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Syngene International Limited
Biocon Special Economic Zone
Biocon Park, Plot 2 & 3
Bommasandra Industrial Area
Bommasandra IV Phase,Jigani Link Road
Bangalore 560 099, India.
T +91 80 2808 2808
F +91 80 4014 3150 / 2852 3423
CIN No. L85110KA1993PLC014937
www.syngeneintl.com

**Sept 07, 2020**

To,

**Biocon Biologics India Limited,**
Biocon House, Ground Floor, Tower-3,
Semicon Park, Electronics City Phase-II,
Hosur Road, Bengaluru-560100, India.

## Declaration

Syngene International Limited ('Syngene') has executed a voluntary license agreement with Gilead Sciences Inc., ('Gilead') dated May 29, 2020 ('GVL').

Pursuant to the GVL, Syngene is having licensed to manufacture and sale of remdesivir (RDV) drug substance and drug product to treat patients with coronavirus disease 2019 ("**COVID-19**") in 127 countries.

Please also access the following link below, wherein Gilead has published the list of voluntary license holders, including Syngene International Limited.

https://www.gilead.com/purpose/advancing-global-health/covid-19/voluntary-licensing-agreements-for-remdesivir

This declaration is issued upon request by Biocon Biologics India Limited.

For Syngene International Limited,

Nandakumar Krishnachar

Authorised Signatory
Nandakumar Krishnachar

Digitally signed by Ostapciuc Alexandr
Date: 2021.04.01 16:09:11 EEST
Reason: MoldSign Signature
Location: Moldova

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# LICENSE AND SUPPLY AGREEMENT

This License and Supply Agreement (the "**Agreement**") is entered on October 6, 2020, is effective from September 14, 2020 ("**Effective Date**") by and between

**Syngene International Limited** ('Syngene'),
a company incorporated under the laws of India, having its principal place of business at Biocon Special Economic Zone, Biocon Park, Plot No. 2 & 3, Bommasandra Industrial Area IV Phase, Jigani Link Road, Bengaluru 560 099, India

and

**Biocon Biologics India Limited** ("Biocon Biologics"),
a company duly incorporated under the laws of India, having its registered office at Biocon House, Ground Floor, Tower-3, Semicon Park, Electronics City Phase-II, Hosur Road, Bengaluru-560100, India.

## RECITALS

I. WHEREAS Syngene and Gilead Sciences, Inc., ('Gilead') are parties to RDV License Agreement dated May 29, 2020 ('Gilead License Agreement') under which Syngene obtained license to manufacture and sale of remdesivir (RDV) and the product incorporating remdesivir (the "Product") to treat patients with coronavirus disease 2019 ("**COVID-19**") in the Territory (as defined below) as per the License Agreement.

II. WHEREAS Biocon Biologics is engaged in the business of promoting and marketing pharmaceutical products.

III. WHEREAS Syngene and Biocon Biologics wish to enter into an agreement pursuant to the flow-down terms of Gilead License Agreement and Biocon Biologics will pursue Regulatory Approval (as defined below) for the Product in the Territory and shall promote, market, distribute and sell the Product in the Territory under a sub-license from Syngene.

IV. WHEREAS Syngene will provide Product Data (as defined below) subject to the terms mentioned herein to Biocon Biologics for the purpose of obtaining Regulatory Approval for the Product in the Territory and promote, market, distribute and sell the Product in the Territory.

**NOW, THEREFORE**, in consideration of the mutual covenants, representations and warranties made herein and for other good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, the Parties hereto agree as follows:

## Article 1 Definitions and Interpretation

As used in this Agreement, each capitalized term has the meaning given thereto in this Article 1 or elsewhere in this Agreement:

BIOCON [redacted] LEGAL

SYNGENE LEGAL

[redacted]

**IN WITNESS WHEREOF**, the Parties hereto have caused this Agreement to be executed by affixing their signatures below

**Syngene International Limited**

[redacted]

Name: [redacted]
Title: CFO


**Biocon Biologics India Limited**

[redacted]

Name: [redacted]
Title: [redacted]

[redacted]

Name: [redacted]
Title: [redacted]

