Document prepared by Nerve Center of TFORD, Venture Center, Pune

Task Force on Repurposing of Drugs (TFORD) for COVID19

S&T Core Group on COVID19 constituted by PSA to GoI

Molecule Brief: Sepsivac

Ref: TFORD/MB/024	**Date:** 18 June 2020
About this document: *This document summarizes information available on drug candidates for COVID19. One Molecule Brief document covers one candidate at a time.*	
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1. Summary Information on Sepsivac

Information About the Candidate for Approved Indication(s)	
Common Name of Drug	Mycobacterium w (heat killed) injection (Mw)/ *Mycobacterium indicus pranii*
Brand Name	Sepsivac
Category/ Type	Immunomodulator
Drug Bank ID/Link	Biologic
Mode of Action	• Shares a number of common B and T cell determinants with *Mycobacterium leprae* and *Mycobacterium tuberculosis*. Elicits Th1, Th2 type cell mediated lympho-proliferative immune response, resulting in the release of type-1 cytokines, predominantly IFN-γ, and thereby propagates cell-mediated immune responses. https://www.cadilapharma.com/sepsivac-sepsis-saviour-cadila/ • Shares an immunogenic determinant with prostate specific antigen (PSA) and may induce host T-cell responses against tumor cells expressing PSA. • https://www.cancer.gov/publications/dictionaries/cancer-drug/def/mycobacterium-w
Therapeutic Target	Th1 Th2 cells
Is action Host or Virus directed?	Host
Currently Approved for which Indication(s)	• Leprosy • Non-Small Cell Lung Cancer (NSCLC) • Sepsis
Approved Dose	0.5×10^9 cells/0.1 ml • Leprosy: First dose: 2 injections of 0.1 ml, Second dose: 0.1ml injection once avery 3 months for 2 years • NSCLC: 0.1ml injection per site • Sepsis: 3 injections of 0.1ml 1 day each at 3 different sites for 3 days
Route of Administration	Intradermal injection
Safety Profile of drug (dose range in	Data not available

which it has been tested to be safe in humans)	
Adverse events/Side effects reported at the current approved dose	Injection site erythema and ulceration, keloid formation. For NSCLC - anemia, leucopenia, neutropenia
Reported Drug-Drug Interactions	None *(Clinicians need to note relevant drug-drug interactions depending on nature of use)*
Link to Datasheet	https://www.cadilapharma.com/sepsivac-sepsis-saviour-cadila/
Current TRL level of the Drug	TRL 9; Approved drug
Has the drug been repurposed for any other indication before?	No
Is the Drug being sold in India?	Yes
Indian Manufacturer(s)	Cadila Pharmaceuticals
International Manufacturer(s)	Data not available
Cost of the Drug in India	5303/- per dose
Information About the Candidate for COVID-19	
Repurposing Claim	New Indication (COVID-19) + New Dose (not confirmed)
Rationale for Repurposing for COVID19/MoA?	• Clinical studies with Mw has shown that is has immune-modulatory effects in Sepsis, TB, HIV, and HPV patients. Key observations: • Mw is shown to be effective in clinical resolution of Severe Sepsis caused due to gram negative bacteria. https://www.cadilapharma.com/sepsivac-sepsis-saviour-cadila/ • Mw is also shown to be effective in achieving clinical and virologic clearance for HPV in patients with external anogenital warts. https://jamanetwork.com/journals/jamadermatology/article-abstract/1893936 http://www.ijdvl.com/article.asp?issn=0378-6323;year=2019;volume=85;issue=4;spage=355;epage=366;aulast=Chandra • Mw is shown to be effective as an adjunct therapy in TB, where it results in higher curative rates and a significant reduction in the time to sputum conversion in patients with a high bacterial load. https://www.sciencedirect.com/science/article/pii/S1878331710600204
Proposed use as Primary or Adjuvant?	Primary
Pre-Clinical Data available for COVID-19	Data not available
Status of Clinical Trials	3 Ongoing Trials – 2 in India
Trial Details	See table below

Trial ID/Link	Type of Trial	No. of patients	Drug Combination/Dose/ Stage of Disease	Primary and Secondary Measures	Has data from the trial been published? (Yes/No)

