From Accessible Diagnosis to Treatment Continuity

REBUILD MEDICINE ARTICLE

Tuberculosis (TB) remains one of the most persistent challenges in global public health. It rarely makes global headlines, yet it continues to claim lives in mining settlements, urban peripheries, and communities where diagnostic infrastructure is scarce and treatment is long, toxic, and difficult to complete. Rebuild Medicine's work over the past year has been built on a simple premise that is too often overlooked: detection and care only matter if they actually reach the people who need them.

That premise took concrete shape in Oruro, Bolivia, a region where TB and its multidrug-resistant variants (MDR-TB) hit mining and peri-urban populations especially hard — communities long overlooked by conventional health systems.

An Access Problem, Not Just a Scientific One

Before turning to results, it is worth understanding the starting point. Molecular diagnosis of tuberculosis — the fastest and most accurate way to detect the disease — depends heavily on technologies such as GeneXpert, the standard endorsed by the World Health Organization. The problem is that these machines require infrastructure, maintenance, and logistics chains that many regions of the world simply do not have. In the department of Oruro, for instance, only one in every 50 laboratories had a GeneXpert unit at the time of this study; the rest relied almost entirely on conventional smear microscopy, a far less sensitive method that misses a significant share of real cases — and one that is also unsafe for the laboratory technician or operator, since manual sample handling generates infectious aerosols without the biosafety controls that molecular platforms are designed to avoid.

This gap is not a technical footnote — it is the difference between a timely diagnosis and months of silent transmission within a community. Closing that gap was the starting point for the work carried out by the Rebuild Medicine team together with the Universidad Técnica de Oruro (UTO) and the Oruro Tuberculosis Network.

Orange G3 TBC: How the Platform Works

The centerpiece of this first year of work was the validation of Orange G3 TBC, a molecular assay developed to detect *Mycobacterium tuberculosis* DNA in clinical samples, with an operational design built specifically for low-resource settings.

The process begins with liquefaction of the sample inside a sealed container. It then undergoes heat inactivation — the sample is heated to roughly 88 °C — which kills any viable bacteria before DNA extraction, a key safety step for the operator. Purification relies on a closed circuit of

syringes, filters, and absorbents, and amplification takes place in a sealed tube inside an end-point thermocycler-fluorometer, reducing the risk of cross-contamination between samples. Results are reported as detectable, non-detectable, or indeterminate, depending on bacillary load.

Perhaps the platform's most decisive feature is that it does not require a laminar-flow hood. That single characteristic changes what is possible: it opens the door for laboratories that could never host a GeneXpert unit — due to cost, space, or unreliable electrical infrastructure — to offer molecular diagnosis. In the Oruro study, a team with just two days of training was able to operate the platform and produce consistent results.

The Results: Rigorous Science, Real-World Impact

In 2025, the team led by Dr. Juan Carlos Garberi and researcher and logistics coordinator Gabriel Alejandro Estryk, together with their institutional partners, published a head-to-head comparison of Orange G3 TBC against GeneXpert Ultra in the scientific journal *Therapeutic Advances in Infectious Disease*.

The study analyzed 71 clinical specimens — 67 sputum samples and 4 cerebrospinal fluid samples — from patients with presumptive TB seen at rural and inter-urban centers in Oruro. The results were as follows:

- Sensitivity of 90% and specificity of 97%.
- Diagnostic efficiency of 94% to 96%.
- Negative predictive value of 98% and positive predictive value of 82%.
- High agreement with GeneXpert Ultra, with a Pearson correlation coefficient of 0.834 and a Kappa index of 0.832.

Of the total samples, nine positive and 59 negative results were concordant between the two platforms; only two samples were positive exclusively on Orange G3, and one exclusively on GeneXpert.

> *These numbers point to something beyond statistics: a Latin American technology, low in cost and requiring no complex infrastructure, can approach the performance of one of the world's most sophisticated and trusted diagnostic tools.*

For the mining and peri-urban communities of Oruro — far from the few laboratories equipped with advanced molecular technology — this means access to fast, biosafe diagnosis without depending on complex logistics chains or travel that many patients simply cannot afford.

