

Landscape analysis of therapeutics as 21st March 2020

Product type and candidate	Description	Licensed for	Licensed dose	Route of administration	Currently being trialled COVID-19?	Status of clinical development for Coronaviruses	Proposed dose for COVID-19	Status of clinical development for other relevant conditions
Re-purposed/off label								
Corticosteroids	Steroid hormones	Various	Various	Inhaled, parenteral injectables and intravenous injectables	Yes ¹	Clinical trial COVID-19 ¹ , clinical studies SARS ^{2,3} , clinical studies MERS ⁴	COVID-19 clinical trial: Methylprednisolone 40 mg q12h for 5 days	Phase III clinical trial H1N1 ⁵
Chloroquine	Antimalarial agent, heme polymerase inhibitor	Malaria prophylaxis and treatment	Prophylaxis: 500mg chloroquine phosphate once per week. Treatment: 2.5g chloroquine phosphate over 3 days	Oral or injectable	Yes ^{6,29} ChiCTR2000029939, ChiCTR2000029935, ChiCTR2000029899, ChiCTR2000029898, ChiCTR2000029868, ChiCTR2000029837, ChiCTR2000029826, ChiCTR2000029803, ChiCTR2000029762, ChiCTR2000029761, ChiCTR2000029760, ChiCTR2000029740, ChiCTR2000029609, ChiCTR2000029559, ChiCTR2000029542	Clinical trial COVID-19 ⁶ , in vitro study COVID-19 ^{7,29} , In vitro studies, chloroquine was found to block COVID-19 infection at low-micromolar concentration, with a half-maximal effective concentration (EC50) of 1.13 µM and a half-cytotoxic concentration (CC50) greater than 100 µM Gao et al 2020 Chloroquine phosphate has shown apparent efficacy and acceptable safety against COVID-19 associated pneumonia in multicenter clinical trials conducted in China. The drug is recommended to be included in the next version	COVID-19 clinical trial: hydroxychloroquine 400mg per day for 5 days	<u>In vitro studies MERS-CoV^{8-10,30}</u> De Wilde et al 2014: Huh7 cells infected with MERS-CoV isolate EMC/2012 (MOI, 0.005) and incubated for 2 days. 50% effective concentrations [EC(50)s], 3 to 8 µM Cong et al 2018 Primary cells - valuated in MDMs and MDDCs to determine their antiviral effect on MERS-CoV infection. <u>In vitro studies SARS-CoV^{11,12,13, 30}</u> Keyaerts et al 2004: Vero cells, 3 days post infection viable cell quantified. IC50 of chloroquine for antiviral activity (8.8 +/- 1.2 microM) was significantly lower than its cytostatic activity; CC50 (261.3 +/- 14.5 microM), yielding a selectivity index of 30 De Wilde et al 2014: Vero E6 cells infected with SARS-CoV isolate Frankfurt-1 (MOI, 0.005) and incubated for 3 days. Pre and post infection effective. Wang et al 2020 Vero E6 cells were infected with nCoV2019BetaCoV/Wuhan/WIV04/2019

DISCLAIMER: These landscape documents have been prepared by the World Health Organization (WHO) for information purposes only concerning the 2019-2020 global of the novel coronavirus. Inclusion of any particular product or entity in any of these landscape documents does not constitute, and shall not be deemed or construed as, any approval or endorsement by WHO of such product or entity (or any of its businesses or activities). While WHO takes reasonable steps to verify the accuracy of the information presented in these landscape documents, WHO does not make any (and hereby disclaims all) representations and warranties regarding the accuracy, completeness, fitness for a particular purpose (including any of the aforementioned purposes), quality, safety, efficacy, merchantability and/or non-infringement of any information provided in these landscape documents and/or of any of the products referenced therein. WHO also disclaims any and all liability or responsibility whatsoever for any death, disability, injury, suffering, loss, damage or other prejudice of any kind that may arise from or in connection with the procurement, distribution or use of any product included in any of these landscape documents.

