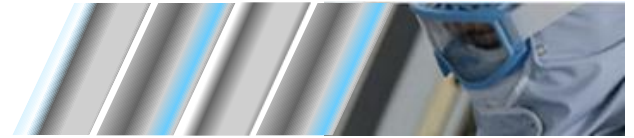


# The RUTI<sup>®</sup> vaccine

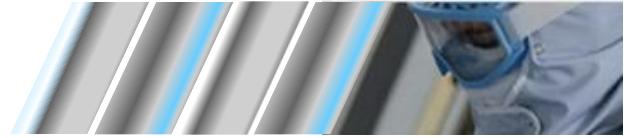


# Caveat



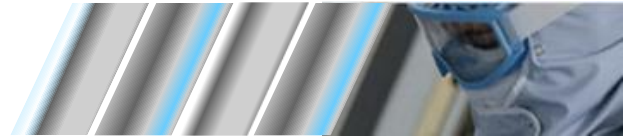
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# Company information

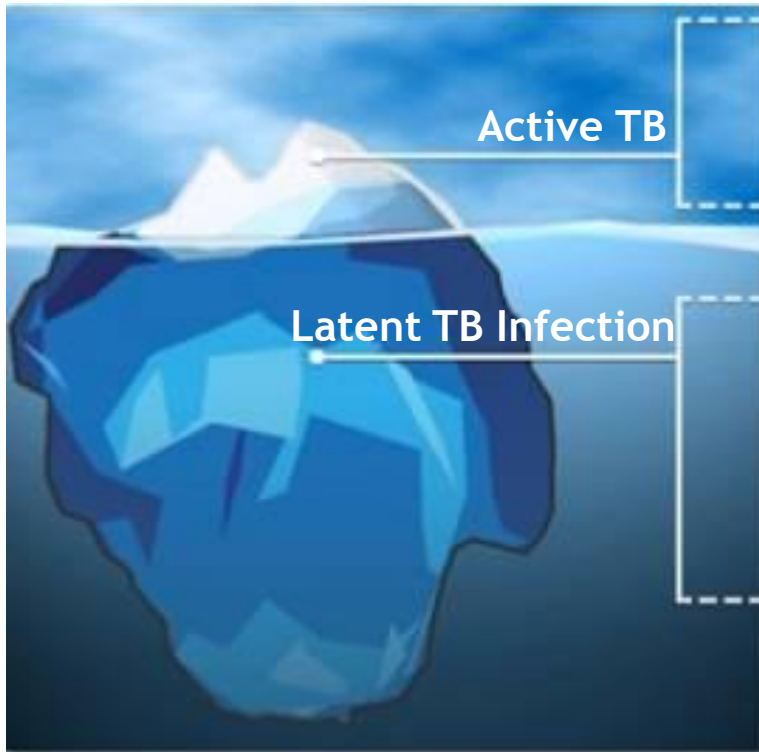


- Private Biopharmaceutical company, created in 2005
- Located in Badalona, at 10 km Barcelona, Catalonia, Spain
- Own production plant + R&D facilities 720 m<sup>2</sup>
- 20 employees