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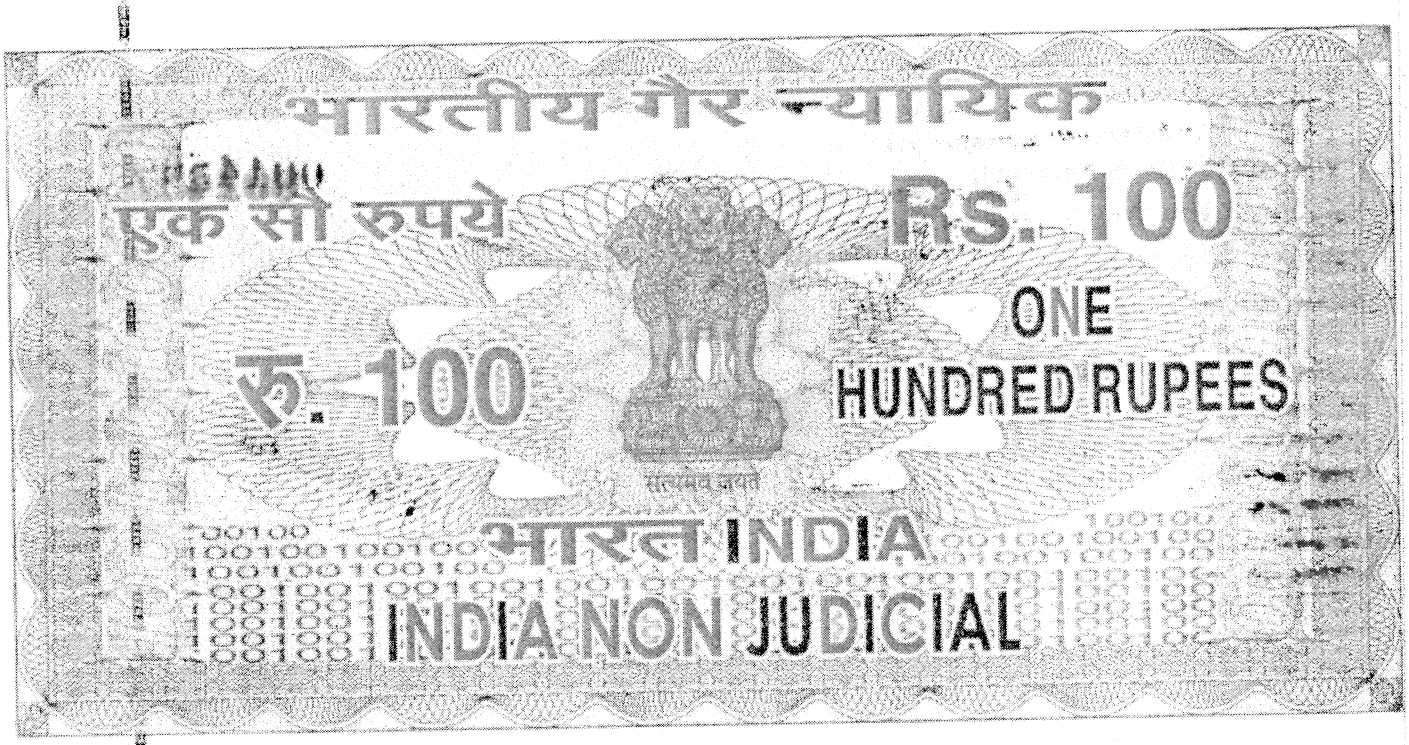


महाराष्ट्र MAHARASHTRA ◑ 2020 ◑ WZ 800310

प्रधान मुद्रांक कार्यालय, मुंबई
प.मु.वि.क्र. ८०००००२
- 7 AUG 2020
सक्षम अधिकारी

श्री. वि. क. गवई

## LOAN LICENSE AGREEMENT

This **LOAN LICENSE AGREEMENT** is entered into as of 27 August 2020 ("**Effective Date**") by and between **SYNGENEINTERNATIONAL LIMITED,** a company incorporated in India with registered office at Biocon SEZ, Biocon Park, Bommasandra Industrial Area – Phase IV Bommasandra-Jigani Link Road, Bangalore, India; (hereinafter referred to as "**SYNGENE**" which expression shall include its assigns, Affiliates, successors and group companies) and

**LYKA LABS LIMITED**, a Company incorporated in India and having place of manufacturing at Registered Office situated at 4801/B & 4802/A, G.I.D.C. Industrial Estate, Ankleshwar – 393 002, Gujarat, India and Administrative Office at Ground Floor, Spencer building,30, Forjett Street, Grant Road (West), Mumbai- 400 036 Maharashtra, India(hereinafter referred to as "**CONTRACTOR**" which expression shall mean and include its successors and assigns, group companies and affiliates).

[redacted]



[redacted]

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**SYNGENE** and **CONTRACTOR** may be referred to herein individually as a "Party" or collectively as the "Parties".

