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MAY 12, 2026

THE CONTROLLER OF PATENT
THE PATENT OFFICE
DELHI

KIND ATTN.: DR. SUNIL KUMAR GAUTAM
DEPUTY CONTROLLER OF PATENTS & DESIGNS

Re: REPRESENTATION U/S 25(1) OF THE PATENTS ACT – BY THE DELHI NETWORK OF POSITIVE PEOPLE AGAINST INDIAN PATENT APPLICATION NO. 201817014361 DATED 16/04/2018
APPLICANT: THE GLOBAL ALLIANCE FOR TB DRUG DEVELOPMENT INC.
R&A REF. NO. OPP0370

Respected Sir,

In response to the reply statement and evidence filed by the Applicant on 07th April, 2025 in the above-mentioned Pre-grant Opposition, the Opponent hereby submits the rejoinder.

We request the Learned Controller to take said documents on record and keep the Opponent apprised of further developments in the matter.

Thanking you,

Yours faithfully,

MARIAM SADAF (IN /PA – 5231)
OF RAJESHWARI & ASSOCIATES
AGENT FOR THE OPPONENT

Encl.: As stated

C.C.: S. MAJUMDAR & CO.
EMAIL.: CAL@PATENTINDIA.COM;

BEFORE THE CONTROLER OF PATENTS, THE PATENT OFFICE, NEW DELHI

IN THE MATTER OF:

The Patents Act, 1970 as amended by the Patents (Amendment) Act 2005, and The Patents Rules, 2003, as amended by The Patents (Amendment) Rules, 2006

AND

IN THE MATTER of Pre-grant opposition under Section 25(1)

AND

IN THE MATTER of Indian Application No. 201817014361

IN THE MATTER OF:

THE DELHI NETWORK OF POSITIVE PEOPLE ….. OPPONENT

VS.

THE GLOBAL ALLIANCE FOR TB DRUG DEVELOPMENT INC. .....APPLICANT

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Dated this 12th day of May, 2025

MARIAM SADAF (IN /PA – 5231)
OF RAJESHWARI AND ASSOCIATES
AGENT FOR THE OPPONENT

TO,
THE CONTROLLER OF PATENTS
THE PATENT OFFICE
DELHI, MUMBAI, KOLKATA, CHENNAI

BEFORE THE OFFICE OF THE CONTROLLER OF PATENTS,

DELHI

IN THE MATTER OF:

The Patents Act, 1970 as amended by the Patents (Amendment) Act 2005, and The Patents Rules, 2003, as amended by The Patents (Amendment) Rules, 2016

AND

IN THE MATTER OF:

Indian Patent Application 201817014361 filed by THE GLOBAL ALIANCE FOR TB DRUG DEVELOPMENT INC.

AND

IN THE MATTER OF:

THE GLOBAL ALIANCE FOR TB DRUG DEVELOPMENT INC. ……. **APPLICANT**

VS

DELHI NETWORK OF POSITIVE PEOPLE ……..**OPPONENT**

REJOINDER TO THE REPLY STATEMENT ON THE BEHALF OF THE OPPONENT

We, Delhi Network of Positive People, hereinafter referred to as "Opponent", submit our rejoinder to the reply statement filed by the applicant against the pre-grant opposition under section 25(1) as under:

The Opponent submits hereunder: -

At the outset, each and every averment, allegation, contention made in the Reply Statement is false, baseless and hereby denied. Nothing in the Reply Statement shall be construed as being admitted unless specifically admitted herein by the Opponent. The Opponent denies each and every averment as set out in the Reply Statement to the opposition unless specifically admitted

herein. It is reiterated that the application 201817014361 is not patentable and all averments made in the opposition are reiterated herein.

The Opponent's response and submissions in detail are as under:

1. The averments made by the Applicant in para 1 relate to the alleged research and development activities of the Applicant in relation to newer drugs for tuberculosis. The Opponent has no knowledge of this, and as such, the Applicant is put to strict proof of the same.

2. In para 2, the Applicant acknowledges the Opponent's filing of representation by way of opposition under section 25(1). The Opponent strongly contests the Applicant's statement that they have understood the documents filed and relied upon by the Opponent.

3. The averments made by the Applicant in para 3 entitled "Preliminary Observations" are completely baseless and without merit. The Applicant avers, without a shred of evidence, that the present opposition has been filed to delay grant of the impugned patent application. In the name of evidence, the Applicant points to the chronology of events related to the application. Specifically, the Applicant alleges that the Opponent waited for the response to the FER to be filed in order to file the opposition and consequently delay the application. The Opponent respectfully submits that the Applicant cannot read intent into the timing of filing of the opposition, as nothing in the Act disallows the same using such chronology. The Applicant is simply making assumptions without evidence to back them up.

4. The averments made by the Applicant in para 4 entitled "The Patent Application" relate to bibliographic details of the impugned patent application. These are not denied insofar as these are matters of record.

5. The averments made by the Applicant in para 5 relate to details of the pre-grant oppositions filed against the impugned patent application. With regard to the opposition filed by the present Opponent (Delhi Network of Positive People), it is pointed out that, even though said opposition was filed on 28 July 2020, the Applicant filed their reply statement on 07 April 2025, almost five years later. This is pertinent because the

Applicant had been copied in the email communication as part of filing the opposition. The pre-grant opposition had been filed in 2020, well before the current amended Rule 55(3) came into the picture. Thus, the Applicant themselves chose to delay filing the reply statement, while accusing the Opponent of delaying the processing of the application.

6. The averments made by the Applicant in para 6 are denied. The Applicant contends that the invention "*...relates to chemically stable combinations of anti-bacterial agents, in a short-course oral dosage regimen for the treatment of multidrug-resistant (MTDR) tuberculosis*." It is submitted that the specification does not include even a single example of an actual composition, let alone a chemically stable one. There is no data at all demonstrating stability of any kind the specification. In fact, it only includes mere statements to this effect.

7. The averments made by the Applicant in para 7 relate to the certain drugs and their combinations, which have previously been used in treatment of tuberculosis, along with problems concerning their toxicity, tolerability and long duration of treatment. Further, certain drug combinations, proven to be promising are enlisted, including BDQ+PMD+SZD. The Applicant acknowledges that the combination of SZD+PMD+BDQ produces a greater sterilizing activity than any dual combinations of its components. It is submitted that this is significant because it teaches the utility of a triple combination of an oxazolidinone (class of antibacterials) in combination with bedaquiline (BDQ) and pretomanid (PMD) in combating TB, with the oxazolidinone contributing important activity.

8. In para 8, the Applicant acknowledges that the utility of linezolid (despite being the only marketed oxazolidinone antibiotic) has been marred by dose- and duration-dependent toxicity. However, the Applicant did not mention here that the manner in which this toxicity was dealt with by the inventors, was by stopping administration of linezolid for one to two weeks as shown below

> The inventors further discovered that linezolid can be re-administered at a lower dose after a one to two week interruption (e.g., drug or treatment holiday) based on neuropathy findings and subsequent improvement or, similarly, hematology findings. Clinical doses for pretomanid can be 200 mg qd or 100 mg qd. For bedaquiline, clinical doses can be 400 mg qd for two weeks followed by 200 mg tiw or 200 mg qd. And clinical doses for linezolid are 600 mg bid or 1200 mg qd to start.

9. The averments made by the Applicant in para 9 relate to the rationale (as disclosed in the specification), for the development of the regimen BDQ+PMD+LZD. Page 4 of the specification, quoted by the Applicant, discloses two important observations
    - The additive sterilizing activity of LZD (to BDQ and PMD) is indistinguishable from that of SZD, as seen in Example 1
    - LZD did not appear as effective as SZD, as seen from example 3 where bacterial burden and dose of PMD were higher
    - The impact of substituting LZD for SZD in terms of duration needed to cure mice is small.

10. Thus, the averments in para 9 actually strongly suggest that LZD and SZD in a triple-drug combination produce anti-TB activity indistinguishable from one another, and are substitutable.

11. The averments made by the Applicant in para 10 relate to the purported development of the invention claimed in the impugned application. The Applicant has quoted portions of the specification dealing with the impact of dose and duration (of LZD) on TB treatment. It can be seen that the specification and the pending claims are divergent in important respects as discussed below
    - The example 2 referenced herein shows the effect of addition of LZD to BDQ+PZA+PMD. However, PZA is not an essential element of the invention. It is optional (as per pending claims). This means that the invention ought to work without PZA.
    - It was observed that LZD, at a certain does (600 mg) produced myelotoxicity and neuropathy. The inventors sought to work around this problem by contemplating reducing the dose and duration of LZD.
    - Significantly, "*In the absence of PZA, reducing the LZD dose to 50 mg/kg, which produces a mean $AUC_{0\text{-}24h}$ equivalent to a 600 mg daily dose in humans, reduced*

the bactericidal activity over the first month of treatment" meaning that without PZA the regimen had reduced activity against the TB bacteria.

- Reducing dose (of LZD) from 100 mg/kg to 50 mg/kg did not affect antiTB activity as in both cases small colony-forming units (CFU) were recovered at both doses.
- Applicant further quotes the specification, which says *"These results suggest that use of LZD 600 mg once daily for the first 1-2 months of treatment and/or front-loading therapy with higher doses for even shorter periods may enable LZD to contribute important bactericidal and sterilizing activity before the onset of potentially irreversible neuropathy develops"*
- The reply statement goes on to conclude, from the above, that "*the present invention provides dose of LZD less than 1000 mg; preferably 600mg once daily for 1-2 months in combination with BDQ+PMD, which combination is in form of a composition*"
- The Opponent submits that, the above statement is another example of the lack of sync between pending claims and specification. Claim 1 includes a dose of LZD upto 1 g (1000 mg), which directly contradicts the Applicant's statement above, of the invention providing LZD less than 1000 mg.
- Secondly, the above discussion (and quotes) was in relation to a regimen that includes PZA. However, the Applicant has extrapolated from a regimen of BDQ+PMD+PZA+LZD to BDQ+PMD+LZD
- The claims to composition are undermined by the Applicant's admission that interrupting Linezolid for e period of 1 to 2 weeks is the way to deal with toxicity

12. The averments made by the Applicant in para 11 relate to discussing the composition, as disclosed in the specification. Para 11 once again reveal that the invention (as claimed) and the rest of the specification (including treatment strategy) are not in sync with one another. While the specification states that the claimed combination may be formulated in a unit dosage formulation, the same specification recommends removing LZD (for a certain period) from the treatment regimen as shown below:

Summary of the Invention

Provided is a pharmaceutical composition, comprising a therapeutically effective amount of each of linezolid, bedaquiline and pretomanid, and optionally pyrazinamide, or a pharmaceutically acceptable salt of each thereof, and a pharmaceutically acceptable carrier.