# The unmet need

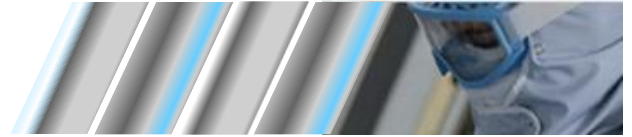


## TB is a major global killer

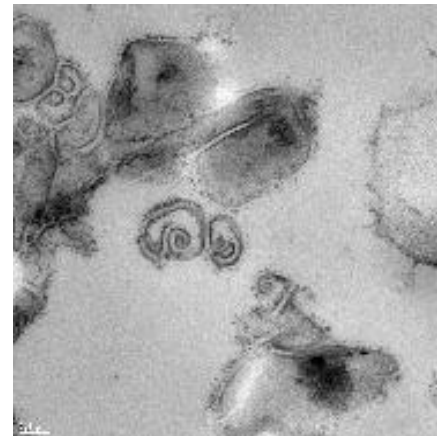
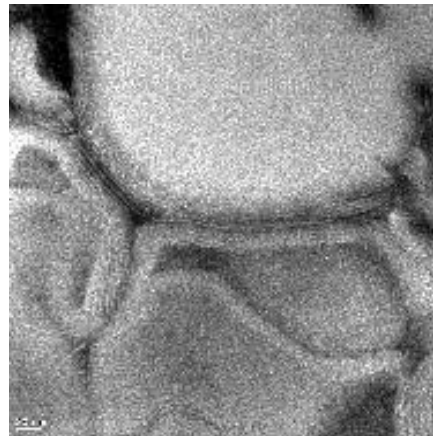


- TB → second cause of death after AIDS
- 9.3 million new cases in 2007
- 1.8 million deaths in 2007 – 1 every 17 seconds
- 1/3 of world population latently infected
- 100 million people infected every year
- Majority of infected people not aware
- 10% will develop active TB during their life

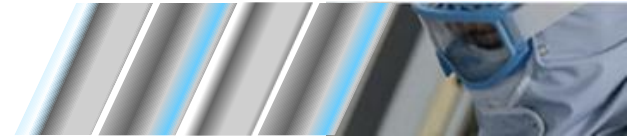
# The RUTI<sup>®</sup> vaccine



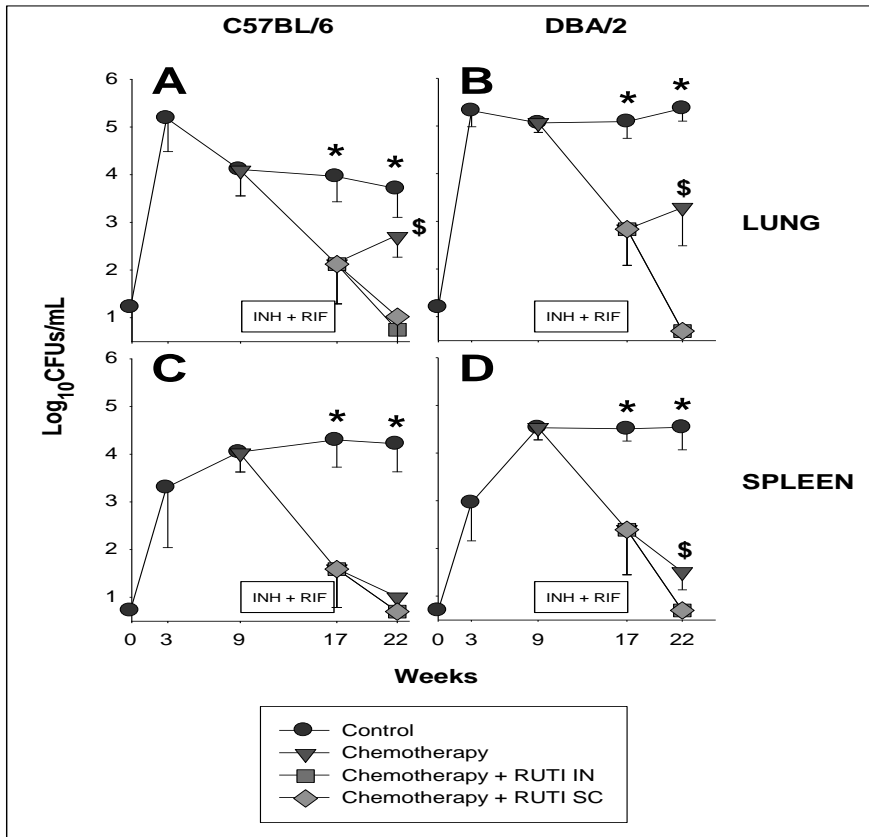
- Discovered at Institut Germans Trias I Pujol , Badalona (“Can Ruti”)
- Made from *M. tuberculosis* grown under anoxic stress
- Non live: fragmented, detoxified and liposomed
- Poly antigenic
- Stable at room temperature



