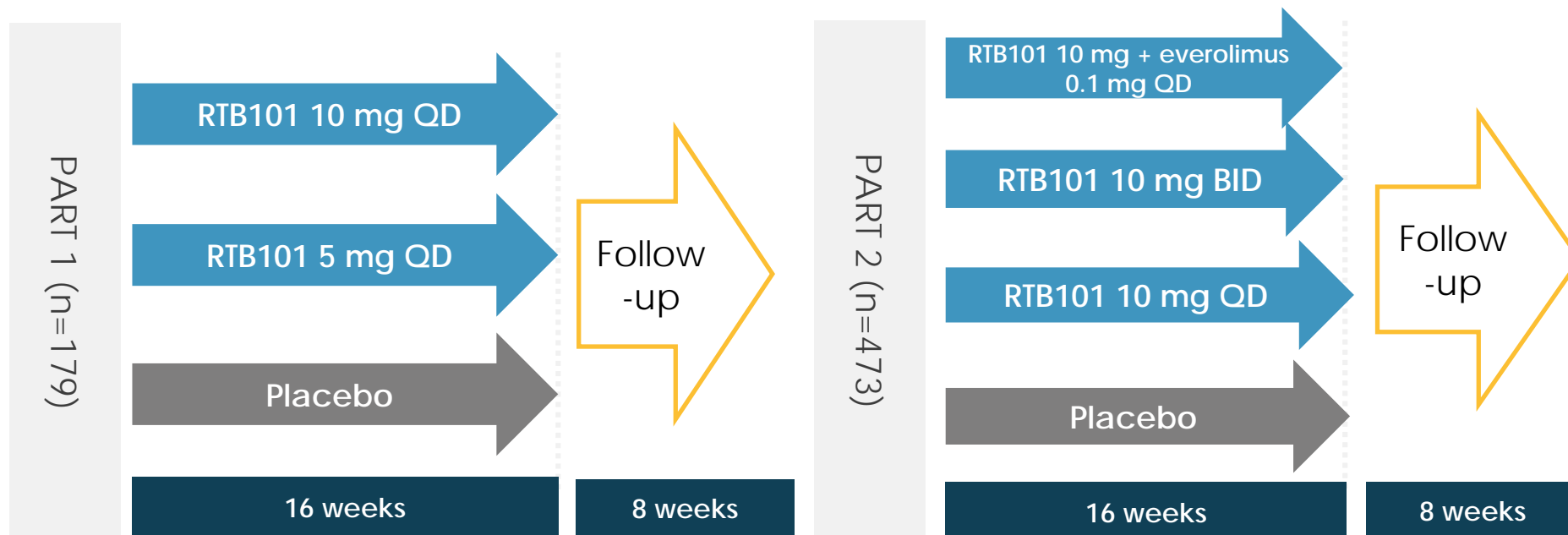
# RTB101 Phase 2b Topline Data

# Goal of Phase 2b dose-finding study: To determine dose and patient population for pivotal trials

- **The study successfully identified dose and patient population for pivotal trials:**
  - **Dose: RTB101 10 mg once daily:**
    - Led to a statistically significant and clinically meaningful 30.6% reduction in the percentage of patients with one or more laboratory-confirmed RTIs (**p=0.026**)
    - RTB101 10 mg once daily decreased the incidence of RTIs in prior Phase 2a by 42% (**p=0.006**)
  - **Pre-specified analyses identified high responding patient population:**
    - 65 and older with asthma: 68.4% reduction in laboratory-confirmed RTIs (**p=0.0002**)
    - 85 and older: 66.7% decrease in laboratory-confirmed RTIs (**p=0.007**)
    - 65 and older non-smokers: 43.9% decrease in laboratory-confirmed RTIs (**p=0.001**)
- All doses, including RTB101 10 mg once daily, were well-tolerated
- Plan to meet with regulatory authorities to discuss design of pivotal trials and initiate pivotal trials in 2019