Also provided is a method for the treatment of tuberculosis, comprising the step of administering to a patient in need thereof a therapeutically effective amount of each of linezolid, bedaquiline and pretomanid, and optionally pyrazinamide, or a pharmaceutically acceptable salt of each thereof, and a pharmaceutically acceptable carrier. In one embodiment of the invention, linezolid is removed from the treatment regimen after one to two months. In another embodiment, linezolid can be re-administered after a one to two week drug holiday.

The inventors further discovered that linezolid can be re-administered at a lower dose after a one to two week interruption (e.g., drug or treatment holiday) based on neuropathy findings and subsequent improvement or, similarly, hematology findings. Clinical doses for pretomanid can be 200 mg qd or 100 mg qd. For bedaquiline, clinical doses can be 400 mg qd for two weeks followed by 200 mg tiw or 200 mg qd. And clinical doses for linezolid are 600 mg bid or 1200 mg qd to start.

13. The question of how a singular component (from a three-drug unitary composition) can be removed (as suggested in the above portion of the spec.) has not been explained by the Applicant.

14. The averments made by the Applicant in paragraphs 12-15 relate to voluntary amendments to the claims carried out by the Applicant. Insofar as these are matters of record, they do not merit a reply.

15. The averments made by the Applicant in paragraphs 16-17 are denied.

16. With regard to the averments made by the Applicant in para 18, it is submitted that the Opponent is a valid and well-known entity, and capable of providing proof of the same at any time.

17. The averments made by the Applicant in para 19 does not merit any reply.

18. The averments made by the Applicant in para 20 are denied. All grounds pled by the Opponent apply to the claimed invention, as demonstrated in the following paragraphs.

19. The averments made by the Applicant in para 21 does not merit any reply.

20. In para 22, the Applicant acknowledges the background on tuberculosis and its treatment (which constitutes state-of-the-art at the application's priority date). The same does not warrant a reply.

21. The averments made by the Applicant in para 23 relate to the prior art cited by the Opponent. It is submitted that the Applicant's averments in this regard are untrue and hence, denied. Under settled patent jurisprudence, prior art documents are the evidentiary foundation for grounds such as lack of novelty and inventive step. It would be legally incorrect to suggest that prior art can only be considered if each document is separately labelled under a ground in every paragraph. Once the statutory grounds are invoked, the supporting prior art is properly on record and must be examined on merits.

22. Furthermore, Section 25(1) does not require hyper-technical pleadings. A pre-grant opposition is a public interest proceeding. The Controller is duty-bound to examine whether the claimed invention satisfies the statutory requirements in light of the materials placed on record. The Applicant cannot seek to exclude relevant prior art merely by alleging absence of "pleadings to the ground," especially when the grounds are clearly invoked in the Notice of Opposition itself

23. The averments made by Applicant in para 24 do not merit a reply.

24. The averments made by the Applicant in para 26-27 relate to the teachings contained in document D3. In para 26, the Applicant has referenced a portion of D3 and contended that "*Accordingly, D3 does not disclose or teach the pharmaceutical composition of the present invention comprising Linezolid, bedaquiline, and pretomamid, and optionally pyrazinamide, where the linezolid, bedaquiline and pretomanid are each present in the unitary dosage form in an amount of 1mg to 1g*." The Applicant's contention that D3 (US20110190199) does not disclose or teach the claimed pharmaceutical composition is misplaced. D3 clearly discloses a method of treating tuberculosis using an oxazolidinone compound in combination with at least two anti-tuberculosis agents selected from a defined group that expressly includes TMC207 (bedaquiline), PA-824 (pretomanid), and pyrazinamide. It is submitted that D3 represent a citation in respect of the ground of inventive step. Although it does not disclose linezolid, it actually does disclose sutezolid, in combination with pretomanid and bedaquiline. Sutezolid is an oxazolidinone, which is also majorly referenced by the Applicant's specification, has

comparable and interchangeable anti-TB activity vis-à-vis linezolid, and is important in this regard. Thus, D3 directly contemplates the very therapeutic combination at the core of the present claims, namely an oxazolidinone together with bedaquiline and pretomanid, optionally with pyrazinamide. The fact that D3 exemplifies sutezolid rather than linezolid does not create a material distinction. Linezolid was a well-known, already approved oxazolidinone antibiotic at the priority date, and the substitution of one known member of a drug class for another closely related member within the same class is a routine and obvious modification for a person skilled in the art. Further D3 discloses the dose of sutezolid to be between 600 mg to 1000 mg as shown below

> **[0050]** In yet another embodiment, the compound of formula (I), or a pharmaceutically acceptable salt thereof, is administered between about 600 mg to about 1000 mg.

25. The Applicant's attempt to distinguish D3 on the ground that it does not disclose a "unitary dosage form" containing linezolid, bedaquiline, and pretomanid in amounts ranging from 1 mg to 1 g is also unpersuasive. The stated dosage range is extremely broad and encompasses virtually all conventional therapeutic doses of small-molecule drugs, and therefore cannot confer novelty. Moreover, the preparation of known active agents into a fixed-dose or unitary dosage form is a routine pharmaceutical formulation exercise once the combination therapy itself is known.

26. The Applicant, in para 27, has contended that D3 discloses that "*Although several case series suggest that LZD may contribute to successful sputum culture conversion in such cases, its individual activity in TB patients and its precise contribution to combination regimens remain unclear. These studies also demonstrate that the duration of LZD administration may be limited by hematologic and neurologic toxicity that can occur with long-term administration*". However, as pointed out by the Opponent before, the Applicant's 'invention' includes discrepancies as elaborated below
    - The Applicant's invention includes linezolid
    - The Applicant's specification mentions the problems associated with the toxicity resulting from longer duration of administration of linezolid
    - The manner in which the Applicant has dealt with this issue, is by interrupting administration of linezolid for a period of time (1-2 weeks)

- Such interruption in administration of one drug is not amenable with a unitary composition, as claimed by Applicant.

27. Critically, such interruption of one active agent is incompatible with the concept of a single, fixed, unitary dosage composition containing all claimed agents together. If linezolid is physically co-formulated in a unitary dosage form with bedaquiline and pretomanid, it cannot be selectively discontinued without simultaneously discontinuing the other components. Conversely, if the drugs are administered separately to permit interruption of linezolid, then the claimed unitary composition loses its functional relevance.

28. Without prejudice to the above submission, with respect to paragraph 27, the Applicant's reliance on the extract from D3 is misconceived. The cited portion of D3 does not discourage the use of linezolid in tuberculosis regimens; rather, it acknowledges that case series suggested linezolid contributed to successful sputum culture conversion, while noting that its precise contribution and toxicity profile required further evaluation. This observation would not deter a skilled person but would instead motivate optimization of dose and duration within combination therapy. Recognition of dose- and duration-dependent toxicity does not negate therapeutic relevance; it reinforces the need for rational regimen design, something already under active investigation before the priority date. Accordingly, paragraph 27 does not support patentability but instead highlights the absence of a genuine technical advance.

29. Further, D3 also states the following

[0006] Oxazolidinones with more potent activity against *Mycobacterium tuberculosis* have previously been described. (See Barbachyn, M. R. et al., J Med Chem. 39:680-685, 1996; Sood, R., et al., Antimicrob Agents Chemother 49:4351-4353, 2005). The antituberculosis activity of the compound of formula (I), (S)—N-[[3-[3-fluoro-4-(4-thiomorpholinyl) phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide, was first described in 1996. (See Barbachyn, M. R., et al., J Med Chem. 39:680-685, 1996). Subsequent experiments in a murine model found the compound of formula (I) to be more active than LZD when both drugs were administered at 100 mg/kg, but the clinical relevance of this LZD dose was not established and the activities of the compound of formula (I), and LZD were not clearly different when compared at lower doses. (See Cynamon, M. H., et al., Antimicrob Agents Chemother 43:1189-1191, 1999). Moreover, although the compound of formula (I) appeared to have modest activity when combined with rifampin (RIF) in an acute (early) infec-

30. Thus, the difference between SZD and LZD was not as clear as the Applicant suggest. In fact, D3 would prompt a person to investigate LZD at lower doses.

31. With respect to paragraph 28, the Applicant's objection that certain documents were cited without providing copies is factually incorrect. The Opposition clearly identified the relevant publications and, where applicable, provided document links to publicly accessible sources. The references cited—such as the 14-day bactericidal activity study of PA-824, bedaquiline, and pyrazinamide; the US FDA approval of Sirturo (bedaquiline); the publication on principles for designing future multidrug-resistant TB regimens; WHO guidance on Group 5 drugs; and the 2015 update on new anti-tuberculosis drugs and regimens—are publicly available scientific and regulatory documents forming part of the common general knowledge in the field. The provision of links to these materials sufficiently identifies them and enables verification. Further, together, these documents seek to establish that by 2012–2013, the use of combination therapy for multidrug-resistant tuberculosis (MDR-TB) was already scientifically recognized and established. They show that newer drugs such as Bedaquiline were approved specifically for use as part of a combination regimen rather than as standalone treatments, reinforcing the principle that multiple effective drugs must be used together to prevent resistance and improve outcomes. The scientific literature at the time also recommended that treatment regimens include several active drugs, preferably incorporating at least one new drug class, and be designed to be shorter in duration and more tolerable for patients. Additionally, Linezolid was already known and discussed

in the context of drug-resistant TB treatment, including consideration of lower dosages to reduce adverse side effects while maintaining efficacy.

32. In pre-grant proceedings under Section 25(1), the emphasis is on substantive examination of patentability in light of the prior art and public domain knowledge. The Controller is empowered to consider relevant publicly available documents, particularly when they are clearly cited and readily accessible. The Applicant's objection does not negate the technical relevance of these documents, nor does it diminish their evidentiary value in assessing novelty, inventive step, and patentability under Section 3. Accordingly, the contention that the references were improperly raised is without merit.