# Preclinical data (I)



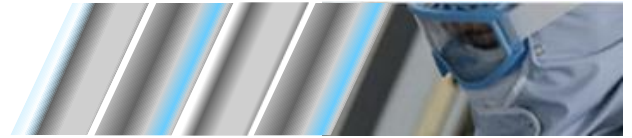
## RUTI<sup>®</sup> acts therapeutically and reduces the need of antibiotic treatment



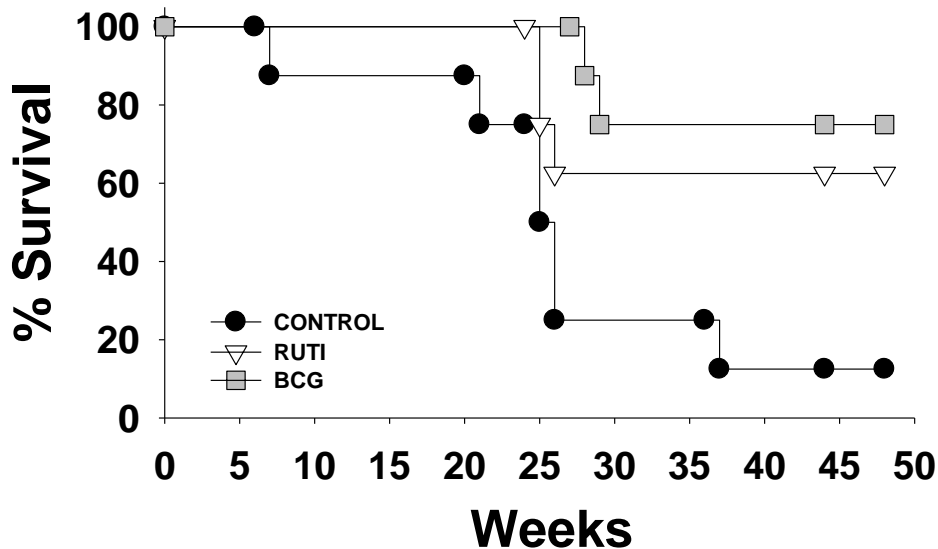
- Mice infected with *M. tuberculosis*
- Treated with antibiotics +/- RUTI
- RUTI potentiates the antibiotic effect
- RUTI acts therapeutically