Landscape analysis of therapeutics as 21st March 2020

						of the Guidelines for the Prevention, Diagnosis, and Treatment of Pneumonia Caused by COVID-19 issued by the National Health Commission of the People's Republic of China for treatment of COVID-19 infection in larger populations in the future		(MOI) of 0.05. Quantification of viral copy numbers by qRT-PCR confirmed with visualization of virus nucleoprotein (NP) expression through immunofluorescence (EC ₅₀ = 1.13 μM; CC ₅₀ > 100 μM, SI > 88.50) Barnard et al 2006 <i>In vitro</i> inhibition of SARS-CoV replication in African green monkey kidney cells <u>In vitro H-Cov OC43³¹</u> Shen et al 2016 chloroquine strongly inhibited HCoV-OC43 replication <i>in vitro</i> , with a 50% inhibitory concentration (IC ₅₀) of 0.33 μM <u>In vivo study MERS⁸</u> <u>In vivo study SARS-CoV¹¹</u> , Barnard et al 2006 Effect of i.p. and i.n. treatment on SARS-CoV replication in female BALB/c mice. Day 3 viral load – no effect. <u>In vivo study H-Cov OC43³²</u> Keyaerts et al 2009 Pregnant mice treated – offspring protected from lethal challenge
Ritonavir + Lopinavir (Kaletra)	Protease inhibitors	HIV infection	Adults 5 ml of oral solution (400/100mg) twice a day	capsule oral, solution oral, tablet oral	Yes ^{14–21}	Clinical trials COVID-19 ^{14–21} , case report COVID-19 ³⁵ , clinical studies SARS ²² , <i>in vitro</i> and clinical studies SARS-CoV ²³ , <i>in vivo</i> studies MERS-CoV ²⁴ <u>Retrospective cohort COVID-19³⁴</u> Deng et al 2020	500mg once, twice a day, 2 weeks	<u>Clinical trial SARS³³</u> Chu et al 2004 41 patients given intervention (control group Ribavirin 111 patients). The patients had a decreasing viral load and rising peripheral lymphocyte count. <u>Retrospective matched cohort SARS²²</u> Chan et al 2003

DISCLAIMER: These landscape documents have been prepared by the World Health Organization (WHO) for information purposes only concerning the 2019-2020 global of the novel coronavirus. Inclusion of any particular product or entity in any of these landscape documents does not constitute, and shall not be deemed or construed as, any approval or endorsement by WHO of such product or entity (or any of its businesses or activities). While WHO takes reasonable steps to verify the accuracy of the information presented in these landscape documents, WHO does not make any (and hereby disclaims all) representations and warranties regarding the accuracy, completeness, fitness for a particular purpose (including any of the aforementioned purposes), quality, safety, efficacy, merchantability and/or non-infringement of any information provided in these landscape documents and/or of any of the products referenced therein. WHO also disclaims any and all liability or responsibility whatsoever for any death, disability, injury, suffering, loss, damage or other prejudice of any kind that may arise from or in connection with the procurement, distribution or use of any product included in any of these landscape documents.

Landscape analysis of therapeutics as 21st March 2020

						16 patients – 2 groups: LPV/r + Arbidol and LPV/r monotherapy. The SARS-CoV-2 could not be detected for 12(75%) of 16 patients' nasopharyngeal specimens in the combination group after seven days, compared with 6 (35%) of 17 in the monotherapy group ($p < 0.05$). After 14 days, 15 (94%) of 16 and 9 (52.9%) of 17, respectively, SARS-CoV-2 could not be detected ($p < 0.05$).		75 patients – 2 intervention groups: lopinavir/ritonavir as initial treatment, and lopinavir/ritonavir as rescue therapy. The addition of lopinavir/ritonavir to a standard treatment protocol as an initial treatment for severe acute respiratory syndrome appeared to be associated with improved clinical outcome.
Ribavirin + Ritonavir + Lopinavir	Nucleoside Inhibitor + protease inhibitor					Clinical trial SARS ^{25,26}	Clinical trial: (1) lopinavir 400 mg/ritonavir 100 mg orally twice daily, plus (2) ribavirin 2.4 g orally as a loading dose followed by 1.2 g orally every 12 hours. Duration of treatment up to 10 days. Case study: ribavirin 600mg 2x day and lopinavir + ritonavir 1000mg 1x day	

DISCLAIMER: These landscape documents have been prepared by the World Health Organization (WHO) for information purposes only concerning the 2019-2020 global of the novel coronavirus. Inclusion of any particular product or entity in any of these landscape documents does not constitute, and shall not be deemed or construed as, any approval or endorsement by WHO of such product or entity (or any of its businesses or activities). While WHO takes reasonable steps to verify the accuracy of the information presented in these landscape documents, WHO does not make any (and hereby disclaims all) representations and warranties regarding the accuracy, completeness, fitness for a particular purpose (including any of the aforementioned purposes), quality, safety, efficacy, merchantability and/or non-infringement of any information provided in these landscape documents and/or of any of the products referenced therein. WHO also disclaims any and all liability or responsibility whatsoever for any death, disability, injury, suffering, loss, damage or other prejudice of any kind that may arise from or in connection with the procurement, distribution or use of any product included in any of these landscape documents.

