AVIFAVIR® MEDICINAL PRODUCT FOR TREATMENT OF CORONAVIRUS INFECTION (COVID-19)
Briefing note

The ChemRar Group pays its deepest respects to you and presents information about the innovative antiviral drug Avifavir® (INN Favipiravir), which is developed by Chromis LLC - a joint venture between the ChemRar Group (www.chemrar.ru) and the Russian Direct Investment Fund (RDIF, the sovereign wealth fund of the Russian Federation www.rdif.ru).

The direct participation of the state structure represented by the RDIF in the development and promotion of Avifavir® makes it feasible to speak of the large-scale involvement of the Russian Federation in the processes of combating COVID-19, and the scientific partner represented by the ChemRar Group efficiently met expectations by being the first to achieve results and register the drug. Avifavir® medicine development and registration was also supported by the Ministry of Industry and Trade of the Russian Federation and Skolkovo Foundation. The drug Avifavir® is the result of the scientific research carried out by Russian scientists as a response to the challenges posed to society as a whole with the onset of the COVID-19 pandemic.

Avifavir advantages

- Fully developed and scaled technology of API and drug product manufacturing;
- High quality of the product:
  - high purity of API
  - selected particles size and polymorth form for the final composition led to a more rapid release of the active substance from the tablets and better stability;
  - right choice of excipients,
  - 2 years' stability;
- Proprietary IP – Chromis obtained the patent for a composition with Favipiravir as an anti-COVID-19 drug;
- Clinical results showing efficacy in COVID-19 treatement - the effectiveness of Avifavir® has been proven during clinical studies, which in scale and depth significantly exceed those of other manufacturers of Favipiravir. 460 patients in 35 medical centers of the Russian Federation took part in clinical trials (phase II / III) of Avifavir®;
- Fast supply of drug products to any destination. 600 000+ packs per month manufacturing at 3 sites in Russia;
- Option for technology transfer to local partner for a long-term collaboration in the health care field;
- Competitive pricing.

Leading position in Russia and WW

Since June 2020, **more than 1,000,000 packages** of Avifavir® have been delivered to hospitals in **80 regions of the Russian Federation and abroad** by Chromis.
RDIF and the ChemRar Group note a high interest in Avifavir® in the foreign countries, contracts have already been signed for the supply of the drug to **20 countries** (Chile, Bolivia, Mexico, Argentina, Paraguay, Uruguay, El Salvador, Ecuador, Honduras, Czech Republic, Venezuela, Panama, Colombia, Brazil, Slovakia, Kuwait, Saudi Arabia, Serbia, Greece, Morocco).
Avifavir® has taken a leading position among the drugs for the treatment of the coronavirus infection currently exported by the Russian Federation. The drug has already been **delivered to 9 countries**: Belarus, Bolivia, Chile, Brazil, Venezuela, Kazakhstan, Kyrgyzstan, Turkmenistan and Uzbekistan.

Registration status of the drug

- On May 29th, 2020, Avifavir® received a Market Authorization certificate from the Ministry of Health of the Russian Federation, **becoming the world's first registered drug based on Favipiravir against coronavirus infection and the first drug in Russia approved for the treatment of COVID-19.**

- On June 3rd, 2020, the Ministry of Health of the Russian Federation **included Avifavir® in the National Recommendations for the Prevention, Diagnosis and Treatment of New Coronavirus Infection.**
- On October 16th, 2020, the Government of the Russian Federation on the recommendation of the Commission of the Ministry of Health **included Favipiravir in the List of Vital and Essential drugs.**
- On February 8th, 2021, The Russian Ministry of Health named **Favipiravir a priority drug in the COVID-19 treatment regimen** for mild to moderate patients.

Avifavir® has received a **Permanent Market Authorization in Bolivia** (Registro Sanitario № II-74791/2020 dated August 27, 2020) and **Emergency Use Authorization in Indonesia** (Persetujuan Penggunaan Obat dalam Kondisi Darurat № EUA2158200117A1 dated March 17, 2021).

Results of clinical trials

The effectiveness of Avifavir® has been proven during clinical studies, which **in scale and depth significantly exceed those of other manufacturers of Favipiravir**. The drug has a direct antiviral effect, blocking the multiplication mechanisms of coronavirus, relieves symptoms and **reduces the duration of the disease by half** compared to standard therapy.

460 patients in **35 medical centers** of the Russian Federation took part in clinical trials (phase II / III) of Avifavir®. The efficacy of Favipiravir compared to standard therapy has been proven for both primary endpoints:

- The **median time to improvement in clinical status** (reduction by 2 points according to the Ordinal Scale for Clinical Improvement or discharge from hospital) in the Favipiravir group was 7.0 days and in the Standard therapy group was 10.0 days (**statistically significant difference p < 0.001**);
- The **median time to virus elimination** in the Favipiravir group was 4.0 days and in the Standard therapy group was 6.0 days (**statistically significant difference p =0.038**).

In addition, since the beginning of supplies of Avifavir® to medical institutions of the Russian Federation, clinical **monitoring has been conducted based on data from the register of patients with coronavirus of the Ministry of Health of the Russian Federation** (a comparative analysis of the efficacy and safety of Avifavir® therapy has been carried out with **940 patients**).

International publications

- In early August, 2020, **the leading Oxford international journal** in the field of infectious diseases, Clinical Infectious Diseases (CID), published a scientific article devoted to the success of a clinical trial conducted by Chromis in accordance with international standards.

AVIFAVIR for Treatment of Patients with Moderate COVID-19: Interim Results of a Phase II / III Multicenter Randomized Clinical Trial doi: https://doi.org/10.1101/2020.07.26.20154724

- In March, 2021, Chromis reported a summary of the **multicenter, open-labeled, efficacy and safety study of AVIFAVIR in 940 patients with COVID-19** at the **Conference on Retroviruses and Opportunistic Infections CROI2021**: https://en.chemrar.ru/chromis-published-results-of-a-multi-center-open-label-post-marketing-clinical-study-in-940-covid-19-patients-confirming-efficacy-of-avifavir-at-croi2021/

Patents

Chromis received **a Russian patent for a composition with Favipiravir as an anti-COVID-19 drug**. The patent is valid from May 2020.

The reduction of the particle size of Favipiravir in the composition led to a more rapid release of the active substance from the tablets, notes Chromis. In addition, it was possible to improve the processability of the composition (flowability, compressibility), the uniformity of dosage of the active substance in the tablet was increased, as indicated in the description of patent application.

Full cycle production

The production of **a full cycle** of a medicinal product (active pharmaceutical ingredient and finished dosage form) is carried out by the ChemRar Group on the territory of the Russian Federation in accordance with:

- GMP Certificate № GMP-0076-000515/20 dated 13.06.2020 and Pharmaceutical license № 00161-ЛС dated 14.05.2020, Chemical Diversity Research Institute JSC, the manufacturer of DP, being the holder,
- GMP Certificate № GMP-0175-000592/20 dated 29.12.2020 and Pharmaceutical License № 00434-ЛС dated 03.09.2019, API-technologies LLC, the manufacturer of API, being the holder.