*Cardona et al; Vaccine 2005*

# Preclinical data (II)



## RUTI<sup>®</sup> has prophylactic potential (immunization PRIOR to low dose challenge)

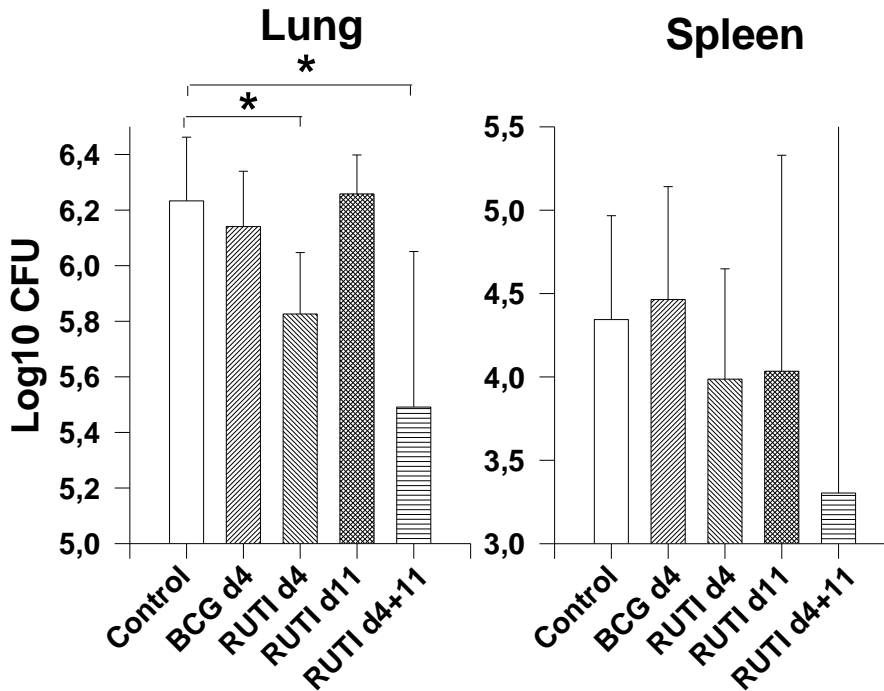


- Guinea pigs
- Vaccination prior to aerosol challenge
- RUTI has prophylactic activity

*Patent application and Vilaplana et al Vaccine Submitted*

# Preclinical data (III)

RUTI<sup>®</sup> has *primary* prophylaxis potential  
(immunization AFTER low dose challenge)



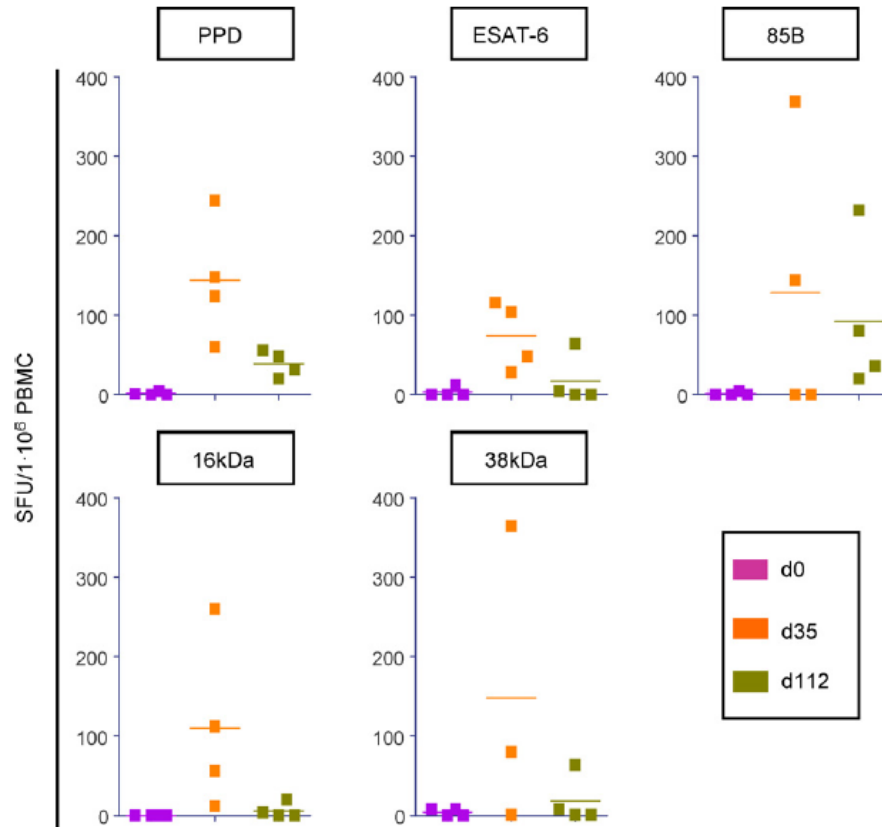
- Mice
- Vaccination after aerosol challenge
- RUTI avoids progression of infection and reduces bacterial load

Patent application and Vilaplana et al Vaccine Submitted

# Clinical data (phase I)

## Phase I trial completed in Spain

C. Vilaplana et al. / Vaccine 28 (2010) 1106–1116



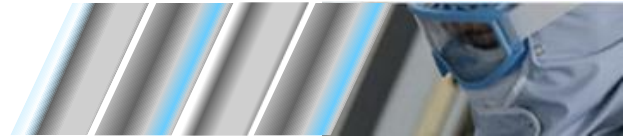
- Three doses tested
- 24 volunteers
- Safe, well tolerated
- Poly-immunogenic

Fig. 4. Cellular immune response (in terms of SFU/1 × 10<sup>6</sup> PBMC) against several *M. tuberculosis* antigens and PPD of volunteers vaccinated with 25 µg of FCMtb. Results of the ELISPOT assay are shown through time, from the baseline value to 1 week after the second inoculation (day 35) and at day 112, almost 5 months after day 0.