# Phase 2b design

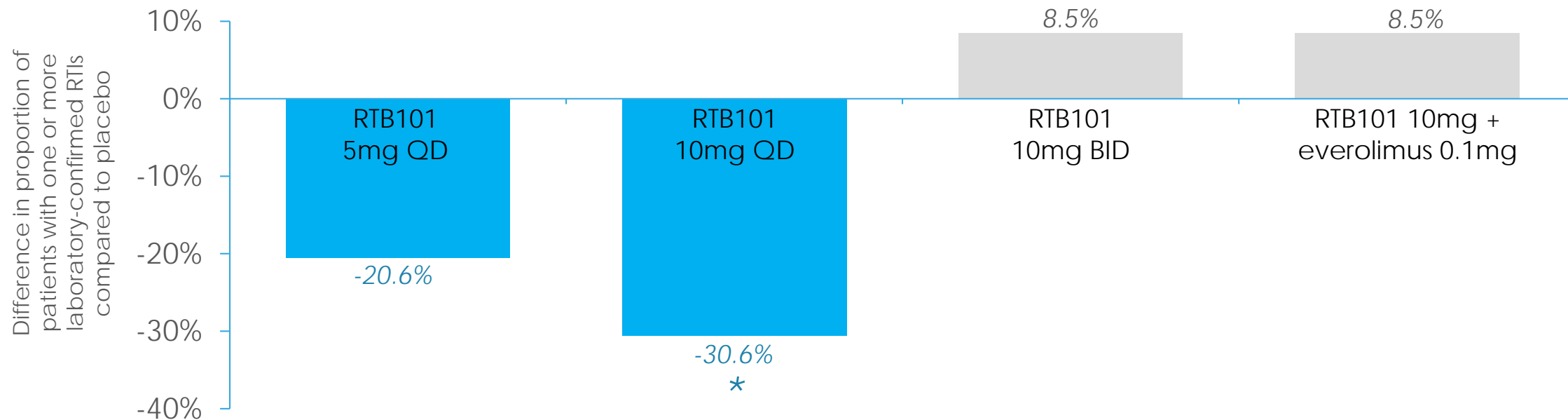
- **Primary Endpoint:** Reduction in the percentage of patients with laboratory-confirmed RTIs through week 16
- **Population:** Elderly subjects at increased risk of RTI-associated morbidity and mortality including:
  - $\geq 85$  years of age
  - 65-84 years of age with one or more of the following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



QD, once daily; BID, twice daily



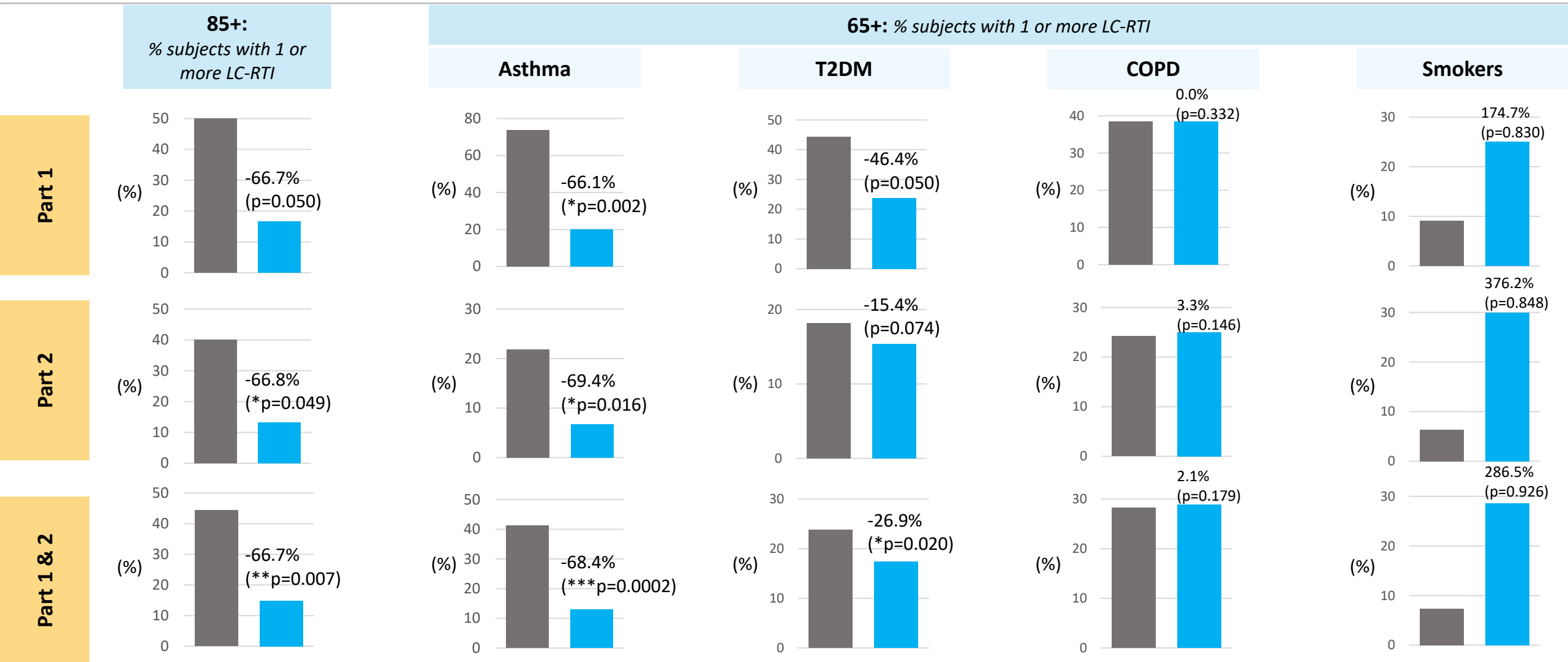
# A significant reduction in the percentage of patients with laboratory-confirmed RTIs was observed in the RTB101 10 mg once daily cohort