Why Bolivia, and Why This Model of Cooperation

Carrying out a project of this scale in Bolivia was not a matter of chance. It responded both to the country's epidemiological urgency and to the opportunity to build scientific sovereignty from the Global South. Developing the project under a framework of interinstitutional and interdisciplinary cooperation — with the Universidad Técnica de Oruro (UTO) at its center, alongside the Departmental Health Service (SEDES Oruro), the Oruro Tuberculosis Network, Clínica del Sur (La Paz), and Rebuild Medicine Foundation — established a model still uncommon in the region: science built from the affected territory itself, with local governance and international standards of rigor.

That model, more than any single result, may be the project's most lasting contribution. It shows that high-level biotechnological innovation does not have to be imported from abroad. It can be designed, validated, and sustained by a country's own institutions — with its own regulatory authority and local bioethics oversight, as is the case with Bolivia.

From Oruro to the International Stage

The impact of these results did not go unnoticed. The combination of results published in a respected scientific journal, institutional backing from an autonomous university like UTO, and a reproducible approach for low-resource settings generated growing interest in international scientific circles.

Today the team is receiving invitations to present this work at conferences and scientific meetings in different parts of the world, carrying the Bolivian experience forward as a case study in decentralized diagnostic innovation. Beyond the institutional recognition they represent, these invitations reflect something more important: genuine interest in an approach developed and evaluated in a real Global South setting, designed from the outset for the communities that conventional science too often leaves behind.

The Next Frontier: When Treatment Itself Becomes the Obstacle

Timely diagnosis is only the first link in the chain. The real bottleneck in the fight against multidrug-resistant tuberculosis is not always a lack of drugs — it is something less visible, and just as deadly: the severe toxic and physical side effects of conventional treatment regimens.

MDR-TB regimens can last for months, combining drugs that cause liver toxicity, hearing damage, gastrointestinal disorders, and other effects that progressively erode a patient's adherence. When a patient stops treatment, they do not only lose their own chance at a cure — they help perpetuate transmission within the community and worsen pathogen resistance, feeding a cycle that hits lower-resource populations hardest.

With that concern as its starting point, and under the same framework of interinstitutional cooperation that made the diagnostic breakthrough possible, the team has begun an ambitious

new phase of preclinical research — strictly *in vitro* — carried out under tightly controlled protocols and with oversight from institutional bioethics and biosafety committees, inside biological containment laboratories.

The work involves evaluating the bactericidal activity of a set of candidate low-cost agents and strategies, in aqueous suspension, directly against viable strains of *Mycobacterium tuberculosis*, including a panel of multidrug-resistant clinical isolates. This exploratory phase has two goals:

1. To identify low-cost alternatives with activity against *M. tuberculosis* strains, including drug-resistant variants, that can be sustained in settings with limited infrastructure.
2. To generate serious scientific evidence on options that, should they successfully pass through the corresponding preclinical stages, could help reduce toxicity and improve treatment tolerability — helping patients complete their regimens instead of abandoning them partway through.

This point deserves the same honesty applied to communicating the diagnostic results: this is early-stage laboratory research with no immediate clinical implications. No finding from this stage, on its own, authorizes any use in patients. Each candidate evaluated must move, step by step, through the validation stages that responsible science requires — further *in vitro* studies, preclinical models, and eventually regulated clinical trials — before any therapeutic application can even be considered.

It is precisely this rigor — combined with the biological containment infrastructure of the Oruro Tuberculosis Network and UTO — that allows the team to move forward with confidence on a problem that, until now, received far less attention than diagnosis: treatment dropout caused by the adverse effects of available drugs.

Why This Matters for the Global South

Connecting accessible diagnosis with research into better treatment conditions is the logic underpinning the entire project, and the core premise of Rebuild Medicine: useful science does not just detect disease — it also works to make sure treatment actually reaches patients, and that they can sustain it through to completion.

Through UTO and its partners, Bolivia positions itself not as a passive recipient of innovation imported from elsewhere, but as an active generator of scientific knowledge capable of scaling to other regions facing similar challenges — mining communities, isolated rural areas, and urban peripheries across Latin America and the wider Global South, all confronting the same combination of high disease burden and limited access to diagnostic technology.

Looking Ahead

One year into this work, the balance is clear: a scientifically validated, internationally recognized diagnostic tool already expanding into new settings, and a new line of research tackling the problem that comes after diagnosis — making treatment something patients can actually complete.

None of this progress would have been possible without the sustained commitment of our sponsors at Rebuild Medicine, whose support allows this model of sovereign, transparent science — oriented toward saving lives where they are needed most — to keep moving forward, one step at a time.