# The RUTI<sup>®</sup> 's potential algorithm in TB

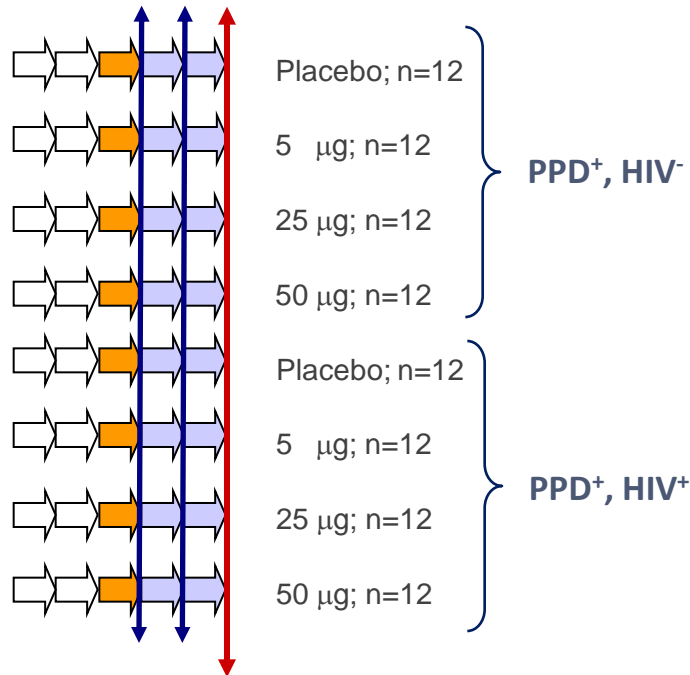
Asymptomatic individuals at risk of developing active tuberculosis	Current treatment	RUTI's potential	Status
LTBI diagnosed /HIV positive	Antibiotic regime, 6 to 9 months	Reduce antibiotic regime to less than 1 month and prevent reinfection	Phase II on-going in South Africa. Phase III to start 2011. Market access 2015
LTBI diagnosed / HIV negative (i.e. TNF alpha therapies candidates)	Antibiotic regime 6 to 9 month before immunosuppressive therapy	Reduce antibiotic regime to less than 1 month and prevent reinfection	Phase II on-going in South Africa. Market access 2018/19
Undiagnosed or non LTBI individuals in close recent contact with an active tuberculosis subject	Antibiotic regime, 3 months until next LTBI test (low active TB prevalence countries)	Prevent antibiotic treatment and development of active or LTBI	Indication not currently pursued. Market access post 2020 or off-label
Undiagnosed individuals who have travelled to active tuberculosis high prevalence areas	None offered (antibiotic regime has relevant side effects)	Prevent development of active or LTBI	Indication not currently pursued. Market access post 2020

# Current clinical development



## Phase II trial, RUTI<sup>®</sup> for the Treatment of LTBI

2 RUTI<sup>®</sup> or Placebo injections (SC)



**No Go/Go and Dose Decision**

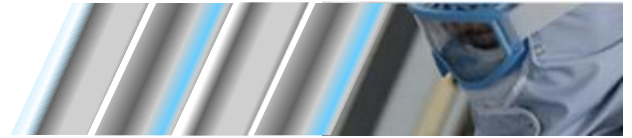
Recruitment   
 Isoniazide   
 Follow up

Each arrow = 1 month

- Recruitment completed
- Trial ends desember 2010
- Draft results available 1Q 2011
- Safety, tolerability , immunogenicity and dose selection for phase III