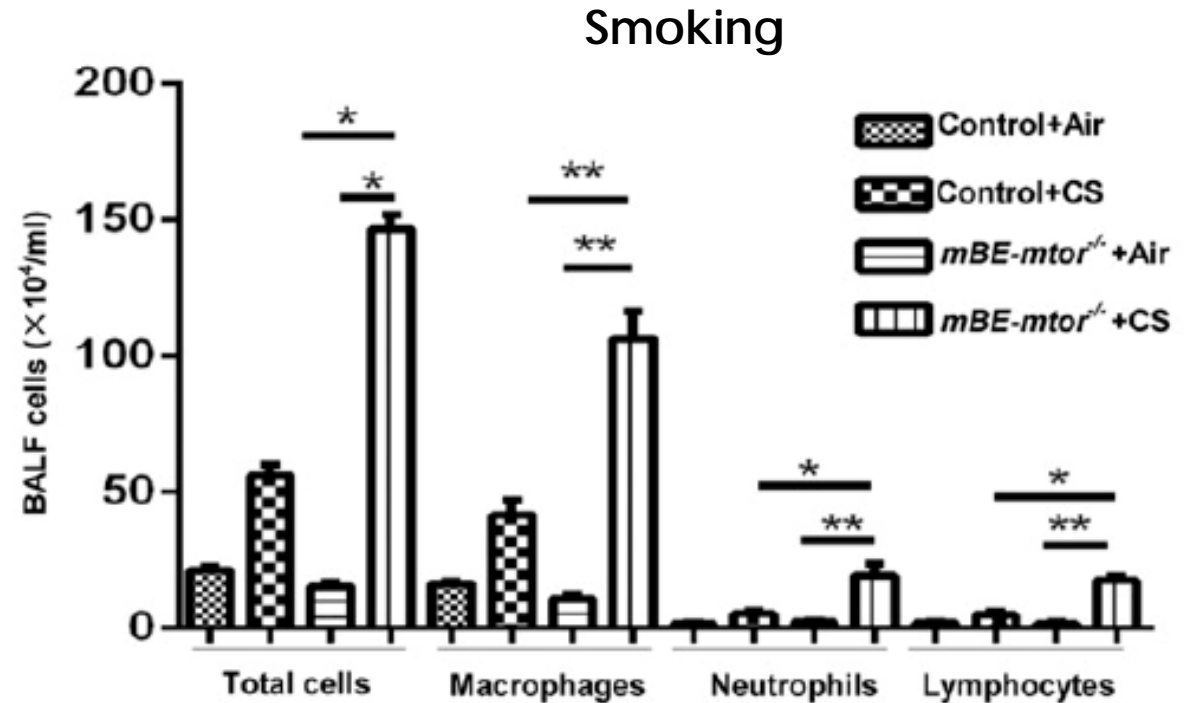
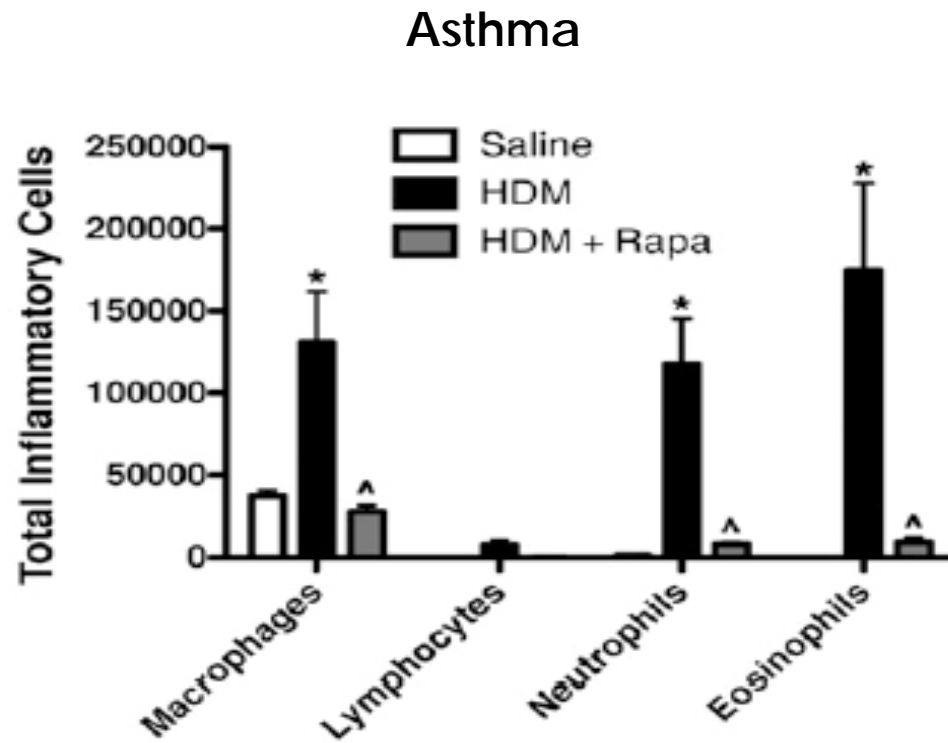
<b>p-value<sup>1</sup></b>		<b>0.108</b>	<b>0.026</b>	<b>0.617</b>	<b>0.694</b>
<b>Odds ratio<sup>2</sup> (CI<sup>3</sup>)</b>		0.615 (0.323; 1.174)	0.604 (0.394; 0.927)	1.100 (0.650; 1.860)	1.180 (0.689; 2.022)
<b>Active</b>	<b>n</b>	61	176	120	115
	<b>n<sub>RTI</sub><sup>4</sup></b>	21	34	26	25
<b>Placebo</b>	<b>n</b>	60	180	120	120
	<b>n<sub>RTI</sub><sup>4</sup></b>	26	50	24	24