## RECITALS

WHEREAS Syngene has been granted certain non-exclusive, non-sublicensable, non-transferable licenses by Gilead Sciences, Inc. (**"the Licensor"**) to sell, have sold and offer for sale of finished pharmaceutical product Remdesivir ("RDV") in the territories as described, solely for use in the territories as stipulated in the license agreement dated May 29, 2020 executed between the Licensor and Syngene (**"the License Agreement"**).

WHEREAS **CONTRACTOR** is having manufacturing facilities owned by them and situated at4801/B & 4802/A, G.I.D.C. Industrial Estate, Ankleshwar – 393 002, Gujarat, India and is holding proper and subsisting registration and Drug Manufacturing License and, is engaged in manufacturing drugs formulations in the Form 25 & 28 under supervision of expert and qualified staff.

AND WHEREAS **CONTRACTOR** has represented to **SYNGENE** that it has the necessary manufacturing facilities and capacity capable of manufacturing the Product for Syngene in accordance with **SYNGENE's** know-how at the aforesaid factory.

AND WHEREAS **SYNGENE** is desirous of utilizing the said manufacturing facilities and the spare capacity of **CONTRACTOR**.

AND WHEREAS **CONTRACTOR** has agreed to manufacture the Products for and on behalf of **SYNGENE** upon and subject to the terms and conditions hereto after appearing and the License Agreement.

**NOW, THEREFORE,** in consideration of the mutual covenants and agreements set forth herein, and for good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, the Parties hereby agree as follows:

1 DEFINITIONS -

1.1 **"Affiliate"** means, in the case of either Party, any corporation, joint venture, or other business entity which directly or indirectly controls, is controlled by, or is under common control with that Party where "control," as used in this Section 1.1, means direct or indirect ownership of at least 50% of the voting stock or interest in a company or control over the composition of the board of directors.

1.2 **"Applicable Laws"** means all international, central, state, provincial and local laws, statutes, codes, rules, regulations, directives, guidelines, ordinances, orders, decrees, standards or other pronouncements of any governmental, administrative or judicial authority, whether currently in existence or hereafter promulgated, enacted, adopted or amended.

1.3 **"Batch"** means a Manufacturing run of a Product which yields a certain amount of each Product as set forth in

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documents and do such acts, deeds, matters and things as the other may reasonably require for the purpose of giving to the other the full benefit of all the provisions of this Agreement.

15.13 Counterparts. This Agreement may be executed in two or more counterparts, each of which shall constitute an original and all of which together shall constitute one and the same agreement.

IN WITNESS WHEREOF, the Parties have executed this Agreement as of the Effective

[redacted]

for and on behalf of
**SYNGENE INTERNATIONAL LIMITED**

By: [redacted]
Name:
Title:

for and on behalf of
**LYKA LABS LIMITED**

By: [redacted]
Name:
Title:

LYKA LABS LIMITED * MUMBAI *

[redacted]

**F. No. SND/MA/20/000286**
**Government of India**
**Directorate General of Health Services**
**Central Drugs Standard Control Organization**
**Subsequent New Drugs Division**

FDA Bhawan, Kotla Road
New Delhi
Dated: 04/11/2020

**To**
**M/s Syngene International Limited,**
**Plot No 2, 3 & 4, IV Phase Bommasandra,**
**Bangalore (India) - 560099**

**Subject:** Grant of permission to manufacture and market Remdesivir for Injection 100 mg/ vial (lyophilized) - regarding

**Reference:** Your application no. SND/CT21/FF/2020/22091 dated 06/10/2020

Sir,

Please find enclosed herewith permission No. **MF/FF/SND/265/2020** dated 04/11/2020 in Form CT-23 under Drugs & Cosmetics Acts and Rules thereunder and New Drug and Clinical Trial Rules, 2019 there under granted based on evaluation in consultation with Subject Expert Committee (SEC) as part of accelerated approval process considering the emergency situation and unmet medical need in light of Covid 19 outbreak for restricted emergency use in the country.

Please acknowledge the receipt of the same.

**Yours faithfully,**

**(Dr. V. G. Somani)**
**Drugs Controller General (India)**

**Copy to: -**

1. Deputy Drugs Controller (India), CDSCO Zonal Office, Ahmedabad.
2. Commissioner, FDCA Gujarat State, Old Sachivalya, Block No.8, 1st Floor, Dr. Jivraj Mehta Bhavan, Gandhi Nagar-382010.