NCT04347174 CTRI/2020/04/024846	Randomized, blinded, two arms, active comparator controlled, clinical trial	40	Mw suspension, heat killed Dose: 0.3 ml (0.1ml x 3 Injection) of intradermal Mw for 3 consecutive days + Standard therapy of COVID-19 Stage: Critically ill adult Covid-19 positive patients (clinical/confirmed)	Primary Outcome: SOFA scores, 7-category ordinal scale that ranges from 1 to 7. Secondary Outcome: All-cause mortality, Incidence of AE / SAE or event of clinical significance, SARS-CoV-2 detectable in nasal or oropharyngeal (OP) sample, ICU length of stay, duration of hospitalization and mechanical ventilation, clinical improvement, time from treatment initiation to death	No
NCT04353518 (Prophylaxis)	Randomized, double-blind, two arms, placebo controlled, clinical trial	4000	Mw suspension, heat killed Dose: Dose 1 at Day 0: 0.2 ml (0.1 ml x 2 injection) of intradermal Mw in two divided doses. Dose 2 at Day 15 after the first dose: 0.1 ml injection of intradermal Mw administered. Stage: Healthy subjects in contact with covid19 patients	Primary Outcome: Number of subject acquiring COVID-19 infection Secondary Outcome: Incidence of Adverse Event and Serious Adverse Event (safety and tolerability), Number of subject developing Upper Respiratory Tract Infection (URTI) symptoms, Number of subject developing severe COVID-19 infection based on ordinal scale	No
NCT04358809 CTRI/2020/05/025271	Randomized, double-blinded, two arms, placebo controlled, clinical trial	480	Mw Suspension, heat killed Dose: 0.3 ml (0.1ml x 3 Injection) of intradermal Mw for 3 consecutive days + Standard therapy of COVID-19 Stage: Hospitalized but not critically ill Covid-19 positive patients (ordinal scale score of 3)	Primary Outcome: Number of patients with increased disease severity Secondary Outcome: Incidence of adverse events and serious adverse events (Safety), Number of COVID-19 patients discharged from hospital, transfer to ICU, reduction in disease severity by 1 ordinal scale; Number of symptom free patients	No
ChiCTR2000030016	Parallel Prospective Double blinded	60	Inhalation of inactivated Mycobacterium vaccae injection	Cause-specific mortality, 30-day cause-adverse events, 30-day all-cause mortality, co-infections, Time from severe and critical patients to clinical improvement, Others (liver function, kidney function, myocardial enzyme)	No

Key Data from Clinical Trials	No published data
TRL Level for COVID19	TRL> 7 (Ph III trial)
Other Key	None

References	

IP Status

Status/ Molecule	Sepsivac
Pending applications	1235/MUM/2007 Title: Mitogen activated protein kinase modulator Assignee: Cadila Pharmaceuticals Filing date: 28/06/2007 Publication date: 19/06/2009 Status: FER issued on 26/02/2014 1929/MUM/2011 Title: Cancer antigen Assignee: Cadila Pharmaceuticals Filing date: 05/07/2011 Publication date: 13/12/2013 Status: Reply to FER issued on 11/02/2019 submitted by the Applicant. 505/MUM/2005 Title: Vaccine adjuvants Assignee: Cadila Pharmaceuticals Filing date: 25/04/2005 Publication date: 06/03/2009 Status: Request for examination filed on 07/07/2009/. No further updates on Indian patent site. 555/MUM/2011 Title: Therapeutic cancer vaccine Assignee: Cadila Pharmaceuticals Filing date: 28/02/2011 Publication date: 31/08/2012 Status: Pending (Reply to FER filed on 10/09/2019)
Approved and Active applications	297641 Title: A process for the preparation of a pharmaceutical composition of killed cells with substantially retained immunogenicity Assignee: Cadila Pharmaceuticals Filing date: 19/02/2010 Grant date: 14/06/2018 Expected expiry date: 19/02/2030
Expired or Lapsed application or examination request not filed	50/MUM/2001 Title: Immnomodulator for the management of human immunodeficiency virus (HIV) disease/infection Assignee: Cadila Pharmaceuticals Filing date: 17/01/2001 Publication date: 08/06/2007 Status: Examination request not filed 47/MUM/2001 Title: The process of manufacturing immunomodulators to treat HIV disease infection Assignee: Cadila Pharmaceuticals Priority date: 17/01/2001 Publication date: 12/08/2005 Status: Examination request not filed 49/MUM/2001 Title: The process of manufacturing immunomodulators to treat HIV disease infection Assignee: Cadila Pharmaceuticals Filing date: 17/01/2001 Publication date: 12/08/2005 Status: Examination request not filed 1167/MUM/2001 Title: The method of treating cancer Assignee: Cadila Pharmaceuticals Filing date: 10/12/2001 Publication date: 01/06/2007 Status: Examination request not filed 1166/MUM/2001 Title: The process of manufacturing a pharmaceutical composition useful for management of cancer Assignee: Cadila Pharmaceuticals