<sup>1</sup>One-sided p-value; <sup>2</sup>Odds ratio represents the odds of experiencing one or more laboratory confirmed RTIs in the active treatment group versus the placebo group; <sup>3</sup>90% confidence interval; \*p<0.05, considered to be statistically significant; <sup>4</sup>No. of patients in cohort with one or more laboratory-confirmed RTIs

# RTB101 10mg once daily monotherapy showed unprecedented efficacy in subpopulations 85+ and 65+ with asthma



# Preclinical data: mTOR inhibition decreased airway inflammation in asthma and increased airway inflammation due to smoking

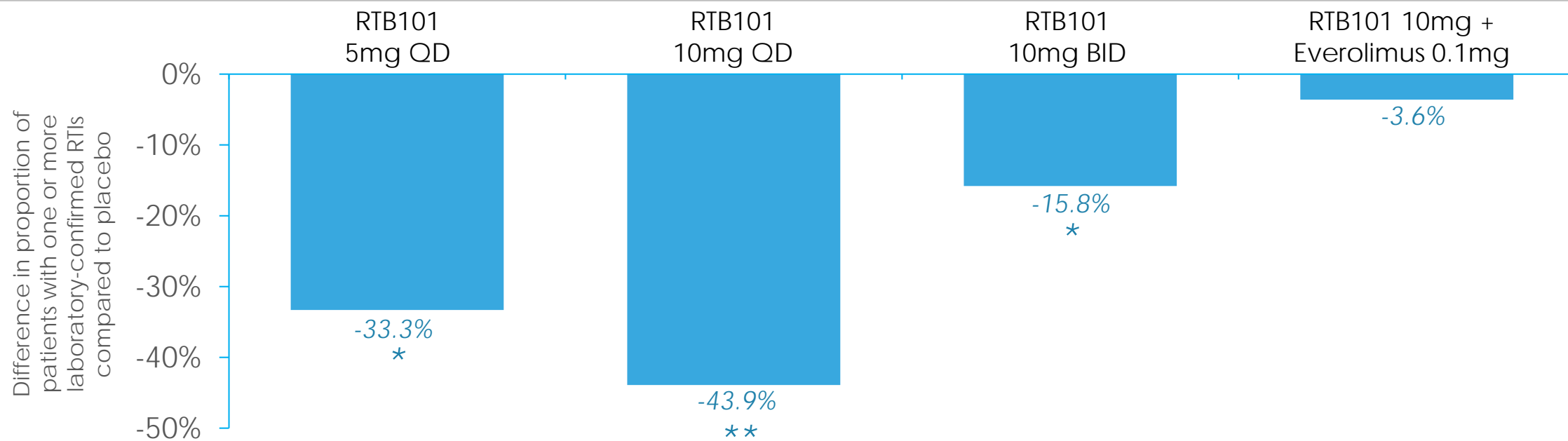


mTOR inhibition with rapamycin (Rapa) significantly **decreased** airway inflammation in a preclinical asthma model in which mice were exposed to intranasal house dust mites (HDM)<sup>1</sup>

Disruption of mTOR selectively in bronchial epithelial cells (mBE-mtor<sup>-/-</sup>) significantly **increased** cigarette smoke (CS)-induced lung inflammation in a COPD model in which mice were exposed to cigarette smoke for 6 months<sup>2</sup>