सत्यमेव जयते

**F. No. SND/MA/20/000286**
**Government of India**
**Directorate General of Health Services**
**Central Drugs Standard Control Organisation**
**(Subsequent New Drugs Division)**

## Form CT-23

*(See Rules 81, 82, 83 & 84)*

## PERMISSION TO MANUFACTURE PHARMACEUTICAL FORMULATION OF A NEW DRUG FOR SALE OR FOR DISTRIBUTION

Number of the permission and date of issue **MF/FF/SND/265/2020 dated 04/11/2020**

The Central Licensing Authority hereby grant permission to M/s Syngene International Limited, Plot No 2, 3 & 4, IV Phase Bommasandra, Bangalore (India) - 560099 to manufacture for sale of pharmaceutical formulation manufactured by a manufacturer specified below.

1. Details of manufacturer and its manufacturing site under the license

| Serial No. | Name and address of manufacturer (Full name and address with telephone and e-mail address of manufacturer | Name and address of manufacturer (Full name and address with telephone and e-mail address of manufacturing site |
|---|---|---|
| 01 | M/s Syngene International Limited,<br>Plot No 2, 3 & 4, IV Phase<br>Bommasandra,<br>Bangalore (India) - 560099<br>Telephone No.: 08028083877<br>FAX: 08028083150<br>E-Mail : srikanta.dutta@syngeneintl.com | M/s Syngene International Limited,<br>C/o M/s. Lyka Labs limited,<br>Plot no. 48011B, 4802/A,<br>G.I.D.C., Dist: Bharuch,<br>Ankleshwar-393002, , Gujarat, |

3. Details of Pharmaceutical formulation

| | |
|---|---|
| **Name of the New Drug to be manufactured:** | Remdesivir for Injection 100mg/vial |
| **Dosage Form:** | Lyophilized powder for injection for IV infusion |
| **Composition** | Each vial contains-<br>Remdesivir .....100mg (Lyphophilised) |
| **Indication** | For treatment of suspected or laboratory confirmed corona virus disease 2019 (COVID-19) in adults and children hospitalised with severe disease. |
| **Shelf life with storage Condition** | Initially 03 months with storage condition - to store Remdesivir for Injection 100 mg/ vial (lyophilized) below 30°C until required for use. |

CENTRAL DRUGS STANDARD CONTROL ORGANISATION CDSCO CDSCO MINISTRY OF HEALTH, GOVERNMENT OF INDIA

4. This is subject to the conditions prescribed in Chapter X of the New Drugs and Clinical Trials Rules, 2019 under the Drugs and Cosmetics Act, 1940.

**Place: New Delhi**

**Date:** 04 **/11/2020**

**Central licensing Authority**
**Stamp**

Dr. V. G. SOMANI
Drugs Controller General (India)
Dte. General of Health Services
Ministry of Health and Family Welfare
FDA Bhawan, Kotla Road, I.T.O.
New Delhi-110002

**Condition of permission**

1. The new drugs shall conform to the specifications approved by the Central Licensing Authority;

2. The labeling of the drugs shall conform to the requirements specified in the Drugs and Cosmetics rules, 1945;

3. The label on the immediate container of the drug as well as the packing in which the container is enclosed should contain the following warning:

   **"WARNING: To be sold by retail on the prescription of specialist for use in hospital/ institutional set up only" and the warning shall be in box with red back ground.**

4. As post marketing surveillance, the applicant shall submit Periodic Safety Update Reports as specified in the Fifth Schedule;

5. All reported serious unexpected adverse reactions related to drug shall be intimated to the Central Licensing Authority and regulatory action resulting from their review shall be complied with;

6. No claims except those mentioned above shall be made for the drug without prior approval of the Central Licensing Authority;

7. **Specimen of the carton, labels, package insert that will be adopted for marketing the drug in the county shall be got approved from the Central Licensing Authority before the drugs is marketed;**

8. **Updated stability study data shall be submitted at periodic interval. If long-term stability data submitted do not cover the proposed shelf-life of the product, the stability study shall be continued to firmly establish the shelf-life and the complete stability data shall be submitted.**

9. **Written informed consent from each patient/ or his representative prior to administration of the drug shall be obtained. Informed consent form to be used should contain in a language understandable to the patient/ or his representative the factual detail about the drug, its restricted emergency use approval, alternative therapy available etc. The copy of the informed consent form should be submitted to CDSCO before launching the drug product for marketing.**

