Annexure – I

Brief details of progress made by CSIR in the development of affordable pharmaceutical technologies and treatment for major diseases

CSIR- Central Drug Research Institute (CSIR-CDRI), Lucknow

The CSIR-Central Drug Research Institute has been functioning with a vision to drive discovery and development of cutting-edge and affordable healthcare technologies. 13 new drugs/products have been developed/discovered by CSIR-CDRI till date towards reaching the national and societal needs of the country. Apart from the drugs, CSIR-CDRI developed several diagnostics for early detection of common diseases. CSIR-CDRI has developed more than 80 cheaper and more convenient technologies for known drugs at pilot plant level and licensed to Industry. The significant progress achieved in the last 5 years is as follows:

- **Technology for Fluorescent Dyes and Quenchers for RT-PCR based Diagnostic Kit for COVID-19**: Under the Indian Government initiatives for 'Atmanirbhar Bharat', CSIR-CDRI team developed indigenous technology of fluorescent dyes and quenchers for Taqman like probe based RT-PCR detection of COVID-19. The commercial fluorescent dyes and quenchers are imported and very costly. This Indian technology of fluorescent dyes and quenchers significantly reduce the dependency on the supply of reagents and kits from foreign manufacturers. Technology was licensed to Biotech Desk Private Limited, Hyderabad.
- **Technology for Corneal Targeted Ophthalmic Formulation of Amphotericin B for fungal keratitis:** CSIR-CDRI has developed a prototype formulation for antifungal drug to enhance ocular bioavailability and reduce dose/dosing frequency. In preclinical evaluation, the formulation exhibited rapid resolution of infection. CSIR-CDRI and Cipla Limited signed an agreement to jointly develop this novel ophthalmic formulation for fungal keratitis.
- **A Standardized Fraction of *Picrorhiza kurroa* for the Treatment of Non Alcoholic Fatty Liver Disease (NAFLD):** The non-alcoholic fatty liver disease is silent epidemic in India with incidence of 9-39%. To date, there are very few FDA approved orally active drugs available for NAFLD. A research team from the CSIR-CDRI, Lucknow and CSIR-IHBT, Palampur have has standardized the candidate drug, Picroliv derived from the plant *Picrorhiza kurrooa*, also known as Kutki. This plant grows in the Himalayan region of northwest India. CSIR-IHBT has developed the high yielding varieties and cultivation techniques for *Picrorhiza kurrooa and also standardised the extraction process.* CSIR-CDRI has established the pre-clinical efficacy and safety in various regulatory animal model systems. Currently, CSIR-CDRI is coordinating the clinical trial at 6 medical institutions with budgetary support from the ICMR and CSIR. Technology was licensed to Themis Medicare Limited, Mumbai.
- **TaqMan-like Probe Based RT-PCR Detection kit for Arboviral Infections (Dengue, Chikungunya, Zika):** During post-monsoon season, there is an increased emergence of arboviral infections and co-infection(s) such as Dengue, Chikungunya and Zika in Asia and Indian subcontinent. The current bottleneck in diagnosis is the cross-reactivity of antibodies leading to false negative results and individual tests are costly and time consuming. Considering the unmet need, the CSIR-CDRI team has developed TaqMan-like probe based RT-PCR kit, a cost-effective and reliable diagnostic for detection of Dengue, Chikungunya and Zika

simultaneously. The technology was licensed to M/s Mylab Discovery Solutions Private Limited (MDSPL), Pune, India for Commercialization

- **Standardized fraction enriched with chebulinic acid (N-012-0001) for the management of Benign Prostatic Hyperplasia:** A licensing agreement with Himalaya Wellness, Bengaluru to commercialize the Standardized fraction of *Terminalia chebula* for the treatment of benign prostatic hyperplasia (BPH) has been signed.

CSIR-IMTECH

CSIR-IMTECH's progress in developing affordable pharmaceutical technologies, therapeutics, and diagnostics has focused heavily on several diseases as listed below:

- **Infectious Diseases:** Tuberculosis (TB) Therapeutics & Diagnostics Tuberculosis remains a massive healthcare burden in India. IMTECH has spearheaded several projects targeting drug-resistant TB strains and has tied up with pharma companies for developing a drug for treatment of tuberculosis. IMTECH developed a rapid, wash-free, fluorescence-based probe that can detect live Mycobacterium tuberculosis in under 15 minutes.

- **Vaccine Infrastructure: Affordable Carrier Proteins**

  - Gram-Scale CRM197 Carrier Protein: Conjugate vaccines (like those for pneumonia and meningitis) rely on a highly expensive carrier protein called CRM197 to trigger a strong immune response. Imported CRM197 can cost up to thousands of dollars per milligram, bottlenecking local vaccine production.
  - IMTECH developed a high-yielding, soluble recombinant clone and bioprocess to produce tag-free CRM197 in E. coli at a gram scale.

- **Addressing Antimicrobial Resistance (AMR) & Pathogens:** With the rise of "superbugs" rendering standard antibiotics useless, the institute has developed several innovative clinical alternatives:
- IMT-P8 Topical Peptide Delivery: To tackle Methicillin-resistant Staphylococcus aureus (MRSA) and severe skin infections, CSIR-IMTECH designed a cell-penetrating peptide (IMT-P8). When paired with older, hydrophobic, FDA-approved antibiotics, IMT-P8 dramatically increases their absorption rate across the skin.
- Metallo-Beta-Lactamase Inhibitors: IMTECH's medicinal chemistry divisions are patenting novel chemical scaffolds (such as Dihydrochromeno-pyrrole compounds) to inhibit metallo-beta-lactamases. These compounds prevent bacteria from destroying carbapenems (the last-line class of antibiotics), restoring the potency of standard, affordable therapies.