Landscape analysis of therapeutics as 21st March 2020

Product type and candidate	Description	Licensed for	Licensed dose	Route of administration	Currently being trialled COVID-19?	Status of clinical development for Coronaviruses	Proposed dose for COVID-19	Status of clinical development for other relevant conditions
Darunavir (with cobicistat) (Prezista® / Prezcoibix® and Generic)	Antiretroviral, protease inhibitor. Used with low doses of cobicistat to increase bioavailability and half life	HIV infection	Treatment-naïve and those with no resistance associated substitutions: 800 mg taken with ritonavir 100 mg per day	Oral suspension and tablets	Yes ^{19,27}	Clinical trials COVID-19 ^{9,27}	Darunavir 800 mg/Cobicistat 150 mg QD	
Emtricitabine + tenofovir (Truvada)	Non-nucleoside reverse transcriptase inhibitor + nucleotide reverse transcriptase inhibitor	HIV infection	1 tablet (emtricitabine (200 mg) and tenofovir disoproxil (245 mg)) per day in those weighing at least 35kg	Oral	Yes ¹⁶	Clinical trial COVID-19 ¹⁶	Dosage clinical trial not available	
Ruxolitinib (Jakafi or Jakavi)	Myelofibrosis and polycythaemia vera treatment	Myelofibrosis and polycythaemia vera		Oral	Yes ²⁸	Clinical trial COVID-19 ⁸	Dosage clinical trial not available	
Baricitinib (Olumiant or Baricinix)	Inhibitor of janus kinase	Rheumatoid arthritis	4 mg per day, can be reduced to 2 mg per day when disease under control, impaired kidney function, increased risk of infections, aged >75, or taking certain other medicines.	Oral				

DISCLAIMER: These landscape documents have been prepared by the World Health Organization (WHO) for information purposes only concerning the 2019-2020 global of the novel coronavirus. Inclusion of any particular product or entity in any of these landscape documents does not constitute, and shall not be deemed or construed as, any approval or endorsement by WHO of such product or entity (or any of its businesses or activities). While WHO takes reasonable steps to verify the accuracy of the information presented in these landscape documents, WHO does not make any (and hereby disclaims all) representations and warranties regarding the accuracy, completeness, fitness for a particular purpose (including any of the aforementioned purposes), quality, safety, efficacy, merchantability and/or non-infringement of any information provided in these landscape documents and/or of any of the products referenced therein. WHO also disclaims any and all liability or responsibility whatsoever for any death, disability, injury, suffering, loss, damage or other prejudice of any kind that may arise from or in connection with the procurement, distribution or use of any product included in any of these landscape documents.

Landscape analysis of therapeutics as 21st March 2020

Product type and candidate	Description	Licensed for	Licensed dose	Route of administration	Currently being trialled COVID-19?	Status of clinical development for Coronaviruses	Proposed dose for COVID-19	Status of clinical development for other relevant conditions
Sirolimus (Rapamycin, Rapamune®)	mTor inhibitor IL2, immunosuppressant	Anti-rejection medicine in those aged >=13 who received a kidney transplant. Also used to treat LAM	Organ rejection: 6 mg given soon after the transplantation followed by 2 mg once a day S-LAM: 2 mg daily and after 10 to 20 days dose adjustment	Oral		In vitro studies MERS-CoV: Kindrachuk et al. Antimicrob Agents Chemother. 2015 ;59(2):1088-99 - Huh7 cells ; Sirolimus largely retained inhibitory activity against MERS-CoV whether it was added pre- or postinfection.	Influenza: 1 mg 1xday. Severe H1N1 pneumonia: 2mg 1xday	RCT for H1N1: Wang et al. Crit Care Med. 2014 ;42(2):313-21. RCT, 38 patients - early adjuvant treatment with corticosteroids and sirolimus (Rapamune 2 mg/d) was associated with improvement in outcomes, such as hypoxia, multiple organ dysfunction, virus clearance, and shortened liberation of ventilator and ventilator days.

DISCLAIMER: These landscape documents have been prepared by the World Health Organization (WHO) for information purposes only concerning the 2019-2020 global of the novel coronavirus. Inclusion of any particular product or entity in any of these landscape documents does not constitute, and shall not be deemed or construed as, any approval or endorsement by WHO of such product or entity (or any of its businesses or activities). While WHO takes reasonable steps to verify the accuracy of the information presented in these landscape documents, WHO does not make any (and hereby disclaims all) representations and warranties regarding the accuracy, completeness, fitness for a particular purpose (including any of the aforementioned purposes), quality, safety, efficacy, merchantability and/or non-infringement of any information provided in these landscape documents and/or of any of the products referenced therein. WHO also disclaims any and all liability or responsibility whatsoever for any death, disability, injury, suffering, loss, damage or other prejudice of any kind that may arise from or in connection with the procurement, distribution or use of any product included in any of these landscape documents.