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

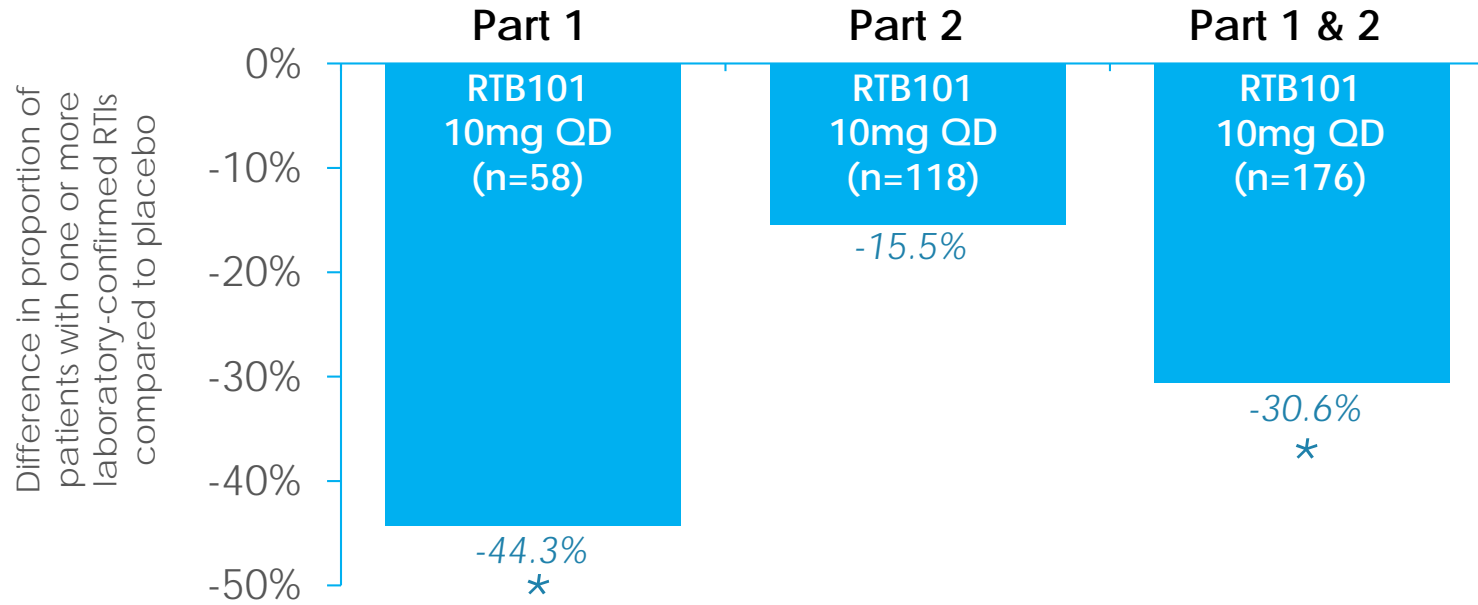
# A significant reduction in the percentage of patients with laboratory-confirmed RTIs was observed in all monotherapy doses [non-smokers]



<b>p-value<sup>1</sup></b>		<b>0.043</b>	<b>0.001</b>	<b>0.041</b>	<b>0.140</b>
<b>Odds ratio<sup>2</sup> (CI<sup>3</sup>)</b>		<b>0.413</b> (0.177; 0.962)	<b>0.309</b> (0.165; 0.577)	<b>0.344</b> (0.126; 0.941)	<b>0.579</b> (0.253; 1.328)
<b>Active</b>	<b>n</b>	53	148	102	94
	<b>n<sub>RTI</sub><sup>4</sup></b>	18	26	19	20
<b>Placebo</b>	<b>n</b>	49	153	104	104
	<b>n<sub>RTI</sub><sup>4</sup></b>	25	48	23	23

<sup>1</sup>One-sided p-value; <sup>2</sup>Odds ratio represents the odds of experiencing one or more laboratory confirmed RTIs in the active treatment group versus the placebo group; <sup>3</sup>90% confidence interval; \*p<0.05, \*\*p<0.01, \*\*\*p<0.001; <sup>4</sup>No. of patients in cohort with one or more laboratory-confirmed RTIs