33. The averments made by the Applicant in para 29-30 relate to cited prior art D4. The Applicant has misrepresented the teachings of D4 in para 29. The actual teaching in D4 with respect to incidence of adverse effects for linezolid is as shown below

> The significant beneficial effect of linezolid was tempered, as expected, by the high rates of drug-related adverse events, although almost all events resolved quickly with a reduction in the dose or the temporary cessation of linezolid, and only three patients discontinued the study owing to adverse events. As we also expected, adverse events were significantly reduced in patients who subsequently received the reduced dose of 300 mg per day. The pharmacokinetic profile of the 300-mg dose, as compared with the minimum inhibitory concentration of the isolates, showed that this dose was sufficient to maintain serum levels above the minimum inhibitory concentra-

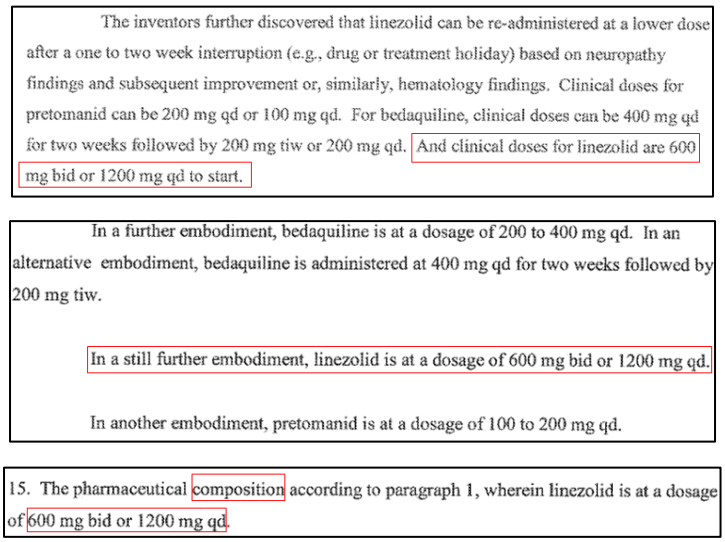
34. Thus, D4 would work as a document motivating a POSITA to consider regimens including linezolid for treatment of TB. D4 would, in fact, not teach away from the use of linezolid based on the above.

35. The averment made by the Applicant in paragraphs 31-32 relate to cited prior art D1. While D1 will be discussed in detail in the following section, it is pertinent to point out that the Applicant has focused on two specific aspects of D1

- The disclosure of linezolid being dosed at 1200 mg
- The disclosure of LZD, BDQ and PMD as "*administration of a combination of separate drugs that are each in separate tablet form*"

36. The Opponent is herein addressing both issues as follows:

- The Applicant's specification itself recommends a dosage of either 600 mg or 1200 mg as shown below



The inventors further discovered that linezolid can be re-administered at a lower dose after a one to two week interruption (e.g., drug or treatment holiday) based on neuropathy findings and subsequent improvement or, similarly, hematology findings. Clinical doses for pretomanid can be 200 mg qd or 100 mg qd. For bedaquiline, clinical doses can be 400 mg qd for two weeks followed by 200 mg tiw or 200 mg qd. And clinical doses for linezolid are 600 mg bid or 1200 mg qd to start.

In a further embodiment, bedaquiline is at a dosage of 200 to 400 mg qd. In an alternative embodiment, bedaquiline is administered at 400 mg qd for two weeks followed by 200 mg tiw.

In a still further embodiment, linezolid is at a dosage of 600 mg bid or 1200 mg qd.

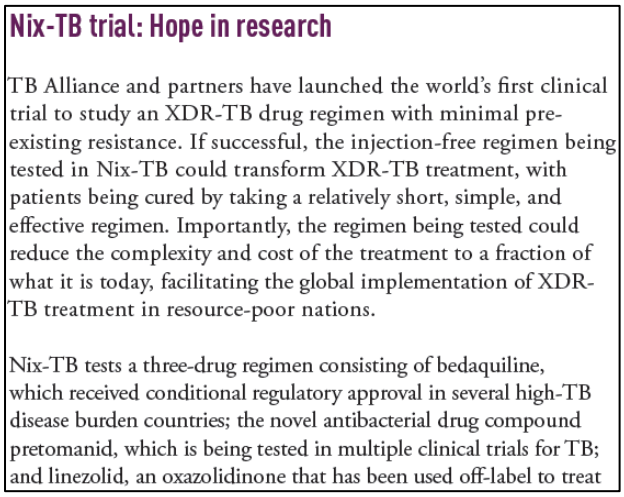
In another embodiment, pretomanid is at a dosage of 100 to 200 mg qd.

15. The pharmaceutical composition according to paragraph 1, wherein linezolid is at a dosage of 600 mg bid or 1200 mg qd.

- The Applicant cannot, now, state that the invention is confined to linezolid lower dose upto 1000 mg, when the specification recommends 1200 mg as one of the doses.

  According to the Applicant, the claimed invention resides in a unitary composition of the active agents. However, the recommendation in the specification to remove LZD in order to circumvent toxicity, clearly shows that the specification and claims diverge.

37. The averments made by the Applicant in para 33 are denied. It is submitted that D2 discloses the combination of bedaquiline, pretomanid and linezolid to treat TB. D2 discloses the aims of developing a short course treatment for extensively drug-resistant TB as shown below



Nix-TB trial: Hope in research

TB Alliance and partners have launched the world's first clinical trial to study an XDR-TB drug regimen with minimal pre-existing resistance. If successful, the injection-free regimen being tested in Nix-TB could transform XDR-TB treatment, with patients being cured by taking a relatively short, simple, and effective regimen. Importantly, the regimen being tested could reduce the complexity and cost of the treatment to a fraction of what it is today, facilitating the global implementation of XDR-TB treatment in resource-poor nations.

Nix-TB tests a three-drug regimen consisting of bedaquiline, which received conditional regulatory approval in several high-TB disease burden countries; the novel antibacterial drug compound pretomanid, which is being tested in multiple clinical trials for TB; and linezolid, an oxazolidinone that has been used off-label to treat

38. With respect to paragraph 33, the Applicant's attempt to exclude D2 is untenable. D2 (Nix-TB) clearly discloses the very same three-drug combination of bedaquiline, pretomanid, and linezolid being evaluated for drug-resistant tuberculosis prior to the priority date. Even if D2 does not expressly disclose specific dosage amounts or confirm treatment within 1.5–2 months, it nonetheless establishes that the identical therapeutic triad was known and under active clinical investigation for shortened regimens. Once the combination itself is publicly known, routine optimization of dose and duration falls within ordinary clinical skill and cannot confer inventiveness.

39. Further, the fact that D2 is acknowledged in the specification does not remove it from consideration as prior art. On the contrary, such acknowledgment confirms that it forms part of the state of the art. An Applicant cannot neutralize a prior art disclosure merely by citing it in the background section. Accordingly, D2 remains highly relevant for assessing novelty and inventive step, irrespective of whether it specifies precise dosage values or treatment duration.

40. The averments made by the Applicant in para 34 do not merit a reply.

41. The averments made by the Applicant in para 35 are denied. It is indeed true that D4 teaches re-administration of linezolid after interruption/stoppage for a period of time (also known as drug holiday). This is shown below

If adverse events occurred that were considered to be related to linezolid, a reduction in the dose or a rechallenge at a dose of 300 mg per day was allowed after a limited drug holiday (described in Table 2 in the Supplementary Appendix). Linezolid was administered by means of directly observed therapy during hospitalization. The study

Supplemental Table 4: Linezolid stoppage and dose adjustments*

Subject ID	Stoppage period (days)	Reason	Relationship to LZD	Dose adjustment
F101	2	Hepatic enzyme elevation	Possibly related	Re-challenge with 600mg
F103	–	Anemia	Probably related	Permanently stopped
F104	1	Joint pain	Unrelated	Re-challenge with 600mg
	18	Neutropenia	Probably related	De-escalation to 300mg
F106	18	Peripheral neuropathy	Probably related	Re-challenge with 300mg
F110	11	Peripheral neuropathy	Probably related	De-escalation to 300mg
F112	–	Optic neuropathy	Possibly related	Permanently stopped
F113	21	Peripheral neuropathy	Probably related	De-escalation to 300mg
F114	5	Hepatic enzyme elevation	Possibly related	Re-challenge with 300mg
	20	Rhabdomyolysis	Possibly related	Re-challenge with 300mg
F117	23	Hepatic enzyme elevation	Possibly related	Re-challenge with 300mg
F119	17	Optic neuropathy	Probably related	De-escalation to 300mg
F121	34	Peripheral neuropathy	Probably related	De-escalation to 300mg

42. Opposition clearly identifies that the alleged inventive contribution—namely, the retained bactericidal/sterilizing role of linezolid when used for a limited duration and its re-administration after a treatment interruption—is already taught in D4. D4 expressly reports the use of linezolid in drug-resistant TB regimens along with dose modification, temporary discontinuation, and re-introduction to manage toxicity while maintaining therapeutic benefit. Thus, the core clinical strategy relied upon by the Applicant was already part of the prior art.

43. It bears repeating that D4 has been cited by the Opponent in relation to the ground of inventive step. The Applicant's contention that D4 does not disclose the exact combination with bedaquiline and PA-824 is misplaced. Paragraph 25 does not rely on D4 alone to disclose the full triad; rather, D4 is cited to show that the specific handling of linezolid (shortened duration and re-administration after interruption) was known. When read together with D2/D3, which disclose the BDQ + pretomanid + linezolid regimen, the Applicant's alleged contribution represents no more than an obvious

application of known teachings. Accordingly, the objection in paragraph 35 does not overcome the prior art case.

44. The averments made by the Applicant in para 36-37 are denied. The Opponent reserves the right to rely upon documents cited in the pre-grant representation. The bald accusation of wishing to delay the grant of the application is not tenable without evidence, which the Applicant has not provided. The opposition fully includes all grounds pled, and prior art cited to substantiate the same. The Opposition has shown that entire sections of the specification—including definitions of chemical stability, synergy, prodrugs, stereochemistry, excipients, and related boilerplate—are substantially reproduced from WO2004064846 with minimal adaptation. While such definitions may be generally known, their wholesale reproduction underscores the absence of any meaningful technical contribution in large portions of the specification and supports the Opponent's grounds under Section 25(1)(f) and 25(1)(g), including lack of invention and insufficiency.

45. The averments made by the Applicant in para 38 relates to matters of record, and hence does not merit a reply.

46. The averments made by the Applicant in para 39 are denied. All the grounds pled by the Opponent are valid and the claimed invention ought to be rejected on each ground alone. The Opponent does not deny the grounds pled in the opposition, as enlisted by the Applicant.