Landscape analysis of therapeutics as 21st March 2020

Product type and candidate	Description	Licensed for	Licensed dose	Route of administration	Currently being trialled COVID - 19?	Status of clinical development for Coronaviruses	Proposed dose for COVID-19	Status of clinical development for other relevant conditions
IFN- α / PEGIFN- α	type I interferons - signaling proteins made and released by host cells in response to the presence of several viruses, that help regulate the activity of the immune system.					<p>In vivo studies SARS-CoV: - Haagmans et al. Nat Med. 2004;10(3):290-3 - Prophylactic positive outcome / postexposure treatment less effective. - Smits et al. PLoS Pathog. 2010; 6(2):e1000756 - reduced pathology without affecting virus replication ; pro-inflammatory gene expression significantly diminished</p> <p>Clinical studies MERS: Al Ghamdi et al. BMC Infect Dis 2016;16:174 (case series ; 8 patients) - 6/8 died.</p>		

DISCLAIMER: These landscape documents have been prepared by the World Health Organization (WHO) for information purposes only concerning the 2019-2020 global of the novel coronavirus. Inclusion of any particular product or entity in any of these landscape documents does not constitute, and shall not be deemed or construed as, any approval or endorsement by WHO of such product or entity (or any of its businesses or activities). While WHO takes reasonable steps to verify the accuracy of the information presented in these landscape documents, WHO does not make any (and hereby disclaims all) representations and warranties regarding the accuracy, completeness, fitness for a particular purpose (including any of the aforementioned purposes), quality, safety, efficacy, merchantability and/or non-infringement of any information provided in these landscape documents and/or of any of the products referenced therein. WHO also disclaims any and all liability or responsibility whatsoever for any death, disability, injury, suffering, loss, damage or other prejudice of any kind that may arise from or in connection with the procurement, distribution or use of any product included in any of these landscape documents.

Landscape analysis of therapeutics as 21st March 2020

<p>IFN-α2a (Pegasys® and others PEGylated IFNα2a)</p>	<p>type I interferon made by leukocytes during viral infection</p>	<p>Hepatitis C (with ribavirin) and hepatitis B</p>	<p>Pegasys is given once a week for 48 weeks for hepatitis B and once a week for between 16 and 72 weeks for hepatitis C. Adult dose is usually 180 micrograms but the children's dose varies depending on their height and weight.</p>	<p>Parenteral injection, for subcutaneous use</p>		<p>Clinical study MERS: Arabi et al. Clin Infect Dis. 2019. pii: ciz544 (Retrospective observational study ; 349 patients) - no decrease in mortality nor faster virus RNA clearance.</p>	<p>MERS: Pegylated interferon alfa-2a (Pegasys): 180 µg subcutaneously per week for 2 weeks</p>	
---	--	---	---	---	--	---	---	--

DISCLAIMER: These landscape documents have been prepared by the World Health Organization (WHO) for information purposes only concerning the 2019-2020 global of the novel coronavirus. Inclusion of any particular product or entity in any of these landscape documents does not constitute, and shall not be deemed or construed as, any approval or endorsement by WHO of such product or entity (or any of its businesses or activities). While WHO takes reasonable steps to verify the accuracy of the information presented in these landscape documents, WHO does not make any (and hereby disclaims all) representations and warranties regarding the accuracy, completeness, fitness for a particular purpose (including any of the aforementioned purposes), quality, safety, efficacy, merchantability and/or non-infringement of any information provided in these landscape documents and/or of any of the products referenced therein. WHO also disclaims any and all liability or responsibility whatsoever for any death, disability, injury, suffering, loss, damage or other prejudice of any kind that may arise from or in connection with the procurement, distribution or use of any product included in any of these landscape documents.

Landscape analysis of therapeutics as 21st March 2020

Product type and candidate	Description	Licensed for	Licensed dose	Route of administration	Currently being trialled COVID-19?	Status of clinical development for Coronaviruses	Proposed dose for COVID-19	Status of clinical development for other relevant conditions
IFN-α2b (PegIntron®, Sylatron®, IntronA®)	type I interferon made by leukocytes during viral infection	- Hepatitis C (with ribavirin) - Melanoma - AIDS-Related Kaposi's Sarcoma, Chronic Hepatitis C, Chronic Hepatitis B	PegIntron®: once a week. In adults, used in combination treatments at a dose of 1.5 mg per kg body weight, or on its own at 0.5 or 1.0 mg/kg. In children and adolescents, the dose is 60 mg per m ² body surface area. Treatment duration from 6 months to a year. IntronA®: 3 times per week. Dose and duration of treatment depend on the disease being treated and the response of the patient, with doses ranging from 2 to 20 million IU per square metre of body surface area.	- Parenteral injection SC - Parenteral injection SC - intramuscular, subcutaneous, intralesional, or intravenous	Yes http://www.hictr.org.cn/showprojen.aspx?proj=48684	Clinical trials COVID-19 Clinical study MERS: Arabi et al. Clin Infect Dis. 2019. pii: ciz544 (Retrospective observational study ; 349 patients) - no decrease in mortality nor faster virus RNA clearance.	MERS: Pegylated interferon alfa 2b (PEG-Intron): 1.5mcg/kg subcutaneously once per week x 2	