<http://clinicaltrials.gov/ct2/show/NCT01136161>

# Next step: phase III trial

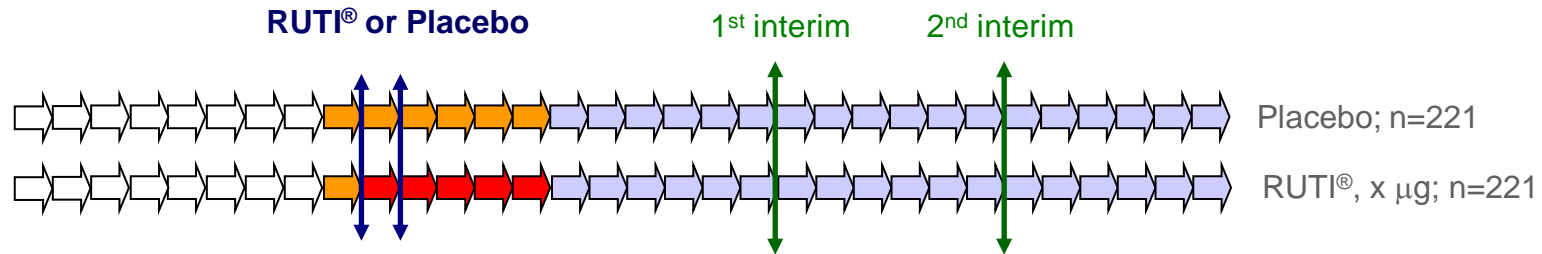


## RUTI<sup>®</sup> for the Treatment of LTBI

### Non-inferiority, Safety, and Efficacy Phase III Trial, 90% Power

- Prospective start 4Q 2011
- PI Prof. Gavin Churchyard, Aurum Institute, South Africa

