Content

XXVI Encuentro de Cooperación Farma-Biotech

19 de noviembre de 2025

RUTI®, a therapeutic vaccine for multidrug-resistance Tuberculosis

Mercè Amat

INSTITUTION

Archivel Farma is a biopharmaceutical company based in Barcelona, focused on developing innovative immunotherapies. Its lead **product, RUTI®, is a therapeutic vaccine designed to boost immunity against tuberculosis**, currently in clinical phase IIb development for multidrug-resistant TB.

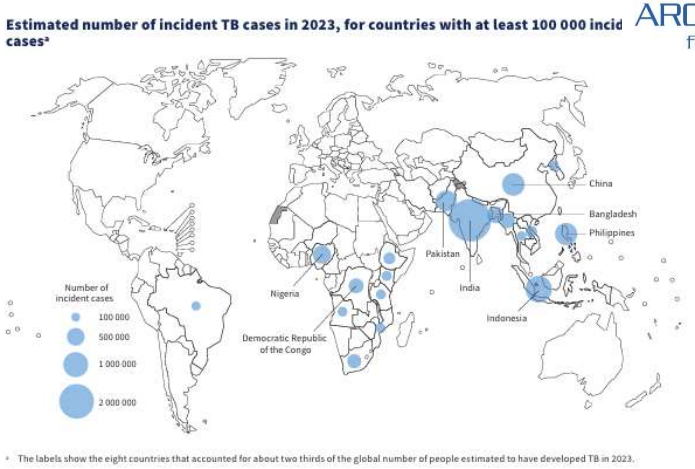
Since 2022 Archivel also operates as a CDMO, specialized in injectable and freeze-dried products. The facilities are engineered to manufacture small-customized clinical batches under GMP pharmaceutical laboratory authorization. Laboratory authorization (4202E).

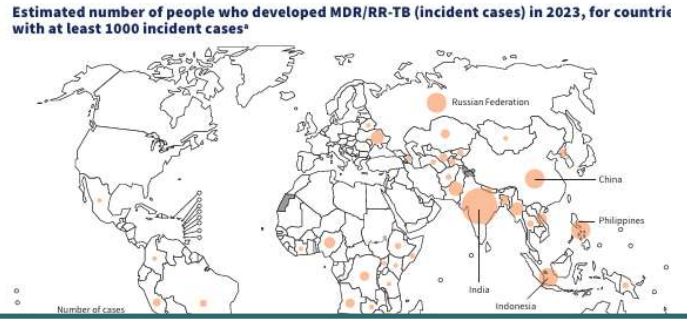
The company funding provides mainly from the **private investors TACTIE group (80%)**, Archivel Technologies and Reig Jofre Lab.

TUBERCULOSIS DATA

According to the WHO Global Tuberculosis Report 2024, an estimated **10.8 million people developed active TB (400,000 DR-TB)** worldwide in 2023, and about 8.2 million were newly diagnosed. More **1,25 millions of deaths per year**

Men (around 60% of cases).
Young adults, 15–45 years
In Low – and Middle- income countries





Standard of Care, antibiotic treatment

Treatment of **drug-sensitive TB** uses a combination of 4 antibiotic for **6 mo**.

Drug-resistant TB requires second-line antibiotics, with treatment **9–20 mo** and greater toxicity.
Shorten oral regimens extending

Why the antibiotic treatment is so long?
Latency (dormant-bacilli)

PRODUCT- RUTI® vaccine

The IMP RUTI® is presented as a **dry powder for reconstitution** with water for injection, and it is **stable at 5ºC at least for 4 years**. RUTI® is a liposomal suspension of the Drug Substance with sucrose as charge excipient.

The RUTI® Drug Substance (DS) consists of purified, heat-inactivated and freeze-dried cell-wall nanofragments from Mycobacterium tuberculosis (RUTI® strain), **which has grown under stress conditions**.

RUTI® is administrated **subcutaneously at 25µg dose**.

Archivel Farma is the manufacturer of Drug Sustance and IMP RUTI®.

PRODUCT- INNOVATIVE MECHANISM OF ACTION

The mechanism of action of the RUTI® it **to boost and refocus the immune-response** inducing (1) a **specific poly-antigenic cell-mediated immune response**, mainly T1, that helps to kill bacilli (replicating and latent) and (2) boost innate immunity through the mechanism of trained immunity.