DISCLAIMER: These landscape documents have been prepared by the World Health Organization (WHO) for information purposes only concerning the 2019-2020 global of the novel coronavirus. Inclusion of any particular product or entity in any of these landscape documents does not constitute, and shall not be deemed or construed as, any approval or endorsement by WHO of such product or entity (or any of its businesses or activities). While WHO takes reasonable steps to verify the accuracy of the information presented in these landscape documents, WHO does not make any (and hereby disclaims all) representations and warranties regarding the accuracy, completeness, fitness for a particular purpose (including any of the aforementioned purposes), quality, safety, efficacy, merchantability and/or non-infringement of any information provided in these landscape documents and/or of any of the products referenced therein. WHO also disclaims any and all liability or responsibility whatsoever for any death, disability, injury, suffering, loss, damage or other prejudice of any kind that may arise from or in connection with the procurement, distribution or use of any product included in any of these landscape documents.

Landscape analysis of therapeutics as 21st March 2020

Product type and candidate	Description	Licensed for	Licensed dose	Route of administration	Currently being trialled COVID - 19?	Status of clinical development for Coronaviruses	Proposed dose for COVID-19	Status of clinical development for other relevant conditions
IFN-β	type I interferons - signaling proteins made and released by host cells in response to the presence of several viruses, that help regulate the activity of the immune system.					Clinical study MERS: Al Ghamdi et al. BMC Infect Dis 2016;16:174 (case series ; 23 patients) - 18/23 died.		

DISCLAIMER: These landscape documents have been prepared by the World Health Organization (WHO) for information purposes only concerning the 2019-2020 global of the novel coronavirus. Inclusion of any particular product or entity in any of these landscape documents does not constitute, and shall not be deemed or construed as, any approval or endorsement by WHO of such product or entity (or any of its businesses or activities). While WHO takes reasonable steps to verify the accuracy of the information presented in these landscape documents, WHO does not make any (and hereby disclaims all) representations and warranties regarding the accuracy, completeness, fitness for a particular purpose (including any of the aforementioned purposes), quality, safety, efficacy, merchantability and/or non-infringement of any information provided in these landscape documents and/or of any of the products referenced therein. WHO also disclaims any and all liability or responsibility whatsoever for any death, disability, injury, suffering, loss, damage or other prejudice of any kind that may arise from or in connection with the procurement, distribution or use of any product included in any of these landscape documents.

Landscape analysis of therapeutics as 21st March 2020

Product type and candidate	Description	Licensed for	Licensed dose	Route of administration	Currently being trialled COVID - 19?	Status of clinical development for Coronaviruses	Proposed dose for COVID-19	Status of clinical development for other relevant conditions
IFN-β1a (Avonex®, Plegridy® (peginterferon β1a), Rebif®, CinnoVex®)	type I interferon made by leukocytes during viral infection	Relapsing forms of multiple sclerosis	In adults, the recommended dose of Avonex is 30 micrograms, given by injection into a muscle once a week. Plegridy treatment should start with a dose of 63 micrograms, followed by a dose of 94 micrograms after two weeks, and then 125 micrograms every two weeks thereafter. The recommended dose of Rebif is 44 micrograms given three times a week by injection under the skin. A 22-microgram dose is recommended for patients who cannot tolerate the higher dose.	IM injection SC injection		In vitro study SARS-CoV: Hensley et al. Emerg Infect Dis. 2004; 10(2): 317–319 Clinical study MERS: Arabi et al. Clin Infect Dis. 2019. pii: ciz544 (Retrospective observational study ; 349 patients) - no decrease in mortality nor faster virus RNA clearance.	MERS: rIFN-β1a (Rebif): 44 mg subcutaneously three-times weekly	In vivo study ARDS: - In an animal model of ARDS (mice), administration of subcutaneous IFN-β 1 before bacterial challenge reduced the odds ratio for 7-day mortality by 85% - Hiruma et al. Am J Respir Cell Mol Biol. 2018;59(1):45-55. Clinical studies ARDS: - In an open-label, nonrandomized, phase 1–2 study of intravenous IFN beta-1a (FP-1201) in ARDS, IFN was associated with lower mortality day 28, 8% vs 32%, odds ratio 0.19 [95% CI 0.03–0.72]; p=0.01. - Bellingan et al. Lancet Respir Med. 2014 ;2(2):98-107. - A multicenter phase III, double-blind, randomized, parallel-group trial (PHASE III TRIAL (INTEREST STUDY, NCT02622724) has been completed. - Bellingan et al. Trials. 2017 Nov 13;18(1):536.

DISCLAIMER: These landscape documents have been prepared by the World Health Organization (WHO) for information purposes only concerning the 2019-2020 global of the novel coronavirus. Inclusion of any particular product or entity in any of these landscape documents does not constitute, and shall not be deemed or construed as, any approval or endorsement by WHO of such product or entity (or any of its businesses or activities). While WHO takes reasonable steps to verify the accuracy of the information presented in these landscape documents, WHO does not make any (and hereby disclaims all) representations and warranties regarding the accuracy, completeness, fitness for a particular purpose (including any of the aforementioned purposes), quality, safety, efficacy, merchantability and/or non-infringement of any information provided in these landscape documents and/or of any of the products referenced therein. WHO also disclaims any and all liability or responsibility whatsoever for any death, disability, injury, suffering, loss, damage or other prejudice of any kind that may arise from or in connection with the procurement, distribution or use of any product included in any of these landscape documents.