10. **The dose of the drug for adult and paediatric patients weighing more than 40kg should be a single dose of 200mg infused intravenously over 30 to 120 minutes on day 1 followed by once daily maintenance dose of 100mg, infused intravenously over 30 to 120 minutes for 4 days and the dose for paediatric patients with body weight between**

10. The dose of the drug for adult and paediatric patients weighing more than 40kg should be a single dose of 200mg infused intravenously over 30 to 120 minutes on day 1 followed by once daily maintenance dose of 100mg, infused intravenously over 30 to 120 minutes for 4 days and the dose for paediatric patients with body weight between 3.5kg and less than 40kg should be single loading dose of 5mg/kg IV infused over 30-120 minutes on day 1 followed by 2.5mg/kg IV infused over 30-120 minutes once daily for 4 days. Extension of administration of drug beyond 5 days to 10 days is not recommended.

11. The package insert of the product should contain the following:-
    a) Use of drug in patient with renal Impairment: Use in patients with renal impairment are based on potential risk and potential benefit considerations. Patients with eGFR greater than or equal to 30 mL/min are reported to have received remdesivir for treatment of COVID-19 with no dose adjustment of remdesivir. All patients must have an eGFR determined before dosing. Remdesivir is not recommended in adult and pediatric patients (>28 days old) with eGFR less than 30 mL/min or in full-term neonates (≥7 days to ≤28 days old) with serum creatinine greater than or equal to 1 mg/dL unless the potential benefit outweighs the potential risk.
    b) Use of drug in patient with hepatic Impairment: It is not known if dosage adjustment is needed in patients with hepatic impairment and remdesivir should only be used in patients with hepatic impairment if the potential benefit outweighs the potential risk. Hepatic laboratory testing should be performed in all patients prior to starting remdesivir and daily while receiving remdesivir.

12. The Label of the product should mention "For use in hospital/ institutional set up only".
13. The Package Insert containing all details including the information as above and Informed Consent Form should be provided along with the drug product for use in hospital/ institutional.
14. Active surveillance data of all treated patients should be submitted to CDSCO on monthly basis.
15. The Risk Management Plan including active Post Marketing Surveillance (PMS) and reporting of Serious Adverse Events (SAEs) etc. should be submitted to CDSCO within one month of approval of the drug product.
16. Phase IV clinical trial is required to be conducted after getting the Phase IV clinical trial protocol approved from CDSCO.



CENTRAL DRUGS STANDARD CONTROL ORGANISATION
CDSCO CDSCO
MINISTRY OF HEALTH, GOVERNMENT OF INDIA

**F. No. SND/MA/20/000286**
**Government of India**
**Directorate General of Health Services**
**Central Drugs Standard Control Organization**
**(Subsequent New Drugs Division)**

**FDA Bhawan, New Delhi**
**Dated:**

**To**
**M/s. Syngene International Limited,**
**Plot No. 2, 3 & 4, IV Phase Bommasandra,**
**Bangalore (India) – 560099.**

18 DEC 2020

**Sub: Amendment in Manufacturing and Marketing permission (Form CT-23) of Remdesivir for Injection 100mg/vial (Lyophilized) - Reg.**

**Reference: Your letter No. RA/SYNG/DCGI/20/354 dated 18-11-2020**

Sir,
This Directorate's permission No. **MF/FF/SND/265/2020** dated **04/11/2020** for Manufacturing and Marketing of **Remdesivir for Injection 100mg/vial (Lyophilized)** is hereby amended to read the composition as follow:-

**Read as**

| | |
|---|---|
| **Name and address of manufacturer:** | M/s. Syngene International Limited,<br>C/o M/s. Lyka Labs Limited,<br>Plot No. 4801/B, 4802/A, G.I.D.C, Dist – Bharuch,<br>Ankleshwar – 393002, Gujarat |
| **Composition:** | Each vial contains:<br>Remdesivir.....100mg (Lyophilized) |

**Instead of**

| | |
|---|---|
| **Name and address of manufacturer:** | M/s. Syngene International Limited,<br>C/o M/s. Lyka Labs Limited,<br>Plot No. 48011B, 4802/A, G.I.D.C, Dist – Bharuch,<br>Ankleshwar – 393002, Gujarat |
| **Composition:** | Each vial contains:<br>Remdesivir.....100mg (Lyphophilised) |

All other contents & conditions of the earlier Manufacturing and Marketing permission no. **MF/FF/SND/265/2020 dated 04/11/2020** will remain same.

Yours faithfully,

**(Dr. V. G. Somani)**
**Central Licensing Authority**