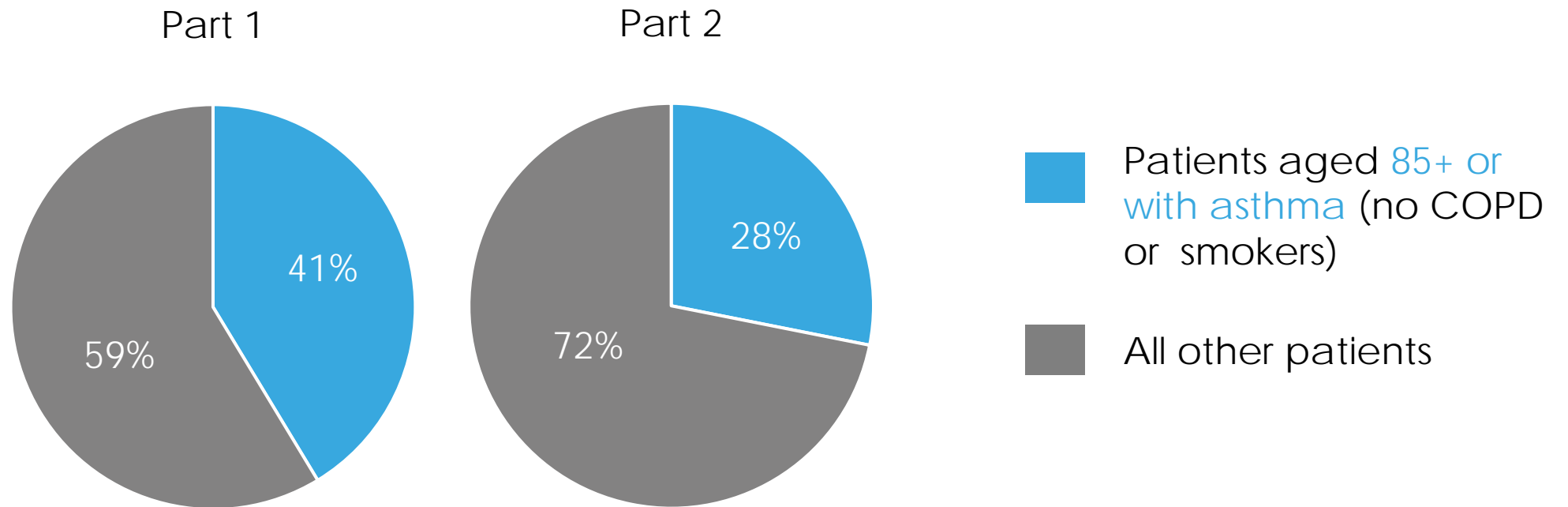
# RTB101 10mg once daily, all parts



<b>p-value<sup>1</sup></b>		<b>0.013</b>	<b>0.272</b>	<b>0.026</b>
<b>Odds ratio<sup>2</sup> (CI<sup>3</sup>)</b>		<b>0.394</b> (0.197; 0.787)	<b>0.815</b> (0.468; 1.419)	<b>0.604</b> (0.394; 0.927)
<b>RTB101 10mg QD</b>	<b>n</b>	58	118	176
	<b>n<sub>RTI</sub><sup>4</sup></b>	14	20	34
<b>Placebo</b>	<b>n</b>	60	120	180
	<b>n<sub>RTI</sub><sup>4</sup></b>	26	24	50

<sup>1</sup>One-sided p-value; <sup>2</sup>Odds ratio represents the odds of experiencing one or more laboratory confirmed RTIs in the active treatment group versus the placebo group; <sup>3</sup>90% confidence interval; \*p<0.05, considered to be statistically significant; <sup>4</sup>No. of patients in cohort with one or more laboratory-confirmed RTIs

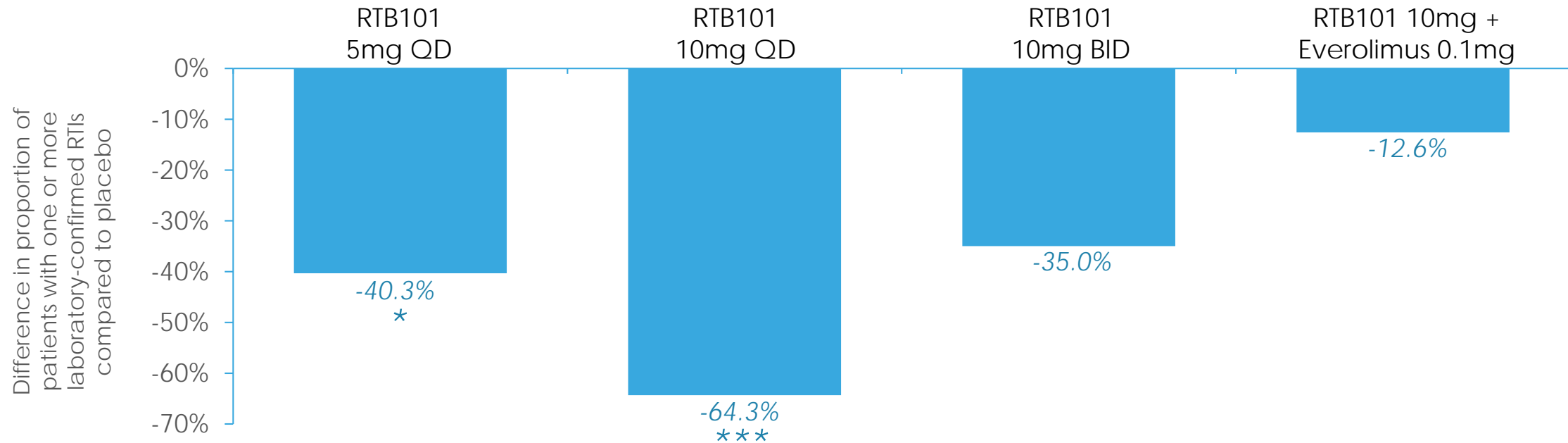
# Greater proportion of high responders in Part 1