Landscape analysis of therapeutics as 21st March 2020

Product type and candidate	Description	Licensed for	Licensed dose	Route of administration	Currently being trialled COVID - 19?	Status of clinical development for Coronaviruses	Proposed dose for COVID-19	Status of clinical development for other relevant conditions
IFN-β1b (Betaseron®/ Betaferon®, Extavia®)	type I interferon made by leukocytes during viral infection	Relapsing forms of multiple sclerosis	Treatment should start with 62.5 micrograms (a quarter of the dose) every other day, increasing progressively over 19 days to reach the recommended dose of 250 micrograms given every other day.	SC injection		<p>In vitro study SARS-CoV: Cinatl at al. Lancet. 2003;362(9380):293-4 (Vero and Caco2 cells) - IFN-β1b > IFN-α2b or IFNγ1b</p> <p>In vivo study MERS-CoV: Chan et al. J Infect Dis. 2015. 212(12):1904-13 (Betaferon® SQ) - less severe disease and lower mean viral loads in necropsied lung and extrapulmonary tissues compared with untreated animals.</p>		

DISCLAIMER: These landscape documents have been prepared by the World Health Organization (WHO) for information purposes only concerning the 2019-2020 global of the novel coronavirus. Inclusion of any particular product or entity in any of these landscape documents does not constitute, and shall not be deemed or construed as, any approval or endorsement by WHO of such product or entity (or any of its businesses or activities). While WHO takes reasonable steps to verify the accuracy of the information presented in these landscape documents, WHO does not make any (and hereby disclaims all) representations and warranties regarding the accuracy, completeness, fitness for a particular purpose (including any of the aforementioned purposes), quality, safety, efficacy, merchantability and/or non-infringement of any information provided in these landscape documents and/or of any of the products referenced therein. WHO also disclaims any and all liability or responsibility whatsoever for any death, disability, injury, suffering, loss, damage or other prejudice of any kind that may arise from or in connection with the procurement, distribution or use of any product included in any of these landscape documents.

Landscape analysis of therapeutics as 21st March 2020

<p>IFN-γ (Actimmune®)</p>	<p>type II IFNs - immune interferon activated by Interleukin-12</p>	<p>Serious infections associated with Chronic Granulomatous Disease (CGD) ; severe, malignant osteopetrosis (SMO)</p>	<p>50 mcg/m² for patients whose body surface area is greater than 0.5 m² and 1.5 mcg/kg/dose for patients whose body surface area is equal to or less than 0.5 m² three times weekly.</p>	<p>SC injection</p>		<p>In vivo study SARS-CoV: Nagata et al. Am J Pathol. 2008; 172(6):1625-37 - IFN-γ treatment protected the animals from the lethal respiratory illness.</p> <p>In vitro study SARS-CoV: Cinatl at al. Lancet. 2003;362(9380):293-4 (Vero and Caco2 cells) Sainz et al. Virology. 2004 ; 329(1):11-7 (Vero E6 cells) Spiegel et al. J Clin Virol. 2004; 30(3):211-3 (Vero cells) Scagnolari et al. Antivir Ther. 2004; 9(6):1003-11 (Vero cells) - IFN-β + IFN-γ > IFN-β or IFN-γ (synergic effect) .</p>		
---	---	---	--	---------------------	--	---	--	--

DISCLAIMER: These landscape documents have been prepared by the World Health Organization (WHO) for information purposes only concerning the 2019-2020 global of the novel coronavirus. Inclusion of any particular product or entity in any of these landscape documents does not constitute, and shall not be deemed or construed as, any approval or endorsement by WHO of such product or entity (or any of its businesses or activities). While WHO takes reasonable steps to verify the accuracy of the information presented in these landscape documents, WHO does not make any (and hereby disclaims all) representations and warranties regarding the accuracy, completeness, fitness for a particular purpose (including any of the aforementioned purposes), quality, safety, efficacy, merchantability and/or non-infringement of any information provided in these landscape documents and/or of any of the products referenced therein. WHO also disclaims any and all liability or responsibility whatsoever for any death, disability, injury, suffering, loss, damage or other prejudice of any kind that may arise from or in connection with the procurement, distribution or use of any product included in any of these landscape documents.