47. The averments made by the Applicant in para 40 relate to the prior art cited by the Opponent, along with the publication dates of each, and the grounds for which they have been cited. Insofar as these are matters of record, the Opponent does not deny them.
48. The averments made by the Applicant in para 41 do not merit a reply.

Section 25 (1)(b): Lack of Novelty

49. The averments made by the Applicant in para 42-43 relate to the ground of novelty pled by the Opponent. The Applicant avers that the impugned patent application is not anticipated by the prior art cited in the opposition. The Opponent denies this contention,

and submits that, as will be demonstrated herein below, the impugned application is fully anticipated by the disclosure contained in documents D1 and D2.

50. The averments made by the Applicant in para 44 relate to the two documents cited in the opposition in relation to novelty viz. D1 (NCT02333799) and D2 (Nix-TB – Testing a New Potential Treatment for XDR-TB). The Applicant avers that document D2 ought not to be taken on record as it is already referenced in the impugned application. The Opponent strongly objects to these averments. There is simply no basis in the Act, or Rules debarring citation of a document in an opposition proceeding, if it has been previously cited in the application. Since the Applicant's own specification acknowledges this state of the art, that is D2, such prior disclosure is highly material to novelty under Section 25(1)(b), and mere amendment of claim language cannot confer novelty where the claimed subject matter substantially overlaps with what was already made available to the public.

51. The averments made by the Applicant in para 45 relate to the document D1 cited in the opposition in relation to novelty of the claimed invention. The Opponent strongly denies the selective reading of the disclosure in D1 by the Applicant, to exclude elements that demonstrate anticipation of the alleged invention.

52. The Applicant avers that "*D1 is a clinical trial report assessing the safety and efficacy of Bedaquiline plus PA-824 plus Linezolid in subjects with drug resistant pulmonary tuberculosis after 6 months of treatment. The subjects were provided 400 mg Bedaquiline once daily for 2 weeks then 200 mg 3 times per week plus PA-824 200 mg once daily plus <u>Linezolid 1200 mg once daily</u>*." The portion relating to 1200 mg once daily has been underlined by the Applicant, presumably to demonstrate that the linezolid administered exceeds the 1g limit as specified in the amended claims. However, the amount of linezolid (1200 mg) is only specified in the experimental arm of the clinical trial. The 'intervention' arm specifies the following amounts for each drug (a) bedaquiline 100 mg tablets (b) pretomanid 200 mg and (c) <u>linezolid 600 mg</u> tablets. Thus, D1 clearly discloses the amount of linezolid as being within the range recited in even the amended claims.

53. The averments made by the Applicant in para 45 are erroneous and misleading. The Applicant avers that "*D1 discloses in Arms and Interventions on page 3,*

"administration of a combination of separate drugs that are each in separate tablet form". Thus, the essential features of the present invention, "a unitary dosage formulation comprising all three active ingredients, i.e., Bedaquiline plus PA-824 plus Linezolid wherein the linezolid, bedaquiline and pretomanid are each present in the unitary dosage form in an amount of 1 mg to 1 g", is not disclosed in D1". However, if we actually consider the original claims, it can be seen that unitary dosage form is not necessarily an essential feature of the invention. Not only was the limitation of unitary dosage form not present in the as-filed claims, some of these claims recite use of the drugs e.g. linezolid separately for treatment of tuberculosis as shown below

> 10. The method according to paragraph 4, wherein linezolid is administered for up to one month at 100 mg/kg per day.
>
> 11. The method according to paragraph 4, wherein linezolid is administered at a dosage of 600 mg once daily for the first one to two months.
>
> 12. The method according to paragraph 4, wherein linezolid is re-administered after a one to two week drug holiday.

54. This is bolstered by the Applicant's own specification, where it is disclosed that

> The inventors further discovered that linezolid can be re-administered at a lower dose after a one to two week interruption (e.g., drug or treatment holiday) based on neuropathy findings and subsequent improvement or, similarly, hematology findings. Clinical doses for pretomanid can be 200 mg qd or 100 mg qd. For bedaquiline, clinical doses can be 400 mg qd for two weeks followed by 200 mg tiw or 200 mg qd. And clinical doses for linezolid are 600 mg bid or 1200 mg qd to start.

55. The above disclosures in the claims and specification clearly shows regimen where drug e.g. linezolid is administered separately. Also, the entire specification presents a very different picture of what the invention is than what the Applicant is now presenting. The clinical regimens detailed in the specification demonstrate no administration involving unitary dosage form of the three drugs. Rather they show regimens with separate administration of the drugs. Thus, D1 discloses the invention in its entirety, including all its elements. It is clear that the amended claims diverge from the substance of the actual 'invention' disclosed in the specification.

56. The averments made by the Applicant in para 47-48 relate to the prior art D2, which was also cited in relation to novelty of the alleged invention claimed in the impugned application. D2 discloses the grave problems associated with the emergence of extensively drug-resistant tuberculosis (XDR-TB) and the paucity of effective treatments for the same. It importantly discloses that TB Alliance and partners have launched the world's first clinical trial to study an XDR-TB drug regimen with minimal pre-existing resistance. It also discloses the following

> Nix-TB tests a three-drug regimen consisting of bedaquiline, which received conditional regulatory approval in several high-TB disease burden countries; the novel antibacterial drug compound pretomanid, which is being tested in multiple clinical trials for TB; and linezolid, an oxazolidinone that has been used off-label to treat

> TB. The trial brings hope to those with XDR-TB who have no other treatment options. It includes patients as young as 14 and those who are co-infected with HIV with a CD4 count of 50 or higher.
>
> Nix-TB is an open-label trial that enables patients to be assessed at regular intervals with the aim of being cured in six to nine months. After completing treatment, participants are monitored for two years to ensure they do not relapse. The trial has an adaptive design; if improved treatments become available during the course of the study, they can be incorporated into the trial.

57. The Applicant has averred that D2 does not disclose a pharmaceutical unitary dosage form specifically. However, as stated in relation to D1 above, the Applicant's own specification contains all regimens where the components (drugs) are separately administered.

58. As elaborated in relation to D1, Linezolid is disclosed as being administered separately in the regimen indicated by the recommendation to halt linezolid administration for one or two weeks. This regimen does not comport with a unitary dosage form. Thus, the amended claims do not align with the invention that is disclosed in the specification.
59. The Applicant, in para 49, alleges that neither D1 nor D2 anticipate the invention claimed in the impugned application. However, as shown above, the Applicant has not clearly disclosed the actual invention, which is not, in fact, a unitary dosage form. Thus, in light of the above, D1 and D2 anticipate the invention fully.

Section 25 (1) (d): Publicly known / used in India

60. The averments made by the Applicant in para 50 relate to the claimed invention being publicly known in India before the priority date of the claim(s) in light of documents D1/D2. The Opponent strongly denies these averments, and submits that the Applicant provides no basis for their contention that *"…availability in the internet of the documents D1 /D2 does not amount to prior knowledge of the present invention as required under Section 25(1)(d) as none of them disclose the present invention as claimed.*". The usage of the internet as a source of public knowledge has been widespread for more than two decades now- it has not been confined to a only a select group of populations/individuals. In fact, it is a primary mode of dissemination of information now. Thus, no documents can automatically be disqualified as sources of public knowledge for being available on the internet. Besides, documents that are publicly accessible before the priority date—such as clinical trial records and scientific publications—form part of the prior art regardless of whether the Applicant subjectively acknowledges them. Further, the Opponent has already demonstrated in the section dealing with novelty, that the actual invention disclosed in the specification diverges from the latest amended claims. In fact, the Applicant's belated amendment introducing the limitation of a "unitary dosage form" is nothing but a transparent afterthought and cannot cure the fundamental defects in the claims. The amendment has been made only in response to the objections raised in the opposition and not on the basis of any clear and unambiguous disclosure in the original specification. Thus, while the latest amended claims are directed towards a unitary dosage form, the invention (and even as-filed claims) is completely different and discloses a regimen where administering a unitary dosage form is just not possible. The disclosure in D1 and D2 completely tracks the actual invention as disclosed in the specification, which recommends halting linezolid administration for a period of time. This is completely contrary to the claims, which claim a unitary dosage form. D1 and D2 were available before the priority date and disclose the regimen that is the actual invention in the impugned application. Thus, the impugned application totally falls within the purview of section 25(1)(d) and ought to be rejected on this ground alone.

Section 25 (1) (e): Lack of inventive step

61. The averments made by the Applicant para 51 relate to the inventive step arguments as elaborated in the pre-grant opposition. The Applicant contends that the case law cited

by the Opponent would be dealt with at the time of hearing. The Opponent strongly objects to the same as these case laws are pertinent to the assessment of inventive step. The unwillingness of the Applicant to address the same in the reply statement in indicative of their relevance to the impugned application.

62. The Applicant's denial regarding D3 (US20110190199) is based on an unduly narrow reading of the prior art. As set out in the Opposition, D3 expressly teaches that the oxazolidinone compound of formula I (sutezolid) may be administered in combination with at least two anti-tuberculosis agents, and the listed agents explicitly include TMC-207 (bedaquiline), PA-824 (pretomanid), and pyrazinamide. The Applicant itself acknowledges in its Reply that D3 provides combination therapy frameworks involving these agents. It is settled law that prior art is not confined to worked examples; the explicit disclosure of permissible combinations constitutes a clear technical teaching. Thus, D3 directly points the skilled person toward the therapeutic triad underlying the present claims.

63. The Applicant's reliance on the absence of a single express three-drug example is legally insufficient. D3 repeatedly emphasizes synergistic multi-drug regimens and guides the selection of companion TB agents, which would have motivated the skilled person to select bedaquiline and pretomanid alongside an oxazolidinone. The optional nature of pyrazinamide in the claims does not confer patentability, as D3 already teaches flexible multi-drug combinations. Moreover, when read with D1 and D2—both acknowledged in the specification—the path to the claimed regimen becomes even more direct. Accordingly, the Applicant's characterization of D3 as "baseless" is without merit, and D3 at minimum renders the claimed subject matter obvious.