- **Peptide-based therapeutics against Parkinson's disease:** CSIR-IMTECH has made a breakthrough in neurodegenerative disease research by developing a cell-penetrating peptide-based therapeutic designed to halt the progression of Parkinson's Disease (PD). This technology addresses the root cellular cause of Parkinson's rather than just offering symptomatic relief. Parkinson's disease is characterized by the abnormal clumping of a protein called α-synuclein into toxic amyloid aggregates (known as Lewy bodies) within the dopaminergic neurons of the brain, leading to cell death and motor dysfunction. IMTECH's technology relies on a specially screened, blood-brain barrier (BBB)-permeable cell-penetrating peptide (such as Penetratin and its derivatives) designed to block this aggregation process.

CSIR-IGIB

Pharmacogenomics: CSIR-IGIB is the lead for pharmacogenomics initiative in GenomeIndia. The institute's analysis reveals extensive pharmacogenomic (PGx) diversity, capturing 2339 of 4245 cataloged variants across 82 populations and 31 of 34 Very Important Pharmacogenes. The unique PGx profiles reported by CSIR-IGIB emphasize the need for population-specific guidelines to optimize drug efficacy and safety.

Sequencing and Research Infrastructure for Next-Generation Sequencing (NGS): CSIR-IGIB houses a dedicated facility equipped with high-throughput platforms, including Illumina NovaSeq, NextSeq and MiSeq, to support human whole-genome, transcriptome, and metagenomic sequencing projects. CSIR-IGIB has contributed immensely during the COVID pandemic by sequencing thousands of COVID genomes. CSIR-IGIB has made major contributions to the GenomeIndia Program, which aims to catalog genetic variations in the people of India by sequencing 10,000 Indian genomes.

Diagnostic and Therapeutic Development: CSIR-IGIB spearheads the Genomics for Understanding Rare Diseases India Alliance Network (GUaRDIAN). This network is heavily involved in decoding the genetic basis of rare Mendelian disorders, neurodegenerative conditions, and metabolic diseases on discovery module. While GOMED programme catered to delivering rare disease diagnostics on cost effective manner by targeted screening in a PanIndia approach. At the institute have developed over 300 genetic diagnostics for rare disorders.

Population Genomics: Through the IndiGen program and GenomeIndia, CSIR-IGIB sequenced thousands of Indian genomes to map population-specific genetic variations, creating resources like the Indigen database and GenomeIndia database to support precision medicine and clinical interpretation

BIRSA-101 gene-editing therapy for Sickle Cell Disease: CSIR-IGIB has translated its indigenous Engineered FnCas9 CRISPR gene-editing technology into BIRSA-101, India's first indigenous gene-editing therapy for Sickle Cell Disease. The technology has been licensed to Serum Institute of India Pvt. Ltd. for further development, regulatory advancement, manufacturing and commercialization, representing a major milestone in the translation of publicly funded research into an advanced therapeutic for public healthcare.

FELUDA (FnCas9 Editor Linked Uniform Detection Assay), an indigenous CRISPR-based paper-strip diagnostic for COVID-19, was successfully translated from laboratory research to public healthcare through a technology licensing partnership with Tata Sons, leading to commercialization of the

technology for rapid and affordable COVID-19 testing in India. The technology subsequently formed the basis of the Tata MD CHECK diagnostic platform.

Engineered FnCas9 technology for genetic material modification (CRISPR-based gene-editing platform) has been licensed to industrial partners, including Serum Institute of India Pvt. Ltd., CrisprBits Pvt. Ltd., and East Ocyon Bio Pvt. Ltd., to support the development and commercialization of indigenous gene-editing therapeutics and advanced healthcare products.

IndiGenome Allele Frequency Database, an indigenous genomic knowledgebase developed by CSIR-IGIB, has been licensed to Indus Health Plus Pvt. Ltd., Semantic Web India Pvt. Ltd., and HaystackAnalytics Pvt. Ltd. for development of genomics-based diagnostics and precision medicine applications.

Molecule (SCHL1)-mediated suppression of telomerase, a potential oncology-related technology, has been licensed to Rejuvas Biotech India Pvt. Ltd. for further research, development, and commercialization

India's first GMP-compliant facilities: CSIR-IGIB has also established one of India's first GMP-compliant facilities for CRISPR-based gene therapy, enabling translation of laboratory discoveries into clinical trials for sickle cell disease and rare genetic disorders

CSIR-IICT

CSIR-IICT has made significant progress in developing affordable pharmaceutical technologies, indigenous manufacturing processes, and therapeutic candidates for major diseases. Major achievements include:

- Bempedoic Acid- Cholesterol Lowering Agent
- Nicergoline Intermediate- is an ergoline derivative with vasodilatory, antiplatelet, and α1-adrenergic blocking properties.
- Tapentadol- is a centrally acting analgesic used for the management of moderate to severe pain.
- Lipoic acid- It has antioxidant, antidiabetic, and nutritive applications.
- TLR 7/8 agonist molecule- Synthesized with an imidazoquinoline framework (IMDG) act as an advanced vaccine adjuvant used in COVAXIN (Bharat Biotech)
- Favipiravir-It is a broad-spectrum antiviral prodrug originally developed for influenza that was repurposed during the COVID-19 pandemic to target the viral RNA-dependent RNA polymerase.

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