Landscape analysis of therapeutics as 21st March 2020

IFN + Ribavirin	Combination antiviral + proteins made and released by host cells					<p>Clinical study SARS: Zhao et al. J Med Microbiol. 2003; 52: 715720 (IFN-α + RBV) - Inconclusive</p> <p>Clinical studies MERS: - Al Ghamdi et al. BMC Infect Dis 2016;16:174 (case series ; 23 patients ; IFN-α or IFN-β +/- RBV) - 18/23 died. - Arabi et al. Clin Infect Dis. 2019. pii: ciz544 (Retrospective observational study ; 349 patients ; RBV + rIFN-α2a or rIFN-α2b or rIFN-β1a) - no decrease in mortality nor faster virus RNA clearance. - Shalhoub et al. J Antimicrob Chemother. 2015. 70(7):2129-32 (Retrospective Cohort Study ; 24 patients ; IFNα2a or IFN-β1a SQ + PO RBV) - The fatality rate was 85% in INF-α-2a vs 64% in INF-β-1a (p=0,24) ; Older age and comorbid conditions, Omrani et al. Lancet Infect Dis.2014. 14(11):1090-1095. and Erratum in Lancet Infect Dis. 2015; 211(2):13 (SQ PEG-INF α-2a + PO Ribavirin for 8–10 days ; Retrospective cohort study ; 44 patients) - significantly improved survival at 14 days, but not at 28 days. Khalid et al. Antivir Ther. 2015. 20(1):87-91 (case</p>		
-----------------	--	--	--	--	--	---	--	--

DISCLAIMER: These landscape documents have been prepared by the World Health Organization (WHO) for information purposes only concerning the 2019-2020 global of the novel coronavirus. Inclusion of any particular product or entity in any of these landscape documents does not constitute, and shall not be deemed or construed as, any approval or endorsement by WHO of such product or entity (or any of its businesses or activities). While WHO takes reasonable steps to verify the accuracy of the information presented in these landscape documents, WHO does not make any (and hereby disclaims all) representations and warranties regarding the accuracy, completeness, fitness for a particular purpose (including any of the aforementioned purposes), quality, safety, efficacy, merchantability and/or non-infringement of any information provided in these landscape documents and/or of any of the products referenced therein. WHO also disclaims any and all liability or responsibility whatsoever for any death, disability, injury, suffering, loss, damage or other prejudice of any kind that may arise from or in connection with the procurement, distribution or use of any product included in any of these landscape documents.

Landscape analysis of therapeutics as 21st March 2020

					<p>series ; 2 patients ; SQ PEGINF- α-2b + RBV PO (treatment or prophylaxis) - Complete recovery and discharge home,</p> <p>- Khalid et al. Respir Care 2016;61:340–8 (case series ; 11 patients ; RBV + INF- α-2a) - survival of all patients,</p> <p>- Al-Tawfiq et al. Int J Infect Dis. 2014. 20:42-6 (Retrospective observational study ; 5 patients ; RBV PO for 5 days + SQ INF α-2b (1 or 2 doses)) - Late treatment administration, multiple comorbidities. All patients died.</p> <p>- Tawalah et al. J Infect Dis Ther, 2015, 3(4), pp. 1-5 (Retrospective observational study ; 2 patients ; PEG-IFN α2a or PEG-IFN α2b + RBV) - Both patients recovered. - Malik et al. Emerg Infect Dis 2016. 2013;22 (case report ; 1 patient ; RBN and IFN-α2a day 12 from onset) - died.</p> <p>- Khalid et al. Ann Saudi Med. 2014, 34, pp. 396400 (case series ; 6 patients ; RBV + IFN-α2b) - 3/6 died (delayed diagnosis and treatment).</p> <p>In vivo study MERS-CoV:</p> <p>Falzarano et al. Nat Med. 2013. 19(10):1313-7 (IFNα2b + RBV) - improved outcome.</p>		
--	--	--	--	--	---	--	--

DISCLAIMER: These landscape documents have been prepared by the World Health Organization (WHO) for information purposes only concerning the 2019-2020 global of the novel coronavirus. Inclusion of any particular product or entity in any of these landscape documents does not constitute, and shall not be deemed or construed as, any approval or endorsement by WHO of such product or entity (or any of its businesses or activities). While WHO takes reasonable steps to verify the accuracy of the information presented in these landscape documents, WHO does not make any (and hereby disclaims all) representations and warranties regarding the accuracy, completeness, fitness for a particular purpose (including any of the aforementioned purposes), quality, safety, efficacy, merchantability and/or non-infringement of any information provided in these landscape documents and/or of any of the products referenced therein. WHO also disclaims any and all liability or responsibility whatsoever for any death, disability, injury, suffering, loss, damage or other prejudice of any kind that may arise from or in connection with the procurement, distribution or use of any product included in any of these landscape documents.