	Filing date: 10/12/2001 Publication date: 04/05/2007 Status: Examination request not filed 81/MUM/2002 Title: Method of providing prophylaxis for tuberculosis in hiv positive individuals Assignee: Cadila Pharmaceuticals Filing date: 20/01/2002 Publication date: 01/09/2006 Status: Examination request not filed 80/MUM/2002 Title: Process for preparing a pharmaceutical composition for immunity against tuberculosis in HIV positive individuals Assignee: Cadila Pharmaceuticals Filing date: 29/01/2002 Publication date: 16/06/2006 Status: Examination request not filed 236/MUM/2002 Title: The process of manufacturing a pharmaceutical composition useful for management of tuberculosis Assignee: Cadila Pharmaceuticals Filing date: 08/03/2002 Publication date: 08/06/2007 Status: Examination request not filed 235/MUM/2002 Title: The method of treating tuberculosis Assignee: Cadila Pharmaceuticals Filing date: 08/03/2002 Publication date: 01/09/2006 Status: Examination request not filed 246/MUM/2002 Title: Use of Mycobacterium w in treatment of bronchial asthama Assignee: Cadila Pharmaceuticals Filing date: 13/03/2002 Publication date: 01/09/2006 Status: Examination request not filed 247/MUM/ 2002 Title: Process for manufacturing pharmaceutical composition comprises of Mycobacterium w in the treatment of bronchial asthama attack Assignee: Cadila Pharmaceuticals Filing date: 13/03/2002 Publication date: 01/09/2006 Status: Examination request not filed 1931/MUM/2006 Title: Poly-TLR antagonist Assignee: Cadila Pharmaceuticals Filing date: 23/11/2006 Publication date: 25/07/2008 Status: Abandoned u/s 21 (1) 509/MUM/2007 Title: P38 Inhibitor Assignee: Cadila Pharmaceuticals Filing date: 20/03/2007 Publication date: 21/11/2008 Status: Examination request not filed 92/MUM/2011 Title: Pharmaceutical composition for Non-Small Lung Cancer Assignee: Cadila Pharmaceuticals Filing date: 11/01/2011 Publication date: 17/08/2012 Status: Examination request not filed

2. Background information

About TFORD-COVID19
The Principal Scientific Advisor to the GoI, Dr K VijayRaghavan, has constituted a S&T Core Group on COVID19. Under the aegis of the S&T Core Group on COVID19, a Task Force has been constituted focused on Repurposing of Drugs for COVID19 (in short "TFORD-COVID19"). The Task Force is being coordinated by Dr V Premnath, Head, NCL Innovations at CSIR-NCL and Director, Venture Center and Dr Anurag Agarwal, Director, CSIR-IGIB. The Nerve Center for the Coordination is located be at Venture Center, Pune (located in the campus of CSIR-NCL).

Credits
Editor: Dr Priya Nagaraj; Contributors: Dr Priya Nagaraj, Dr Vidula Walimbe, Dr Smita Kale, Dr Kirtee Wani, Dr Tejas Shah, Dr Mugdha Lele, Mr Navnath Kadam, Dr Manisha Premnath, Dr Premnath V; Information also contributed by Dr Gopakumar Nair, GNAS and GnanLex.

About Advisory Group
The Nerve Center at TFORD-COVID19 has constituted an inter-disciplinary Advisory Group. This Advisory Group reviews the information compiled by the Nerve Center, provides suggestions on data, information sources, organization of data etc. while also providing inputs to refine the analysis and create a structured information base to support decision-making. The Advisory Group also provides expert input and opinions on certain selected points where experience-based inputs are needed. The members of the Advisory Group for each Discussion Paper are listed at https://nclinnovations.org/covid19/teams/ .

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