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: Favipiravir

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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 Favipiravir

Information About the Candidate for Approved Indication(s)	
Common Name of Drug	Favipiravir (Synonyms- Favilavir, Fapilavir)
Brand Name	Avigan in Japan
Category/ Type	Antiviral
Drug Bank ID/Link	DB12466 https://www.drugbank.ca/drugs/DB12466
Mode of Action	Pyrazinecarbox amide derivative viral RNA polymerase inhibitor. It is a prodrug. Host cell enzymes (cellular kinases) convert Favipiravir into Favipiravir ribofuranosyl phosphate, a form that inhibits virus polymerase without affecting host cellular RNA or DNA synthesis. https://drugs.ncats.io/drug/EW5GL2X7E0
Currently Approved for which Indication(s)	Influenza (Approved in Japan)
Approved Dose	Day 1: 1600 mg twice daily Days 2 through 5: 600 mg twice daily https://drugs.ncats.io/drug/EW5GL2X7E0
Route of Administration	Oral
Safety Profile of drug (dose range in which it has been tested to be safe in humans)	Doses ranging from 30-1600mg was tested in Clinical Studies https://www.pmda.go.jp/files/000210319.pdf https://www.pmda.go.jp/files/000210319.pdf
Adverse events/Side effects reported at the current approved dose	Increase in Uric acid level, Teratogenic
Reported Drug-Drug Interactions	Reported with acetaminophen (inhibitory) and Oseltamivir (synergistic)
Link to Datasheet	https://www.pmda.go.jp/files/000210319.pdf
Current TRL level of the Drug	TRL 9; Approved Drug
Has the drug been repurposed for any other indication before?	Was given in 2014 and 2016 by Japan to West Africa and Guinea respectively to treat Ebola patients. Not much data available NCT02329054- Efficacy of Favipiravir Against Ebola (JIKI) NCT02662855- Efficacy of Favipiravir Against Severe Ebola Virus Disease

Is the Drug being sold in India?	No
Indian Manufacturer(s)	Cipla reported to be pursuing it https://www.expresspharma.in/latest-updates/csir-iict-ties-up-with-cipla-to-develop-anti-covid-19-drug/
International Manufacturer(s)	Fujifilm Toyama Chemical: Japan
Information About the Candidate for COVID-19	
Repurposing Claim	New Indication (COVID-19) + New Dose (not confirmed)
Rationale for Repurposing for COVID19/MoA?	Known anti-viral activity. It has been revealed that SARS-CoV-2 has a genome sequence that is 75%–80% identical to that of SARS-CoV and MERS. Since it has been successfully used in SARS-CoV it has been evaluated for its efficacy against SARS-CoV-2.
Proposed use as Primary or Adjuvant?	Primary
Pre-Clinical Data available for COVID19	As a prodrug, FPV effectively inhibits SARS-CoV-2 infection in Vero E6 cells (half maximal effective concentration (EC_{50}) = 61.88 μmol·L^{-1}, half-maximal cytotoxic concentration (CC_{50}) > 400 μmol·L^{-1}, selectivity index (SI) > 6.46) https://www.nature.com/articles/s41422-020-0282-0
Status of Clinical Trials	• Ongoing (See details below)
Number of Trials	8 Ongoing trials (Ph II & Ph III) ChiCTR2000029996 received approval as an investigational therapy in China ChiCTR2000029548 ChiCTR2000029544 ChiCTR2000029600 ChiCTR2000030113 ChiCTR2000030254 NCT04310228 NCT04319900
Dose being tested for COVID-19?	On the 1st day, 1600mg each time, twice a day; from the 2nd to the 7th day, 600mg each time, twice a day. Oral administration, the maximum number of days taken is not more than 7 days.
Countries where Clinical Trials are being/been done	China
Key Data from Clinical Trials	Data not available
TRL Level for COVID19	TRL > 7 (Phase II/Phase III Trials)
IP Status	**Pending applications**: NA **Approved and Active applications**: • IN219369 **Title**: A Pyrazine Derivative **Assignee:** Toyama Chemical Co. Ltd. **Priority date:** 16/02/2000 **Grant date:** 02/05/2008 **Expected expiry date:** 14/02/2021 • IN219547 **Title:** A Pyrazine Derivative **Assignee:** Toyama Chemical Co. Ltd. **Priority date:** 16/02/2000 **Grant date:** 09/05/2008 **Expected expiry date**: 14/02/2021 • IN261641 (Divisional IN 219547) **Title:** Novel Pyrazine Derivatives Or Salts Thereof, Pharmaceutical Composition Containing The Same, And Production Intermediates Thereof **Assignee:** Toyama Chemical Co. Ltd. **Priority date:** 16/02/2000 **Grant date:** 04/07/2014

