Title of the Technology: A Novel Liposomal Amphotericin B (**Cat-LAmB**) for Treatment of Visceral Leishmaniasis and Fungal Infections

Background/Problem to be addressed: Amphotericin B (AmB) has been the mainstay and Gold Standard drug for treatment of invasive fungal infections, such as cryptococcal meningitis (the most common form of fungal meningitis), 3 important endemic mycoses (namely, blastomycosis, histoplasmosis, and coccidioidomycosis), candidemia and invasive candidiasis (the most common forms of nosocomial fungal disease), and invasive aspergillosis (the most common form of invasive mould disease), talaromycosis and mucormycosis. FDA has also approved this for the treatment of leishmaniasis infections (including visceral leishmaniasis and cutaneous leishmaniasis). However, overwhelming nephorotoxicity, liver toxicity and hypokalemia has led to evolving different liposomal formulations. Though, the lipid-based formulations of amphotericin B, have largely replaced amphotericin B deoxycholate due to their improved tolerability, they fail to treat severe invasive fungal infections such as candidiasis. These problems emphasize the need for better liposomal AmB with immunomodulatory activities to treat such complicated cases. We have developed a cationic liposome with phosphatidylcholine (PC) and stearylamine (SA) having inherent leishmanicidal activity. This prompted us to entrap AmB into these liposomes and check their efficacy against both fungal and visceral leishamaniasis (VL) infections. Single shot therapy with this formulation provided complete cure and long lasting protection through immunomodulation against disease resurgence and reinfection with least toxicity in VL. Interestingly, our studies with this formulation demonstrated very potent antifungal efficacy both in invitro and invivo in comparison with Ambisome. Thus, this formulation has prospects for the treatment of severe and complicated invasive fungal infections making it a lucrative commercial product. Moreover, for better stability lyophlisation was necessary for which we standardised the lyophilisation conditions and were able to successfully lyophilise the liposomal AmB formulation.

Scientific merit /Technical highlights over existing solutions: The combination of PC-SA with AmB provides the immunomodulatory effect comparable with that of the AmB deoxycholate with least toxicity. Although Ambisome reduces the toxicity, the immunomodulatory effects of AmB is masked. The single shot treatment with Cat-LAmB offers enhanced efficacy, reduced toxicity, and improved pharmacokinetics compared to conventional anti-leishmanial and antifungal therapies such as amphotericin B deoxycholate, AmBisome and Fungisome.

Societal Relevance: Application of AmB in PC-SA can prove to treat complicated fungal infections such as candidiasis and mucormycosis. Moreover, this formulation provided complete cure of visceral leishmaniasis and resistance to relapse and reinfection, the two major problems prevalent worldwide. It can also prevent chances, if any, of resistance development against the drug.

Market size/Commercial PotentiaL: Invasive fungal infections such as candidiasis, aspergillosis, cryptococcosis and complete cure of visceral leishmaniasis and resistance to relapse and reinfection.

Current stage of Development (Technology Readiness Level (TRL): The product has been lyophilised. The next stage for further development of Liposomal AmB is to undertake pre-clinical development and regulatory toxicology in compliance with GMP/GLP Guidelines. **Drugs category TRL 4**

USP of technology/Competitive products and advantages over competition: Cat-LAmB delivers a potent punch against a broad spectrum of fungal pathogens and leishmaniasis in single dose treatment reducing toxicity of Amp B and overall treatment costs.

Extent of indigenisation & import substitution, if applicable: Two major components phosphotidylcholine and stearylamine are imported which are not expensive and Amphotericin B is manufactured in India Thus low capital investment and labour cost.

Scope for overseas market penetration related to the Technology: Liposomal amphotericin B presents an enhanced efficacy, and reduced toxicity profile to meet the global demand for leishmanianiasis and antifungal therapies, particularly in regions with high incidences of leishmanianiasis and fungal infections and limited access to advanced treatments.

High Resolution image of the technology prototype, if developed:

Number of samples tested/validated: Preclinical studies have been done with promising results

Cost of Sampling/testing: The estimated cost of single dose therapy will be 45000 INR for leishmaniaisis and 70000 INR for fungal infections per person reducing the cost to 1/3rd of existing costs.

Studies conducted for getting regulatory approval, if any: NO
Any other information relevant for evaluating the technology: NO
Novelty, IP and Competitive Landscape and IP/Patent Applications, filed/granted: Indian Patent No 264798 has been granted

Details of PIs, funding agency and third party, if involved in development: Prof Nahid Ali, CSIR.