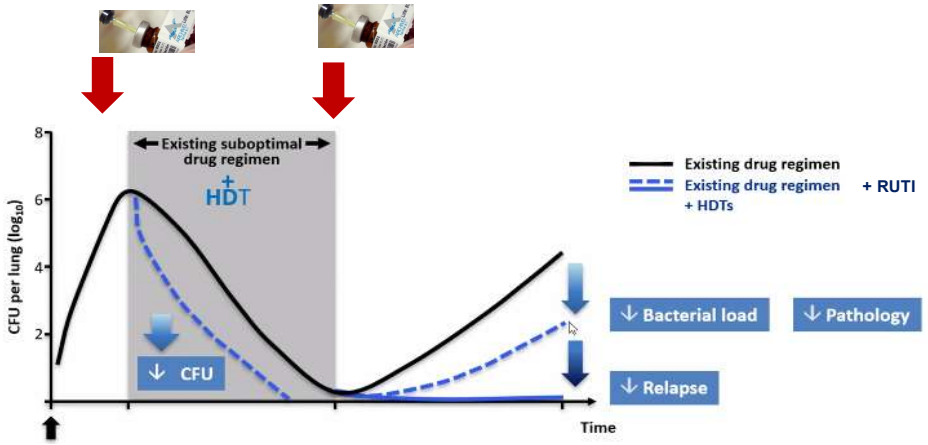
PRODUCT- TARGET INDICATIONS

TUBERCULOSIS

RUTI® is being developed as a **therapeutic vaccine** in combination with Standard of Care (SoC) for **active pulmonary TB,** specifically for **Drug Resistance (DR) –TB patients.**

The main objective is to

- **Shorten and simplify the current SoC**
- **Increasing the cure rate**
- **Reducing the relapse rate**



BLADDER CANCER & COVID-19

PRODUCT- CURRENT STATUS OF DEVELOPMENT, CLINICAL TRIALS – PHASE IIb " PROOF OF CONCL. "

Phase I study in healthy subjects (Vilaplana et al., Vaccine. 2010)
Phase II study in LTBI patients (Nell et al., PlosOne 2014)

CLINICAL TRIALS - RUTI® as a therapeutic vaccine

	Phase IIa	Phase IIb		Phase IIb
Location	Ukraine	India [H2020 Strituvad EU & DBT India]		Argentina
Population	MDR (XDR) -TB	**MDR-TB**	DS-TB	DS-TB
Injection time RUTI®/placebo	Week 16 (After intensive phase)	**Week 4**	Week 1	Day 0
SoC for TB	20-24mo	**18-20mo**	6mo	6mo
Allocation RUTI:Pbo	1:1	**1:1**	1:1	1:1
Size (Recruited/ total)	8/8	**50/50**	90/90	40/44
Outcome	Safety Immunogenicity	**Safety** **Reduction of bacillary load** **immunogenicity**		Early bactericidal activity (EBA) Safety
Status	Immunogenicity pd	**STAT October-2025**	STAT Dec 2023	Finished
Results	Good safety	**Good safety** **Promising SCC effect**	Good safety No significant SCC effect (*)	Good Safety No significant EBA effect (*)

PRODUCT- DIFFERENTIAL FEATURE FACING THE MARKET

RUTI® is a FIRST IN CLASS product

Several vaccines are being developed as a therapeutic vaccine: **H56:IC31 failed** in a Phase 2b trial; **Vaccae**, has limited evidence; and **VPM1002**, BCG recombinant no results since 2023

PRODUCT- CURRENT STATUS OF DEVELOPMENT, CLINICAL TRIALS

SAFETY AND TOLERABILITY

Overall, total of 578 individuals have been enrolled in the RUTI® clinical programme, of which approximately **356 adults (healthy volunteers, LTBI, TB, NMIBC, COVID) have received RUTI® in Spain, South Africa, Ukraine, Argentina, and India** to date.

RUTI® was **safe and well tolerated** and triggered a specific and immunogenic response against multiples Mtb antigens.