64. Further, the Applicant has contended that improved results have been demonstrated with respect to the combination of linezolid + bedaquiline + pretomanid (LZD + BDQ + PMD), as well as the combination of pyrazinamide + linezolid + bedaquiline + pretomanid (PZA + LZD + BDQ + PMD) from examples 2 and 3. However, the specification itself contains an admission that this is not the case. The specification in fact discloses the following

"*Despite the conventional understanding that it is necessary to continuously administer antibacterial agents over a period of many months to obtain the desired antibacterial*

effect, the inventors surprising discovered that LZD in a multi-agent dosage form can be administered for one to two months and still retain sterilizing activity. More specifically, the inventors discovered that LZD adds bactericidal and sterilizing activity in formulation comprising BDQ and PMD. Its additive sterilizing activity was indistinguishable from that of SZD as shown in Example 1. ***In Example 3, in which the bacterial burden and the dose of PMD were higher, LZD did not appear as effective as SZD****, although the difference was not statistically significant*."

65. From the above, it can be seen that linezolid is no better than the compound sutezolid, and in fact, appeared to be less efficacious than the latter, in a combination regimen of BDQ + PMD + LZD. The specification discloses the results of various drug regimens in Example 3, which include the regimens BDQ + PMD + LZD and BDQ + PMD + SZD. In this, regard, it is disclosed that -

"*Treatment with BDQ+PMD produced numerically superior results, with just 3 (21%) of 14 mice relapsing at 3 months, although this difference was not statistically significant. Addition of SZD to BDQ+PMD resulted in only one relapse after just 2 months of treatment, a result that was at least as effective as 3 months of BDQ+PMD and more effective than 3 months of the first-line regimen.* ***Addition of SZD at 50 mg kg also resulted in fewer relapses than did the addition of LZD 300 mg/kg for 2 months****, although the difference did not reach statistical significance.* ***Use of LZD at. 100 mg/kg for the first month only was less effective than SZD for 2 months****, but not significantly different from LZD 100 mg/kg for 2 months. Similarly, among regimens administered for 3 months,* ***no relapse was observed irrespective of whether LZD 100 mg/kg was continued throughout or discontinued after 1 or 2 months, or replaced with LZD 50 mg/kg after 2 months****. In a post hoc analysis comparing BDQ+PMD to all BDQ+PMD+LZD regimens, the addition of LZD 100 mg kg for at least one month resulted in fewer relapses after 3 months of treatment."*

	Mean (±SD) log_{10} CFU count at[a]:				Proportion (%) relapsing after treatment for:	
Regimen	**D-13**	**D0**	**M1**	**M2**	**2 mos**	**3 mos**
Untreated	3.96±0.08	7.74±0.20				
2RIF+INH+PZA/ 1RIF+INH				1.94±0.27		8/14 (57)
BDQ+PMD			4.48±0.20	2.33±0.30		3/14 (21)
BDQ+PMD+TZD			4.20±0.13	1.67±0.41		
BDQ+PMD+AZD			4.07±0.36	1.43±0.36		
BDQ+PMD+RWJ			3.63±0.18	0.54±0.41		
BDQ+PMD+LZD_{50}			3.48±0.36	0.39±0.26		
1BDQ+PMD+LZD_{100}/ BDQ+PMD			2.69±0.37	0.93±0.49	9/15 (60)	0/15 (0)
2BDQ+PMD+LZD_{100}/ BDQ+PMD				0.66±0.39	6/15 (40)	0/15 (0)
2BDQ+PMD+LZD_{100}/ BDQ+PMD+LZD_{50}						0/12 (0)
BDQ+PMD+LZD_{100}						0/15 (0)
BDQ+PMD+SZD			1.88±0.22	0.00±0.00	1/14 (7)	0/14 (0)

66. Thus, it can be seen that the addition of linezolid to the dual drug regimen of bedaquiline and pretomanid does not provide a benefit which cannot be obtained by substituting it with sutezolid. In other words, the effect of linezolid in this regimen is indistinguishable from that of sutezolid. In the absence of any demonstrated superiority of linezolid over the closely related oxazolidinone sutezolid, the observed activity is consistent with a predictable class effect of oxazolidinones. Where prior art (including D3) already teaches the use of oxazolidinones in multi-drug TB regimens, the mere selection of linezolid from within the same known class cannot confer inventiveness. Further, It is well settled that, for a selection within a known class to be patentable, the Applicant must demonstrate a technical advance from all the existing knowledge. The specification contains no such evidence. On the contrary, the Applicant's own data show parity or numerical inferiority relative to sutezolid, thereby negating any alleged inventive merit.

67. With respect to Example 2, the specification discloses the following

"In Example 2, the contribution of LZD to regimens containing BDQ+PMD plus PZA was assessed. Control mice received BDQ+PZA plus PMD at either 50 or 100 mg/kg. Test mice received BDQ+PZA+PMD (100 mg/kg) plus LZD (100 mg/kg) for up to 2

months. One cohort received LZD for the entire 2 months. Another received LZD for the first month only."

68. The above shows that the regimen in Example 2 includes pyrazinamide (abbreviates as PZA) as an essential component. However, pyrazinamide is an **optional** element as per the Applicant's own amended claim 1. It is not an essential feature of the claims at all.

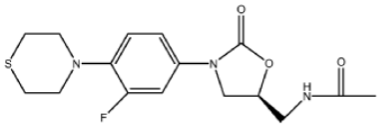
69. The specification discloses that *"In Example 2, it was confirmed that addition of LZD to BDQ+PZA+PMD also significantly increases the bactericidal and sterilizing activity of the regimen, curing all mice after 6 weeks of treatment, while at least 5 months of treatment with the first-line regimen is typically required to produce this result under the same conditions."*

70. The above results indicate that pyrazinamide (PZA) is essential to the above 4-drug combination. However, as pointed out above, the amended claims recite the same as an optional element. It is a settled position that any alleged technical advance must be commensurate with the full scope of the claims. In the present case, the only technical advance demonstrated arises in the presence of pyrazinamide, whereas the claims extend to embodiments in which pyrazinamide is absent. The Applicant has provided no data showing that the claimed three-drug regimen (BDQ + PMD + LZD) achieves the same effect. Accordingly, the asserted technical benefit lacks adequate support across the claim's breadth. Thus in the absence of supporting data for PZA-free embodiments, the Applicant cannot presume that the observed results will extend across the entire claimed scope. Such unsupported generalization renders the claims speculative and undermines any reliance on Examples 2 and 3 to establish inventive step.

71. The averments made by the Applicant in para 52-54 relate to the prior art D3. The Opponent submits that these are outright false and misleading. The Applicant alleges that "*...it is denied that D3 teaches a three drug combination of Sutezolid (SCZ) (compound of formula 1) plus Bedaquiline plus Pyrazinamide and hence the present invention is obvious as baselessly alleged by the Opponent*." The claims of the impugned application are directed towards a combination of linezolid, bedaquiline and pretomanid. Pyrazinamide is only an optional element recited in the claims. Cited prior art D3 discloses the combination of the compound sutezolid (SZD) in combination with

at least two other anti-tuberculosis drugs. Among these drugs are included both bedaquiline (TMC-207) and pretomanid (PA-824). Thus, D3 discloses the combination of sutezolid + bedaquiline + pretomanid as shown below

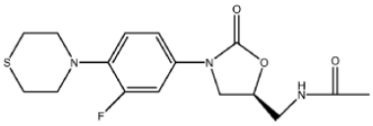
1. Use of a compound of the formula or a pharmaceutically acceptable salt thereof:



[I] in combination with at least two anti-tuberculin agents in the manufacture of a medicament for the treatment of tuberculosis.

2. The use of claim 1, wherein said at least two agents is selected from the group consisting of isoniazid, rifampin, rifapentine, rifabutin, pyrazinamide, ethambutol, streptomycin, kanamycin, amikacin, moxifloxacin, gatifloxacin, levofloxacin, ofloxacin, ciprofloxacin capreomycin, ethionamide, cycloserine, para-aminosalicylic acid, thiacetazone, clarithromycin, amoxicillin-clavulanic acid, imipenem, meropenem, viomycin, terizidone, TMC207, PA-824, OPC-7683, LL-3858 and SQ-109. 3. The use of claim 1, wherein one of said at least two agents is selected from the group consisting of isoniazid, rifampin, rifapentine, rifabutin, pyrazinamide, moxifloxacin, gatifloxacin, levofloxacin, ofloxacin, ciprofloxacin, and ethambutol.

8. A pharmaceutical composition comprising: i) a therapeutically effective amount of a compound of formula (I) or a pharmaceutically acceptable salt thereof:



[I]

[ii] a therapeutically effective amount of at least one agent useful in the treatment of tuberculosis and,

[iii] one or more pharmaceutically acceptable carriers or vehicles.

9. The pharmaceutical composition of claim 8, wherein said at least one agent is selected from the group consisting of isoniazid, rifampin, rifapentine, rifabutin, pyrazinamide, ethambutol, streptomycin, kanamycin, amikacin, moxifloxacin, gatifloxacin, levofloxacin, ofloxacin, ciprofloxacin, capreomycin, ethionamide, cycloserine, para-aminosalicylic acid, thiacetazone, clarithromycin, amoxicillin-clavulanic acid, imipenem, meropenem, viomycin, terizidone, TMC207, PA-824, OPC-7683, LL-3858 and SQ-109.

72. The Applicant further avers that D3 includes the following disclosure regarding linezolid *"Although several case series suggest that LZD may contribute to successful sputum culture conversion in such cases, its individual activity in TB patients and its precise contribution to combination regimens remain unclear. These studies also demonstrate that the duration of LZD administration may be limited by hematologic and neurologic toxicity that can occur with long-term administration"*

73. The Applicant contends that the toxicity profile of LZD prompted the inventors of D3 to look for other oxazolidinones. The Opponent submits that the problem of toxicity of LZD has not been solved by the Applicant's invention also. This can be seen from the Applicant's own specification, where the Applicant, contending with the problem of neuropathy caused by LZD, discovered the following

> The inventors further discovered that linezolid can be re-administered at a lower dose after a one to two week interruption (e.g., drug or treatment holiday) based on neuropathy findings and subsequent improvement or, similarly, hematology findings. Clinical doses for pretomanid can be 200 mg qd or 100 mg qd. For bedaquiline, clinical doses can be 400 mg qd for two weeks followed by 200 mg tiw or 200 mg qd. And clinical doses for linezolid are 600 mg bid or 1200 mg qd to start.

74. The approach of temporarily discontinuing linezolid to manage hematologic or neurologic toxicity was already part of established clinical practice, as reflected in the prior art. The Applicant has not demonstrated any new formulation strategy, dosing paradigm, or mechanistic solution that mitigates linezolid toxicity. The proposed "drug holiday" merely represents routine clinical management rather than a technical advancement.