		Expected expiry date: 14/02/2021 • IN235048 **Title:** A Novel Pyrazine Nucleotide Or Pirazine Nucleoside Analog **Assignee:** Toyama Chemical Co. Ltd. **Priority date:** 14/08/2001 **Grant date:** 30/06/2009 **Expected expiry date:** 13/08/2022 • IN273554 **Title:** Pharmaceutical Composition For Treating Influenza Virus Infection **Assignee:** Toyama Chemical Co. Ltd. **Priority date:** 16/02/2007 **Grant date:** 15/06/2016 **Expected expiry date:** 14/02/2028 • IN274639 **Title:** Process For Producing An Amine Salt Of 6-Fluor0-3-Hydroxy-2-Pyrazinecarbonitrile **Assignee:** Toyama Chemical Co. Ltd. **Priority date:** 27/09/2007 **Grant date:** 01/09/2016 **Expected expiry date:** 25/09/2028 • IN280086 **Title:** Method For Producing Dichloropyrazine Derivative **Assignee:** Nippon Soda Co Ltd **Priority date:** 28/01/2009 **Grant date:** 09/02/2017 **Expected Expiry date:** 14/01/2030 • IN305027 **Title:** Pyrazino[2,3-D]Isoxazole Derivative **Assignee:** Fujifilm Corporation, Toyama Chemical Co., Ltd. **Priority date:** 12/11/2010 **Grant date:** 27/12/2018 **Expected Expiry date:** 11/11/2021
	Expired or Lapsed application	• IN226506 **Title:** Nitrogen-Containing Heterocylic Carboxamide Derivatives Or Salts Thereof And Antiviral Agents Comprising The Same **Assignee:** Toyama Chemical Co. Ltd. **Priority date:** 20/08/1998 **Grant Date:** 19/12/2008 **Expired date:** Patent has expired on 18/08/2019 • 4832/KOLNP/2008 **Title:** Anti-Foot-And-Mouth Disease Virus Agent For Animal Belonging To Family Suidae Or Sheep, And Method For Prevention Or Treatment Of Foot-And-Mouth Disease In Animal Belonging To Family Suidae Or Sheep **Assignee:** Toyama Chemical Co. Ltd.

	Priority date: 31/05/2006 **Status:** Refused for grant by the controller u/s 3(d) • 6955/DELNP/2011 **Title:** Tablet And Granulated Powder Containing 6-Fluoro-3-Hydroxy-2-Pyrazinecarboxamide **Assignee:** Toyama Chemical Co. Ltd. **Priority date:** 13/03/2009 **Status:** Refused for grant by the controller u/s 3(d)
Other Key References	1. https://www.pmda.go.jp/files/000210319.pdf 2. https://newdrugapprovals.org/tag/favipravir/ 3. https://pubchem.ncbi.nlm.nih.gov/compound/Favipiravir 4. https://www.ncbi.nlm.nih.gov/pubmed/28769016 5. WHO: Table of Therapeutics

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 Mugdha Lele, Mr Navnath Kadam, Dr Manisha Premnath, Dr Premnath V; Information also contributed by Dr Gopakumar Nair, GNAS and GnanLex.

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