Greater proportion of high responder group in Part 1 may account in part for the larger reduction in RTIs in Part 1 compared to Part 2



# 65+ with Asthma or 85+ Years of Age (Non-Smokers)



<b>p-value<sup>1</sup></b>		<b>0.0195</b>	<b>0.0003</b>	<b>0.134</b>	<b>0.352</b>
<b>Odds ratio<sup>2</sup> (CI<sup>3</sup>)</b>		<b>0.292</b> (0.110; 0.779)	<b>0.213</b> (0.102; 0.447)	<b>0.557</b> (0.234; 1.326)	<b>0.824</b> (0.356; 1.908)
<b>Active</b>	<b>n</b>	30	68	43	40
	<b>n<sub>RTI</sub><sup>4</sup></b>	11	10	8	10
<b>Placebo</b>	<b>n</b>	26	68	42	42
	<b>n<sub>RTI</sub><sup>4</sup></b>	16	28	12	12

<sup>1</sup>One-sided p-value; <sup>2</sup>Odds ratio represents the odds of experiencing one or more laboratory confirmed RTIs in the active treatment group versus the placebo group; <sup>3</sup>90% confidence interval; \*p<0.05, \*\*p<0.01, \*\*\*p<0.001; <sup>4</sup>No. of patients in cohort with one or more laboratory-confirmed RTIs

# Consistent efficacy of RTB101 10 mg once daily observed in Phase 2 clinical trials

## Phase 2a

(n=264)

23% with comorbidities

- ✓ 42%\*\* ↓ RTIs
- ✓ 47% ↓ RTIs in asthma pts
- No ≥ 85 in placebo

## Phase 2b

Part 1 (n=179)

100% with comorbidities

- ✓ 44%\* ↓ RTIs
- ✓ 66%\*\* ↓ RTIs in asthma pts
- ✓ 67% ↓ RTIs in ≥85

## Phase 2b

Part 2 (n=473)

100% with comorbidities

- ✓ 15% ↓ RTIs
- ✓ 69%\* ↓ RTIs in asthma pts
- ✓ 67%\* ↓ RTIs ≥ 85

## Phase 2b

Parts 1+2 (n=652)

100% with comorbidities

- ✓ 31%\* ↓ RTIs
- ✓ 68%\*\*\* ↓ RTIs in asthma pts
- ✓ 67%\*\* ↓ RTIs ≥ 85

\*p<0.05, \*\*p<0.01, \*\*\*p<0.001

# RTB101 was well-tolerated in high-risk elderly patients

- Adverse events (AEs) were balanced between the RTB101 10 mg once daily and placebo cohorts
- 1 unrelated death occurred in the RTB101 10 mg once daily cohort (patient was hit by car while riding a bicycle), 1 unrelated death occurred in the placebo cohort (unknown cause)
- 4.5% of subjects in the RTB101 10 mg once daily cohort and 7.2% of subjects in the placebo cohort had a serious adverse event, none of which were considered related to study drug
- 4.5% of subjects in the RTB101 10 mg once daily cohort and 6.1% of subjects in the placebo cohort discontinued study drug due to an AE
- All AEs were mild or moderate in severity except for 11 severe AEs in RTB101 10 mg once daily cohort and 22 severe AEs in the placebo cohort

# Summary of 16-week analysis of Phase 2b

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- Study successfully defined the dose and patient populations to include in our pivotal trials:
  - RTB101 10 mg once daily
    - Consistent efficacy seen in two phase 2 trials enrolling more than 900 elderly people
  - 65 years or older with asthma, or 85 years and older, non-smokers
- All doses including RTB101 10 mg once daily were well-tolerated in high-risk elderly patients enrolled in the Phase 2b study
- Plan to meet with regulatory authorities to discuss design of pivotal trials and initiate pivotal trials in 2019

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# Medical Need & Market Opportunity

# RTIs represent a significant healthcare burden

- RTIs are the 4<sup>th</sup> most common cause for hospitalization in 65+<sup>1</sup> (2<sup>nd</sup> in 85+<sup>1</sup>)
- RTIs are the 7<sup>th</sup> leading cause of death in 65+<sup>2</sup> (5<sup>th</sup> in 85+<sup>2</sup>)
- RTIs are the leading cause of asthma exacerbations<sup>3</sup>
- The majority of RTIs are caused by viruses for which there are no approved therapies<sup>4</sup>
- Decreasing the incidence of RTIs in the elderly may significantly decrease health care costs