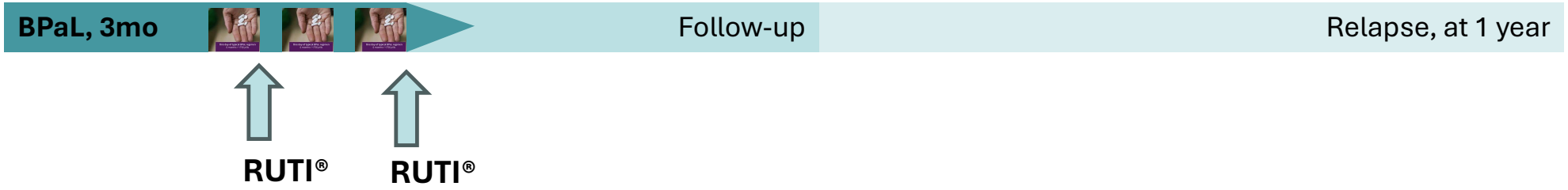
PRODUCT- CURRENT STATUS OF DEVELOPMENT – NEXT STEPS

Next CLINICAL TRIAL (Non-inferiority)

The aim is to evaluate whether combining a shortened antibiotic regimen (six to three months) with vaccination is effective, reducing toxicity, infectious duration, and relapse rate.

Placebo

Intervention



PRODUCT- IPR PROTECTION

Patente CODE	TITLE	Expiration expected	GRANTED
WO2005042013 PCT/ES2004/000482	IMMUNOTHERAPEUTIC AGENT WHICH IS USED FOR COMBINED TREATMENT OF TUBERCULOSIS TOGHETHER WITH OTHER PHARMACEUTICALS	29/10/2024 EXPIRED	EXPIRED
ES2393007 PCT/ES2007/000583	**PROPHILACTIC TUBERCULOSIS VACCINE**	**17/17/2027**	**Brazil, China, Russian Federation, and United States of America**
WO 2010031883 PCT/ES2009/000436	**IMMUNOTHERAPEUTIC AGENT SUITABLE FOR THE PRIMARY PROPHYLAXIS OF TUBERCULOSIS**	**03/09/2029**	**China, Russian Federation and United States of America.**
WO 2012093137 PCT/EP2012/050080	**LIPOSOME FORMULATION SUITABLE FOR TREATING OR PREVENTING TUBERCULOSIS**	**04/01/2032**	**Brazil, Canada, India, Israel, Belgium, Bulgaria, Czech Republic, Germany, Estonia, Spain, France, United Kingdom, Hungary, Lithuania, Latvia, Italy, Slovakia, Turkey, Poland, Romania, Slovenia, Japan, Korea, Mexico, Russian Federation, South Africa, Vietnam, United States of America, United States of America. Rejected: China divisional**
WO2023/062066A1 PCT/EP2022/078375	**LIPOSOME FORMULATIONS FOR TREATMENT OF ACTIVE TUBERCULOSIS**	**14/10/2041**	**It entered in national phase (April 2025) in Brazil, EPO, Eurasia, South Africa, US, China, India, Indonesia, Mexico).**
WO PCT/EP2025/057265	LIPOSOME FORMULATIONS FOR THE TREATMENT OF CANCER	15/03/2044	It will be entered in national phase in Sept-Oct 2026

PRODUCT- PITFALLS RISC TO BE CONSIDERED

- **Manufacturing challenges**

Drug Substance scale up to 100.000 doses of IMP.

RUTI® Stability , up to 4 years at 5ºC.

Medium-cost manufacturing process

- **Safety concerns**

The RUTI® vaccine is **highly safe and well –tolerated** (356 patients administered).

- **Efficacy**

The RUTI® vaccine **reduced the bacillary load and improved clinical symptoms** in MDR-TB population

- **Intellectual property.**

Strong patent portfolios in the relevant jurisdictions

- **Eligible population**:

400,000 MDR-TB cases, with strategic priority given to high-burden regions

- **First in class product. Non-TB therapeutic vaccines on the market** (VP-1002 under development)

PARTNERING OPPORTUNITIES

We are seeking a **licensee or strategic partnerships** with pharmaceutical companies and/or investors to advance the clinical development of the RUTI® vaccine and accelerate its market entry, aiming to improve the treatment of TB, the world's leading infectious disease.