75. The Applicant's own specification recommends drug holiday and re-administration of LZD after such period to avoid toxicity as shown below

> Provided is a pharmaceutical composition, comprising a therapeutically effective amount of each of linezolid, bedaquiline and pretomanid, and optionally pyrazinamide, or a pharmaceutically acceptable salt of each thereof, and a pharmaceutically acceptable carrier.
>
> Also provided is a method for the treatment of tuberculosis, comprising the step of administering to a patient in need thereof a therapeutically effective amount of each of linezolid, bedaquiline and pretomanid, and optionally pyrazinamide, or a pharmaceutically acceptable salt of each thereof, and a pharmaceutically acceptable carrier. In one embodiment of the invention, linezolid is removed from the treatment regimen after one to two months. In another embodiment, linezolid can be re-administered after a one to two week drug holiday.

76. Further, the Applicant's "teaching away" argument based on linezolid toxicity is unpersuasive. D3 merely identifies known limitations of linezolid and motivates the development of improved oxazolidinones; it does not discourage the use of oxazolidinones in TB combination therapy. To the contrary, D3 reinforces the central role of this drug class in multi-drug regimens and teaches that combining an oxazolidinone with multiple TB agents produces synergistic effects and may shorten treatment duration.

77. Further, the Applicant states (in para 54) that "*present invention has showed that the activity of BDQ+PMD known to be antagonistic has been improved by addition of LZD*". However, this is of no significance in the context of D3, because, as already shown in the Applicant's specification, in considering the combination of SZD+BDQ+PMD and LZD+BDQ+PMD, LZD is not more effective than SZD. Therefore, even if LZD did improve the activity of BDQ+PMD, such triple combination is anyway not better than SZD+BDQ+PMD. Further, the Applicant states (in para 54), that "*Therefore the finding of the present inventors, as demonstrated in Example 1, that addition of LZD significantly increased the activity of BDQ+PMD (p< 0.01) and produced activity superior to that of RIF +INH-+PZA after 2 and 3 months of treatment (p<0.001) is unexpected*. *This definitely is technical advancement.*" However, the correct comparison (of the claimed composition) ought to be with D3, and not RIF+INH+PZA, as D3 discloses SZD+BDQ+PMD, which is the closest prior art composition, rather than RIF+INH+PZA. It is well settled that the assessment of inventive step must be made against the closest prior art and not against a clinically inferior baseline regimen. Where the prior art already discloses an oxazolidinone-based BDQ+PMD combination (as in D3), any alleged improvement over RIF+INH+PZA is legally irrelevant to the question of obviousness. In fact, the Applicant's own specification includes a comparison of the two regimens SZD+BDQ+PMD and LZD+BDQ+PMD, in Table 1.

	Mean (±SD) $\log_{10}$ CFU count at[a]:					Proportion (%) relapsing after treatment for:		
Drug Regimen	D-13	D0	M1	M2	M3	2 mos	3 mos	4 mos
Untreated	2.69±0.13	6.17±0.27	6.47±0.06					
2RIF+INH+PZA/ RIF+INH			3.47±0.37	1.59±0.25	0.50±0.51		13/15 (87)	1/20 (5)
BDQ			3.24±0.25					
PMD			4.57±0.32					
LZD			4.97±0.26					
SZD			3.85±0.37					
BDQ+PMD			4.21±0.40	1.62±0.19	0.53±0.34	15/15 (100)	10/15 (60)	2/20 (10)
BDQ+LZD			2.82±0.15	1.91±0.66				
BDQ+SZD			2.88±0.07	0.65±0.50				
PMD+LZD			3.23±0.41	1.48±0.12				
PMD+SZD			1.65±0.33	0.23±0.40				
BDQ+PMD+LZD			3.28±0.65	0.34±0.41	0.00±0.00	12/15 (80)	0/14 (0)	0/20 (0)
BDQ+PMD+SZD			0.94±0.14	0.00±0.00		14/20 (70)	1/14 (7)	

78. Notably, the specification itself records that the observed differences between LZD- and SZD-containing regimens did not reach statistical significance. In the absence of statistically meaningful superiority, the Applicant cannot rely on marginal numerical variations to establish an inventive step.

79. However, in relation to the findings from the above data, the specification (internal page 20) discloses the following

"Addition of SZD significantly increased the initial bactericidal activity of BDQ+PMD (p< 0,001), rendering all mice culture-negative between 1 and 2 months of treatment. The activity of BDQ+PMD+SZD was significantly greater than that of RIF+INH+PZA after 1 and 2 months of treatment (p< 0.00.1). Addition of LZD also significantly increased the activity of BDQ+PMD (p< 0.01) and produced activity superior to that of RIP +INH+PZA after 2 and 3 months of treatment (p< 0.001). All 2-drug combinations had inferior activity compared to the 3 -drag combinations of BDQ+PMD plus SZD or LZD at 2 months (p< 0.01), confirming that each component drug contributes to the efficacy of the 3-drug combinations. However, the 3 -drug LZD-containing regimen was only superior to BDQ+LZD after 2 months of treatment. LZD-containing regimens produced higher CFU counts compared to their SZD-containing comparator regimen."

80. Significantly, the specification discloses the following (internal page with respect to the combinations of SZD+BDQ+PMD and LZD+BDQ+PMD

Relapse after treatment completion. The relapse results are displayed in Table 1. Treatment with the first-line regimen for 3 and 4 months resulted in relapse of 13 (87%) of 15 and 1 (5%) of 20 mice, respectively. The higher cure rate compared to previous examples is due to the lower than usual bacterial burden at the initiation of treatment. Consistent with the CFU count results, treatment with BDQ+PMD produced relapse results similar to the first-line regimen after 3 and 4 months but did not prevent relapse after just 2 months of treatment. However, unlike the more rapid decline in CFU counts with the 3-drug regimen containing SZD compared to LZD, the two BDQ+PMD+oxazolidinone regimens had similar sterilizing activity.

While only the difference between the SZD-containing regimen and BDQ+PMD alone was statistically significant after 2 months of treatment, both oxazolidinone-containing regimens resulted in significantly fewer relapses after 3 months of treatment compared to both BDQ+PMD and the first-line regimen.

81. It is clear from the above, that there is no difference between the effectiveness of the two triple-drug regimens i.e. SZD+BDQ+PMD and LZD+BDQ+PMD. The actual difference in effectiveness lies in the difference between the dual-drug regimens, as compared to the oxazolidinone-containing triple-drug regimens as shown in the excerpts above. In these circumstances, the substitution of one known oxazolidinone

(linezolid) for another closely related member of the same class (sutezolid) represents a routine and predictable modification that would have been obvious to the skilled person. The Applicant has not demonstrated any class-transcending or unexpected property unique to linezolid.

82. The Applicant goes on to state that "*In comparison with D3 which teaches that addition of LZD leads to hematologic and neurologic toxicity and teaches use of SZD as a better active when used alone or when combined with RIF+MXF+PZA, cannot motivate a person skilled in the art to reach the present invention, rather it teaches away*." This contention by the Applicant is extremely deceptive, because the Applicant's specification admits that the manner, in which the problems associated with neurological and haematological toxicity were dealt with, was by stopping administration of linezolid for 1 to 2 weeks. This admission not only undermines the Applicant's "composition" claim, but also undermines any claims to technical advancement. The Applicant has not, in fact, solved any problem via the claimed "composition"; rather, the avoidance of administration of one of its key drugs leads to the solving of the issue of toxicity, as shown below. In fact, D3 teaches both the use of, and composition of, a combination of drugs of the oxazolidinone class (sutezolid) + bedaquiline + pretomanid. The Applicant's contention that "there is no data of the combination of actives with BDQ in D3" is completely irrelevant in light of the above factors. The relevant portions of the Applicant's specification disclosing the stoppage of administration of linezolid is shown below:

> The inventors further discovered that linezolid can be re-administered at a lower dose after a one to two week interruption (e.g., drug or treatment holiday) based on neuropathy findings and subsequent improvement or, similarly, hematology findings. Clinical doses for pretomanid can be 200 mg qd or 100 mg qd. For bedaquiline, clinical doses can be 400 mg qd for two weeks followed by 200 mg tiw or 200 mg qd. And clinical doses for linezolid are 600 mg bid or 1200 mg qd to start.

> Provided is a pharmaceutical composition, comprising a therapeutically effective amount of each of linezolid, bedaquiline and pretomanid, and optionally pyrazinamide, or a pharmaceutically acceptable salt of each thereof, and a pharmaceutically acceptable carrier.
>
> Also provided is a method for the treatment of tuberculosis, comprising the step of administering to a patient in need thereof a therapeutically effective amount of each of linezolid, bedaquiline and pretomanid, and optionally pyrazinamide, or a pharmaceutically acceptable salt of each thereof, and a pharmaceutically acceptable carrier. In one embodiment of the invention, linezolid is removed from the treatment regimen after one to two months. In another embodiment, linezolid can be re-administered after a one to two week drug holiday.

83. Mere acknowledgement of known dose-limiting toxicity does not constitute a teaching away from the use of linezolid in combination therapy. Rather, as recognized in the art, such toxicity concerns typically motivate dose optimisation or regimen adjustment, which are routine activities for the skilled person.

84. From the above submissions, it is evident that D3 motivates a person skilled in the art towards exploring a combination of an oxazolidinone with bedaquiline and pretomanid. Significantly, the Applicant's reliance on temporary interruption of linezolid further demonstrates that the alleged advance lies in clinical management rather than in any inventive pharmaceutical composition. Such regimen adjustments were well within the ordinary skill in the art and cannot confer inventiveness on the claimed subject matter. D3 expressly identifies both TMC-207 (bedaquiline) and PA-824 (pretomanid) among preferred companion agents for use with an oxazolidinone, thereby providing a clear technical pathway toward the presently claimed combination. Further, as already demonstrated above, the claimed invention possesses no technical advancement over the combination of D3. Thus, the invention claimed in the impugned application is obvious and does not involve an inventive step over D3.