# 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%)

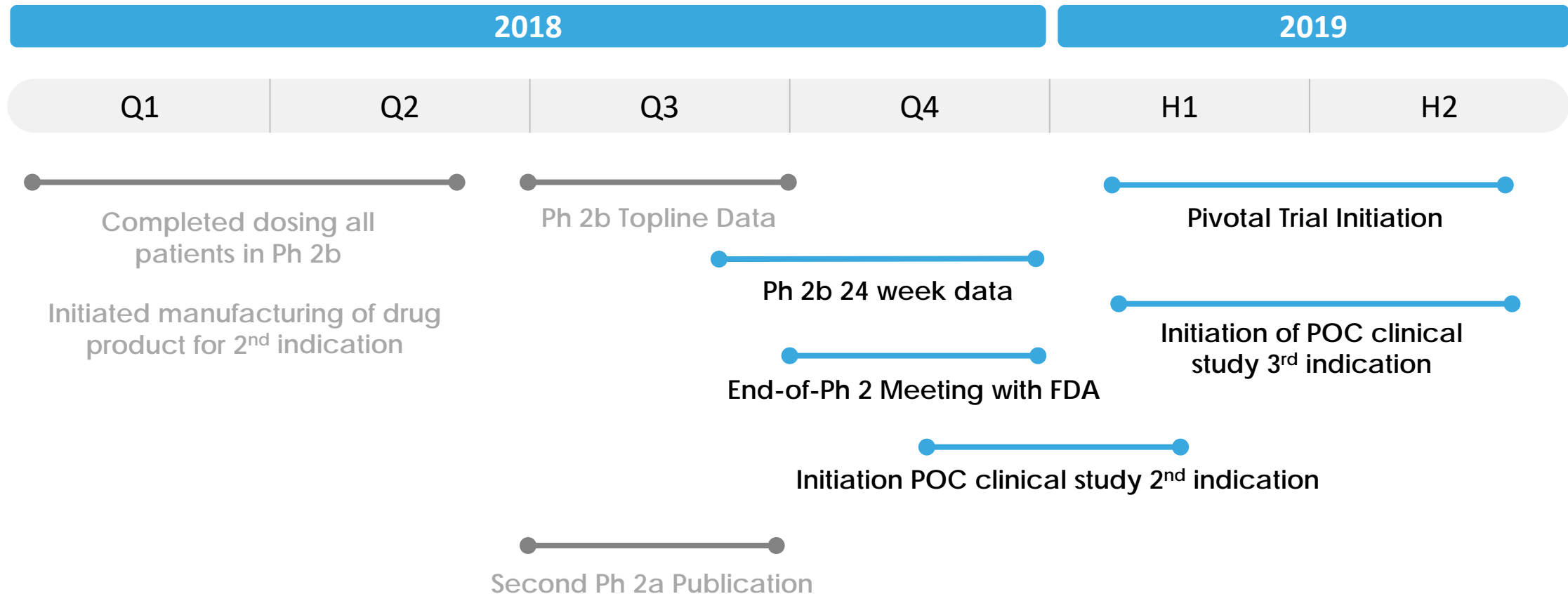
# Broad pipeline targeting aging-related diseases

Program	Indication	Discovery	Preclinical	Phase 1	Phase 2	Phase 3	Anticipated Milestones
TORC1 Program:  RTB101 and RTB101+ Everolimus	Respiratory Tract Infections	[Progress bar: Discovery to end of Phase 2]					
	Other Infections*	[Progress bar: Discovery to end of Phase 1]					
	Heart Failure with Preserved Ejection Fraction	[Progress bar: Discovery to end of Phase 1]					Initiation of at least one Phase 2 trial in 2018**
	Autophagy-Related Diseases	[Progress bar: Discovery to end of Phase 1]					

\* Other infections include those that the elderly are at increased risk of contracting, such as urinary tract infections.

\*\* For heart failure with preserved ejection fraction, autophagy-related neurodegenerative diseases 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.

# Near term planned clinical milestones and path forward



# resTORbio highlights

- **Developing first in class and most advanced selective TORC1 program**
  - TORC1 inhibition improves immune, cardiac and neurologic function in aging preclinical species
  - Proprietary TORC1 inhibitor, RTB101, in clinical development
- **Positive topline results in Phase 2b study of RTRB101 to decrease the incidence of respiratory tract infections (RTIs) in high risk elderly patients**
  - Successfully **identified dose (RTB101 10 mg once daily) and high-responding patient populations** to move forward into pivotal trials
  - All doses of RTB101 observed to be well-tolerated
  - Potential to treat **high unmet need**; RTIs are the 4<sup>th</sup> leading cause for hospitalization in the 65+; 2<sup>nd</sup> in 85+ (US)
- **Data-driven approach to expand into additional indications in 2018**
  - Detecting signals in the Phase 2b trial for two additional aging-related diseases in 2H 2018
  - Initiate at least one Phase 2 trial in an additional indication(s) in Q4 2018/Q1 2019
- **Well financed through 2020 with over \$125 million as of June 30, 2018**

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