THANK YOU VERY MUCH FOR YOUR ATTENTION

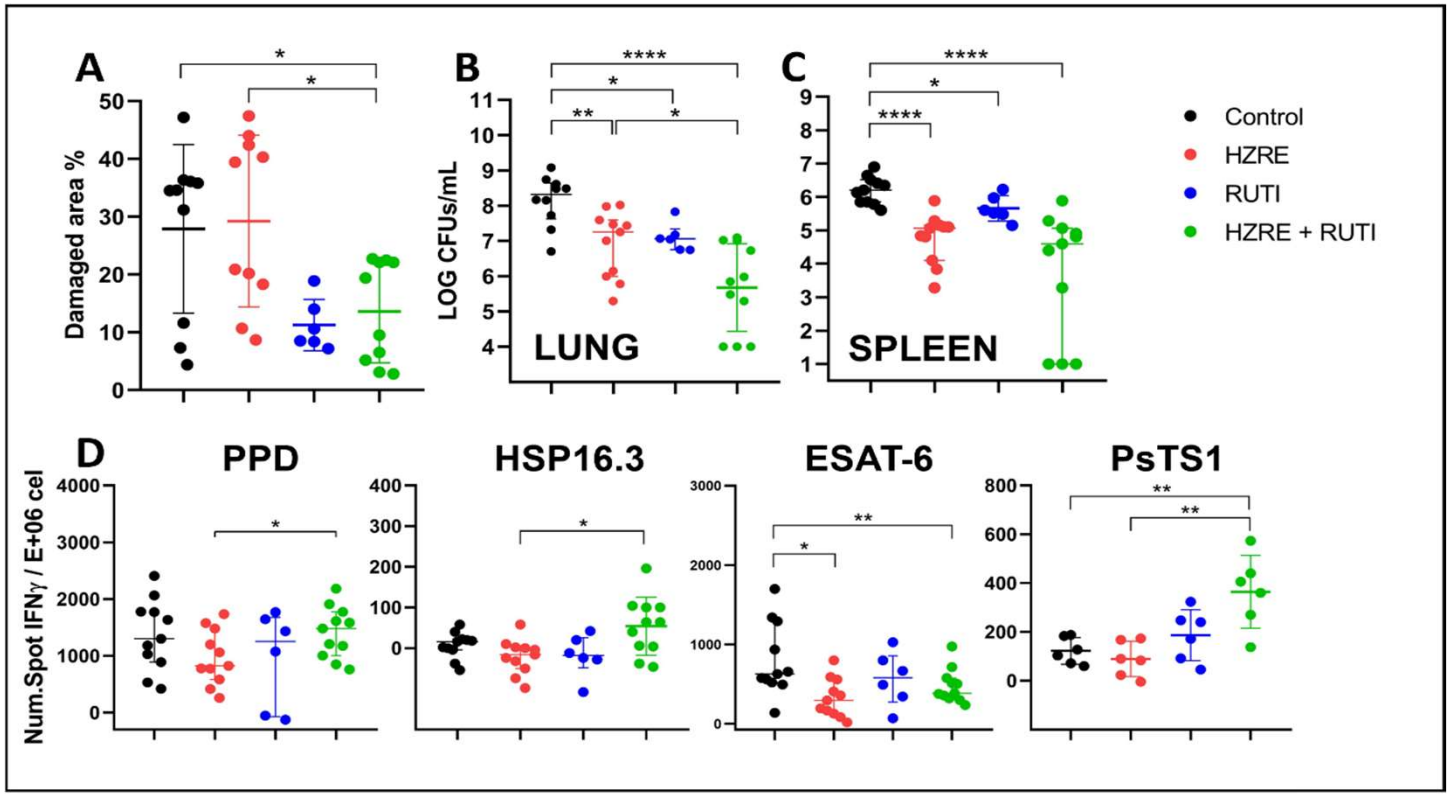
https://archivelfarma.com

merce.amat@archivelfarma.com

TREATMENTS COST

Country / Region	Type of TB	Average cost per patient	Notes
Global (122 countries, WHO 2020)	DS- TB	**$ 1,245**	Direct treatment cost for health systems
Global (122 countries, WHO 2020)	MDR/RR-TB	**$ 3,868**	Higher due to longer treatment and expensive drugs
Europe (18 EU countries)	DS- TB	**€ 7,848**	Total medical costs including hospitalization
Europe (18 EU countries)	MDR-TB	**€ 54,779**	Much higher due to prolonged care
Europe (18 EU countries)	XDR-TB	**€ 168,310**	Extremely high due to extensive drug resistance

NON CLINICAL DATA: TB model in C3H



The administration of RUTI® **at time 0** after the start of antibiotic treatment caused a **reduction in the bacillary load of -1.5 LOG**, together with **a very significant reduction of the damage area** in **the lung**.

Results showed a statistically significant increase of the Th1 response against HSP16.3 antigen, PsTS1 and for PPD.

Top 15 causes of death worldwide in 2021[a,b]

Deaths from TB among people with HIV are shown in grey.