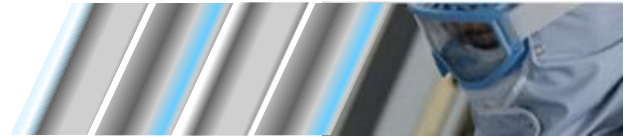
PPD<sup>+</sup>, HIV<sup>+</sup>



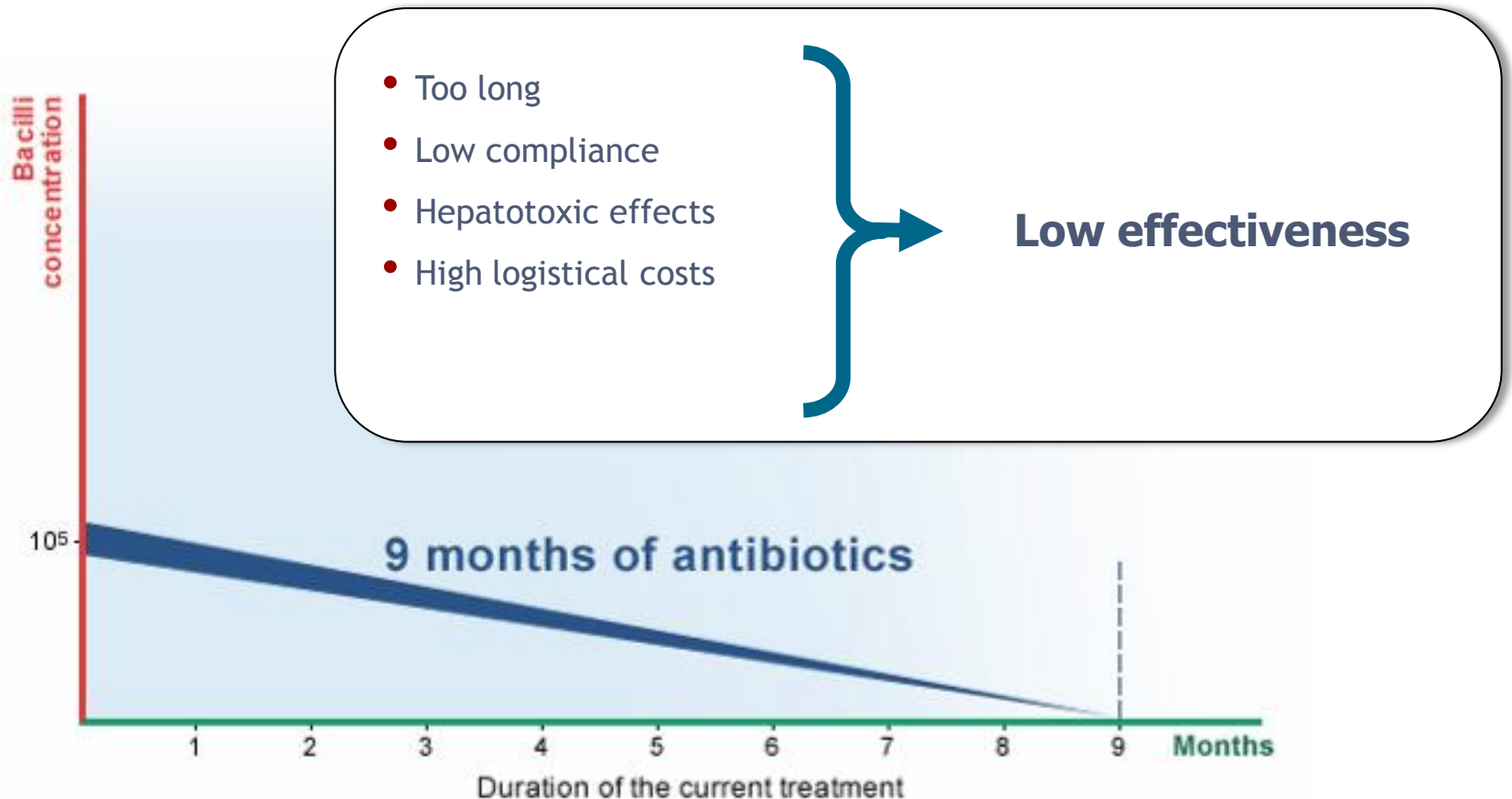
Each arrow = 1 month

⇒ Recruitment    ⇒ Isoniazide    ⇒ Placebo    ⇒ Follow up

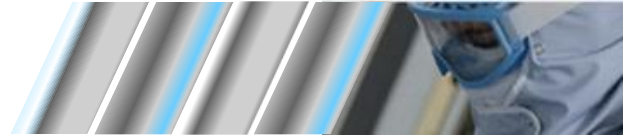
# The business case for LTBI (I)



## Latent TB Infection (LTBI) - Current Treatment



# The business case for LTBI (II)



**RUTI<sup>®</sup> has potential to treat more than 5 million people per year in the LTBI-related indications**

## VIH+ subjects diagnosed with LTBI

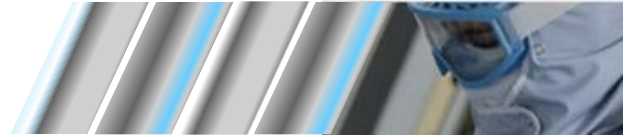
EU5 , Jp and US: 30.000 patients per year

Russia, China, India: 250.000 patients per year

## VIH- Subjects diagnosed with LTBI

EU5, Jp and US: **550.000**

Russia, India, China: 5.000.000



- WO2005/042013 granted in most countries, process, product and therapeutic uses
- WO2008/053055 under accelerated review in EU, national phases worldwide, prophylactic use
- PCT/ES2009/000436, will enter national phases by Q1 2011, primary prophylactic use

# Current development status

- Phase IIa ongoing for LTBI related indication
- Manufacturing Process Development completed, Phase III ready



- Stability tests on going, currently 1 year at room temperature
- IP portfolio under active examination. Seminal product patent granted in most countries. Use patents in prophylaxis and primary prophylaxis actively pursued.