85. The averments made by the Applicant in para 55 are denied. It is submitted that the Applicant's contention that there is "*no disclosure or teaching or even hint in D1 that addition of LZD to BDQ+PZA+PMD can significantly reduce the proportion of mice relapsing after 1.5 months of treatment from 60% to 0% (p< 0.001)*" is irrelevant to claimed invention. Moreover, the Applicant has not demonstrated that the reported statistical improvements arise uniquely from the claimed three-drug combination independent of pyrazinamide. In the absence of such evidence, the asserted efficacy differences cannot be attributed to the claimed invention. This is because PZA (pyrazinamide) is an optional element in claim 1. Notably, the Applicant has not provided any dependent claim in which pyrazinamide is recited as a mandatory component corresponding to the relied-upon data. This further confirms the disconnect between the experimental evidence and the scope of protection sought. It is a settled principle that any alleged technical advance must be commensurate with the full breadth of the claims. Where the claims extend to embodiments lacking pyrazinamide, data derived solely from PZA-containing regimens cannot support inventiveness of the broader claimed subject matter. Therefore, D1 (which discloses LZD+BDQ+PMD) is relevant to the impugned invention. In assessing inventive step, the proper benchmark is the closest prior art disclosing the same core combination. D1 squarely discloses the BDQ + PA-824 + LZD regimen and therefore represents the most relevant starting point for the skilled person. The same applies to Example 2, referenced by the Applicant, where the effect of addition of LZD to BDQ+PZA+PMD was studied. Since PZA is not an essential element of the invention, the above example is not pertinent to the essential features of the invention claimed by Applicant. Any further optimisation of treatment duration, relapse rates, or dosing schedules would constitute routine clinical development once the three-drug regimen itself was known, and cannot by itself confer inventiveness. Further, it can be observed that the Applicant has not even claimed a composition (in the dependent claims) that includes pyrazinamide as an essential element. Thus, if we were to consider the Applicant's own claim set, pyrazinamide is entirely optional to the invention.

86. The averments made by the Applicant in para 56 are denied. The Applicant contends that "*on reading D1 PSITA working on anti-TB treatment would be motivated to use Bedaquiline (200 mg-400 mg tablets), Pretomanid (200 mg tablets) and Linezolid (1200 mg tablets) for six months. There is no indication in D1 about achieving the treatment*

in a shorter regimen of 1.5 months with no relapse." However, the pending claims of the impugned application are directed towards a composition, and not method of treatment. Accordingly, the Applicant's emphasis on an alleged shortened treatment period of 1.5 months is not a distinguishing technical feature of the claims and cannot confer inventiveness over D1. D1 clearly discloses the combined administration of bedaquiline, pretomanid (PA-824), and linezolid in treating drug-resistant tuberculosis, thereby teaching the very combination that forms the core of the present claims. It is well established that features relating solely to treatment duration or clinical outcome cannot impart patentability to a claim directed to a pharmaceutical composition unless such features are structurally reflected in the claimed product. Therefore, the duration of treatment is relevant to the pending claims. Even if we were to take the Applicant at his word regarding the above, it can be seen that the specification contradicts the Applicant's contentions: (1) The specification itself discloses that clinical dose for linezolid can be 1200 mg (page 4, second paragraph; page 7, second-last line; page 27, point 15). (2) The Applicant's contention of a shortened duration of treatment of 1.5 months is not relevant here, as it includes a non-essential element (PZA, pyrazinamide) in the test. The Applicant cannot rely on results obtained from a PZA-containing regimen to support claims that extend to embodiments where pyrazinamide is absent. Such evidence is not commensurate with the scope of protection sought. In any event, optimisation of treatment duration constitutes routine clinical development once the therapeutic combination is known and does not, by itself, establish an inventive step. Further, the overlap between the dosing disclosed in the specification and that taught in D1 further confirms that the claimed subject matter represents, at most, routine implementation of known therapeutic parameters. For a true assessment of the efficacy of claimed combination, only the (efficacy of) essential elements should be taken into account. D1 fully discloses all elements of the invention, and represents a direct motivation to arrive at the same. D1 therefore represents the closest prior art, and the skilled person would have had a clear expectation of success in employing the same three-drug combination in anti-TB therapy.

87. The Applicant's submissions in paragraph 57 are unpersuasive. It is submitted that D4 teaches the use of Linezolid, for the treatment of tuberculosis at a dose of 600 mg. This disclosure would have provided a clear dosage benchmark for further regimen development involving linezolid. Thus, D4 serves as a motivation to select this dose as

a starting point for TB treatment. Importantly, the Applicant acknowledges that "*D4 further discloses the sterilizing activity of Linezolid, i.e. after administration of Linezolid up to 4 months, it can be stopped for 2 week and can be started again for 18 months*" [emphasis added]. It can be seen that the teaching to interrupt the administration of Linezolid for a period of time was already known in the prior art. Management of oxazolidinone toxicity through dose interruption or treatment holidays formed part of established clinical practice at the priority date and would have been routinely implemented by the skilled clinician. Considering that the Applicant's own specification takes this same approach shows that this approach was already well-known in the art. Further, D4 teaches the administration of Linezolid along with other drugs (used in the treatment of TB), one of which is pyrazinamide. The skilled person in the TB field routinely employed multi-drug regimens to prevent resistance and enhance sterilizing activity; will find the inclusion of linezolid within combination therapy was entirely conventional. The Applicant goes on state that "*As already mentioned above the present inventors have found though there is antagonist effect of BDQ+PMD, but when LZD is added there is significant increase in activity which is unexpected*". The Opponent has already demonstrated that the Applicant's own specification does not support this contention. The specification shows that linezolid performs at best comparably to the closely related oxazolidinone sutezolid. Such comparable performance merely reflects the expected behaviour of members of the oxazolidinone class and does not evidence any unexpected or class-transcending effect. The same applies to the disclosures in examples 1 and 2. In summary, it is evident that D4 teaches important elements of the invention, as discussed above, and the invention claimed in the impugned application is obvious in light of D4. To the extent the Applicant relies on treatment scheduling or interruption strategies, such features relate to clinical regimen management rather than to any inventive pharmaceutical composition. In these circumstances, D4—read alone and in the context of the common general knowledge—clearly motivates the skilled person toward the claimed therapeutic combination. Thus the Applicant's assertion of an unexpected improvement upon adding linezolid to BDQ+PMD is not supported by the specification, which shows that linezolid performs at best comparably to the closely related oxazolidinone sutezolid. When D4 is read together with D1 and D3, the skilled person is provided with both the therapeutic components and the clinical rationale for

combining an oxazolidinone with modern anti-TB agents, rendering the claimed subject matter obvious. Accordingly, the impugned claims lack inventive step in view of D4.

88. With regard to the averments made by the Applicant in para 58, the Opponent fully denies the Applicant's contentions, including the contention that "*.....D3 teaches away from use of LZD in view of its toxic effect and sets forth to find another compound i.e. SZD which is demonstrated to have better activity than LZD*". It is submitted that a reference can be said to "teach away" only where it discourages the skilled person from pursuing the claimed path or indicates that such path would be unsuccessful. A mere acknowledgment of known dose-limiting toxicity does not amount to teaching away, particularly where the prior art continues to recognize the therapeutic utility of the compound in combination regimens. D3's acknowledgement of linezolid toxicity falls far short of this standard – the same document continues to enumerate Linezolid within the group of agents suitable for combination therapy, and its disclosure regarding dose optimization would if anything motivates the skilled person to investigate Linezolid at adjusted doses. The teaching away argument advanced by the Applicant is accordingly without legal or factual foundation. The Opponent has already elaborated in detail several times in the preceding paragraphs, that it is disingenuous for the Applicant to keep highlighting the toxic effect of LZD, when the Applicant's specification itself shows that they have not been able to solve the problem with LZD toxicity. What the specification proposes as the solution to this issue is to take a one or two week drug holiday. Management of linezolid-associated toxicity through temporary interruption or dose adjustment formed part of established clinical practice at the priority date, as also reflected in D4. The Applicant has not demonstrated any new formulation strategy or mechanistic solution to this issue. The Opponent has already pointed out that this approach is completely contradictory to the actual "composition" claims. In a true unitary pharmaceutical composition comprising fixed amounts of the active ingredients, selective interruption of only linezolid would not be feasible without affecting the remaining components. This further indicates that the alleged contribution lies in regimen management rather than in any inventive pharmaceutical composition. The actual 'invention' claimed in the impugned application is fully disclosed in documents D1 and D2. The document D3 makes it obvious that the approach involving combining an oxazolidinone anti-TB drug, with other drugs (which includes bedaquiline and pretomanid) was already disclosed in the prior art. D3 expressly

identifies both TMC-207 (bedaquiline) and PA-824 (pretomanid) among suitable companion agents for use with oxazolidinones, thereby providing a clear technical pathway toward the presently claimed therapeutic combination. Further the Applicant states that "*On the other hand D1 teaches use of Bedaquiline (200 mg-400 mg tablets), Pretomanid (200 mg tablets) and Linezolid (1200 mg tablets) for six months.*" The Opponent has already shown that the Applicant's specification itself recommends dosage of 600 mg or 1200 mg, as shown below. The overlap between the dosing disclosed in D1 and that recommended in the Applicant's own specification confirms that the claimed subject matter operates within known therapeutic parameters and does not reflect any non-obvious dosage innovation. In fact, the specification only recommends dosages of 600 or 1200 mg, not a range between 600 to 1200 mg.

> The inventors further discovered that linezolid can be re-administered at a lower dose after a one to two week interruption (e.g., drug or treatment holiday) based on neuropathy findings and subsequent improvement or, similarly, hematology findings. Clinical doses for pretomanid can be 200 mg qd or 100 mg qd. For bedaquiline, clinical doses can be 400 mg qd for two weeks followed by 200 mg tiw or 200 mg qd. And clinical doses for linezolid are 600 mg bid or 1200 mg qd to start.

> In a further embodiment, bedaquiline is at a dosage of 200 to 400 mg qd. In an alternative embodiment, bedaquiline is administered at 400 mg qd for two weeks followed by 200 mg tiw.
>
> In a still further embodiment, linezolid is at a dosage of 600 mg bid or 1200 mg qd.
>
> In another embodiment, pretomanid is at a dosage of 100 to 200 mg qd.

> 15. The pharmaceutical composition according to paragraph 1, wherein linezolid is at a dosage of 600 mg bid or 1200 mg qd.

89. Further, the contention regarding D1 disclosing (study of the) regimen of LZD+BDQ+PMD for six months is irrelevant to the claims, which are directed towards a composition. It is well established that optimisation of treatment duration constitutes routine clinical development once the therapeutic combination is known and cannot, by itself, confer inventiveness on a composition claim. Thus, none of the documents teach way, but rather teach all elements of the 'invention' claimed in the impugned application. When D1, D3 and D4 are read together, the skilled person is provided with (i) the same three-drug therapeutic combination, (ii) the motivation to combine oxazolidinones with modern anti-TB agents, and (iii) established strategies for managing linezolid toxicity, rendering the claimed subject matter obvious.

90. The Applicant cannot be allowed to avoid addressing the incongruence between the claims and the specification, where the specification clearly, and repeatedly, recommends a drug holiday with respect to linezolid. This flies in the face of the pending claims of impugned application, which clearly claim a "composition". It is more than obvious that if you have a drug "composition", you technically cannot make one component be on a drug "holiday" i.e. stopping administration of the same for a certain period of time. The Opponent humbly requests the Ld. Controller to ask the Applicant to offer a coherent explanation of this glaring discrepancy, as it completely undermines the "composition" claims of the application.

91. The averments made by the Applicant in paragraphs 59-61 are misplaced and rely on an artificial distinction.. The Applicant has repeated the same contentions herein, which have shown to be false in the preceding paragraphs, and yet for the sake of brevity the opponent is addressing them briefly. The claims are directed to a pharmaceutical composition comprising bedaquiline, pretomanid and linezolid in broadly defined amounts, and the prior art—particularly D1 and D3—already discloses the same therapeutic triad and expressly motivates combining an oxazolidinone with modern anti-TB agents including bedaquiline and PA-824. The mere presentation of known drugs in a unitary dosage form or within a broad dosage range of 1 mg to 1 g does not, without any demonstrated structural or functional distinction, confer inventiveness. It is well settled that formulation into a single dosage unit and routine dose selection fall within ordinary pharmaceutical development once the combination therapy itself is known.

92. Further, the Applicant's reliance on alleged efficacy at 1.5 months and on PZA-containing regimens is not commensurate with the scope of the claims, where pyrazinamide is optional and no specific treatment duration is claimed. The cited data therefore cannot establish any unexpected technical effect attributable to the claimed three-drug composition. On the contrary, the specification itself shows that linezolid performs at best comparably to the closely related oxazolidinone sutezolid and that toxicity is managed through known interruption strategies. When D1, D3 and D4 are read together, the skilled person is provided with the same components, the motivation to combine them, and routine clinical optimisation tools. In summary, the invention

claimed in the impugned application is obvious, and does not involve an inventive step in view of cited prior art D1-D4, and ought to be rejected on this ground alone.

Section 25(1)(f): Invention not patentable under section 3(d), 3(e) and 3(i)

93. The averments made by the Applicant in para 62-64 are denied. It is submitted that the documents D1 and D2 both disclose combination of LZD+BDQ+PMD. The invention claimed in impugned application claims the same combination of LZD+BDQ+PMD. Thus, they are plainly the same substance and therefore does not introduce any new substance in substance or effect. The mere presentation of the same known active ingredients in a unitary dosage form cannot confer patentability where the therapeutic combination itself was already publicly disclosed. It is reiterated that the specification has no data for the composition *per se.*In particular, the Applicant has not demonstrated any formulation-specific advantage—bioavailability, efficacy—arising from the alleged unitary composition. In the absence of such evidence, the claims are unsupported across their full scope. Further, the Applicant's contention with regard to the combination of LZD added to BDQ+PZA+PMD is irrelevant to the question of efficacy, as the PZA is not an essential element to the invention. It is well settled that any asserted technical advance must be commensurate with the claim breadth; data derived from a PZA-containing regimen cannot support patentability of claims that extend to embodiments lacking that component. The Applicant has not even established greater efficacy against the combination of SZD+BDQ+PMD, let alone against the exact combination disclosed in D1 and D2. In the absence of demonstrated enhancement in therapeutic efficacy, the claims fall squarely within the ambit of Section 3(d) and are liable to be rejected on this ground alone.

94. The reliance placed by the Appellant on *Allergan v. Ajanta Pharma* is misconceived. The observations in that decision are confined to the specific facts and claims before the IPAB and do not constitute a binding ratio laying down a general rule that pharmaceutical combinations fall outside the scope of Section 3(d).

95. It is submitted that in any event, the IPAB, as a tribunal constituted under the statute, lacks the authority to alter, dilute, or read down the express language of Section 3(d), including its Explanation, which unequivocally brings combinations of known substances within its ambit. The Supreme Court's binding ruling in Novartis AG *v.*

Union of India & Others [(2013) 6 SCC 1] conclusively settled that Section 3(d) requires demonstration of enhanced therapeutic efficacy, not merely enhanced physical or chemical properties over the known substance. A combination of known active agents cannot escape the scrutiny of Section 3(d) merely by presenting them in a new dosage form unless a clear and demonstrable improvement in therapeutic efficacy id established over the individual components or prior combinations. The Applicant has not met this burden. The data in the specification does not demonstrate enhanced therapeutic efficacy attributable to the claimed composition per se, distinct from the already known activity of BDQ+PMD+LZD as a therapeutic regimen. The mere formulation of known active agents into a unitary dosage form does not constitute enhance efficacy within the meaning of Section 3(d) as interpreted by the Supreme Court. Any tribunal-level observation that seeks to dilute or bypass this statutory requirement cannot prevail over the plain language of the Act or binding Supreme Court precedent. Accordingly, the Appellant's attempt to rely on *Allergan v. Ajanta Pharma* as laying down a blanket exclusion of combinations from Section 3(d) is legally unsustainable.

96. The averments made by the Applicant in para 65 are denied. It is submitted that the specification shows no data to distinguish the claimed 'composition' from the already-disclosed combination in D1 and D2. In fact, no 'composition' has actually been disclosed in the specification. No concrete composition example of a 'composition' of LZD with PMD and BDQ is disclosed in the specification. Not a single working example of the claimed pharmaceutical composition has been provided in the specification. The Applicant's repeated reference to the data regarding addition of LZD to BDQ+PZA+PMD is not relevant, for the reasons already discussed above. In these circumstances, the claimed subject matter represents, at best, a mere admixture of known drugs without any demonstrated synergistic or technical advantage attributable to the claimed composition. Thus, it is evident that the claimed invention falls squarely within the ambit of section 3(e) of the Act, and ought to be rejected on this ground alone.

97. It is further submitted that the Applicant's own characterization of the invention as one relating to chemically stable combinations, is unsupported by a single stability study or data, or accelerated stability testing result anywhere in the specifications. A claimed

technical feature, particularly one that forms a part of the stated inventive contribution, must be enabled by adequate disclosure. Where the applicant explicitly claims chemical stability as a property of the composition, the complete absence of any stability data renders the specification fatally insufficient under Section 25(1)(g). The skilled person would be unable to prepare a composition meeting the claimed stability requirement without undue experimentation, given that no formulation example, excipient system or stability protocol is described.

98. The averments made by the Applicant in para 66-67 are denied. The Opponent's contention that the invention falls under the ambit of section 3(i) is based on what the application actually discloses. It has already been shown how the disclosure in the specification (solving of a problem, data, results) runs counter to the composition claims. The actual invention is, in fact, nothing but a method of treatment, based on the recommendation for linezolid to be interrupted in order to deal with potential neurological and haematological toxicity. The application should thus be treated as a method of treatment in keeping with the above, and ought to be rejected under section 3(i).

Section 25(1)(g): Insufficiency

99. The averments made by the Applicant in para 68 are denied. It is submitted that, nowhere does the specification demonstrate how to arrive at the composition claimed in the application. There is not a single example where any additive (excipient), method to produce, or dosage form of the composition is shown. In particular, the specification fails to disclose any specific excipient system, formulation process, or manufacturing method that would enable a person skilled in the art to prepare the claimed unitary dosage form without undue experimentation. No ratio(s) between the drugs, and any excipient(s), is shown. It bears repeating that if the claim is to a composition, the examples ought to demonstrate a composition, which has not been shown.

100. Further, the alleged "unitary dosage form" is nowhere meaningfully defined or technically enabled in the specification. The mere listing of conventional dosage forms such as tablets, granules or liquids does not amount to an enabling disclosure of a fixed multi-drug unit, particularly in view of the well-known formulation challenges associated with combining multiple anti-TB agents. The specification is completely

silent on how the three actives—having different dosing requirements and toxicity profiles—can be co-formulated in a single stable dosage unit.

101. It bears emphasis that the Applicant's own disclosure contemplates interruption of linezolid therapy for one to two weeks to manage toxicity. Such selective discontinuation is fundamentally inconsistent with a true unitary dosage form containing all three drugs in fixed proportions, since in a genuine fixed-dose unit the components cannot be independently stopped without affecting the entire regimen. This internal inconsistency further demonstrates that the specification does not teach a workable unitary composition but merely describes a treatment regimen. In the absence of any enabling formulation disclosure, working composition example, or technically credible unitary dosage teaching, the skilled person is left to engage in undue experimentation. Thus, the application falls squarely within the ambit of section 25(1)(g) and ought to be rejected on this ground alone.

102. It is important to note that the WHO, in its 2022 Consolidated Guidelines on Tuberculosis Treatment, recommended the BPaL regimen (bedaquiline-pretomanid-linezolid) as a standard short-course treatment for drug-resistant. Since then, India has implemented this regimen under the National TB Elimination Programme (NTEP). It is administered programmatically as an approximate six-month treatment regimen. This real-world clinical practice underscores that the regimen is implemented as a therapeutic schedule rather than as a single fixed unitary composition. The Applicant has provided no evidence demonstrating that the claimed unitary dosage form is either standard in the art or practically adopted in TB treatment protocols. Accordingly, the claims attempt to capture a formulation concept that is neither enabled in the specification nor reflected in established treatment practice. The grant of the impugned patent over a composition that is now the backbone of India's National TB treatment Programme would have direct and severe consequences for procurement, generic supply and affordability. The Controller is respectfully requested to consider the public health implications of these applications, and implement the patentability requirements of Section 25 in favour of the public interest.

Section 25(1)(h): Non-disclosure of information required u/s 8

103. The averments made by the Applicant in para 69-70 are denied.

104. It is submitted that in light of preceding paragraph as presented that relate to the various grounds raised in the pre-grant opposition, the present impugned patent application lacks inventive step, falls under the purview of section 3(d), lack of sufficiency of disclosure and non-compliance of section 8 requirements. Therefore, the present impugned patent application should be rejected.

Dated this 12th day of May 2026



MARIAM SADAF (IN /PA – 5231)
OF RAJESHWARI AND ASSOCIATES
AGENT FOR THE OPPONENT

TO,
THE CONTROLLER OF PATENTS
THE PATENT OFFICE, NEW DELHI

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