Landscape analysis of therapeutics as 21st March 2020

IFN + Ribavirin + steroids	Combination of proteins made					Clinical study SARS: Wu et al. Chin Med J (Engl)			
----------------------------	------------------------------	--	--	--	--	--	--	--	--

DISCLAIMER: These landscape documents have been prepared by the World Health Organization (WHO) for information purposes only concerning the 2019-2020 global of the novel coronavirus. Inclusion of any particular product or entity in any of these landscape documents does not constitute, and shall not be deemed or construed as, any approval or endorsement by WHO of such product or entity (or any of its businesses or activities). While WHO takes reasonable steps to verify the accuracy of the information presented in these landscape documents, WHO does not make any (and hereby disclaims all) representations and warranties regarding the accuracy, completeness, fitness for a particular purpose (including any of the aforementioned purposes), quality, safety, efficacy, merchantability and/or non-infringement of any information provided in these landscape documents and/or of any of the products referenced therein. WHO also disclaims any and all liability or responsibility whatsoever for any death, disability, injury, suffering, loss, damage or other prejudice of any kind that may arise from or in connection with the procurement, distribution or use of any product included in any of these landscape documents.

Landscape analysis of therapeutics as 21st March 2020

Product type and candidate	Description	Licensed for	Licensed dose	Route of administration	Currently being trialled COVID-19?	Status of clinical development for Coronaviruses	Proposed dose for COVID-19	Status of clinical development for other relevant conditions
	and released by host cells + antiviral + steroid hormones					2003;116(6):811-8 (IFN- α + RBV + steroids) Clinical study MERS: Al Ghamdi et al. BMC Infect Dis 2016;16:174 (case series ; 23 patients ; hydrocortisone + RBV + IFN- α or IFN- β) - Inconclusive.		
Lopinavir + Ritonavir + IFN + Ribavirin	combination of protease inhibitor + proteins made and released by host cells + antiviral					Clinical studies MERS: - Spanakis et al. https://www.ncbi.nlm.nih.gov/pubmed/25288266 - Kim et al. https://www.ncbi.nlm.nih.gov/pubmed/26492219	MERS: Spanakis et al. : oral (p.o.) lopinavir/ritonavir (400/100 mg twice daily), pegylated interferon (180 μ g subcutaneously once per week for 12 days) and ribavirin (2000 mg p.o. loading dose, followed by 1200 mg p.o. every 8 h for 8 days) Kim et al.: LPV/r (per oral, lopinavir 400 mg/ritonavir 10 mg twice per day), ribavirin (per oral, as a loading dose of 2.0 g followed by 1.2 g three times per day) and pegylated IFN α 2a (subcutaneous injection, 180 μ g /0.5 ml)	

DISCLAIMER: These landscape documents have been prepared by the World Health Organization (WHO) for information purposes only concerning the 2019-2020 global of the novel coronavirus. Inclusion of any particular product or entity in any of these landscape documents does not constitute, and shall not be deemed or construed as, any approval or endorsement by WHO of such product or entity (or any of its businesses or activities). While WHO takes reasonable steps to verify the accuracy of the information presented in these landscape documents, WHO does not make any (and hereby disclaims all) representations and warranties regarding the accuracy, completeness, fitness for a particular purpose (including any of the aforementioned purposes), quality, safety, efficacy, merchantability and/or non-infringement of any information provided in these landscape documents and/or of any of the products referenced therein. WHO also disclaims any and all liability or responsibility whatsoever for any death, disability, injury, suffering, loss, damage or other prejudice of any kind that may arise from or in connection with the procurement, distribution or use of any product included in any of these landscape documents.

Landscape analysis of therapeutics as 21st March 2020

IFN-β1a + mycophenolate mofetil	combination of proteins made and released by host cells + immunosuppressant	mycophenolate mofetil (generic) is licensed for preventing organ rejection (used with ciclosporin and corticosteroids)	Dose depend on the type of organ transplant and the patient's age and size (in adults: usually 1.0 to 1.5g twice a day)	Mycophenolate mofetil is available as capsules (250 mg) and tablets (500 mg), and can also be given as an infusion (drip into a vein).		Clinical study MERS: Al Ghamdi et al. BMC Infect Dis 2016;16:174 (case series ; 23 patients ; hydrocortisone + RBV + IFN-α or IFN-β) - Inconclusive.		
---------------------------------	---	--	---	--	--	--	--	--

DISCLAIMER: These landscape documents have been prepared by the World Health Organization (WHO) for information purposes only concerning the 2019-2020 global of the novel coronavirus. Inclusion of any particular product or entity in any of these landscape documents does not constitute, and shall not be deemed or construed as, any approval or endorsement by WHO of such product or entity (or any of its businesses or activities). While WHO takes reasonable steps to verify the accuracy of the information presented in these landscape documents, WHO does not make any (and hereby disclaims all) representations and warranties regarding the accuracy, completeness, fitness for a particular purpose (including any of the aforementioned purposes), quality, safety, efficacy, merchantability and/or non-infringement of any information provided in these landscape documents and/or of any of the products referenced therein. WHO also disclaims any and all liability or responsibility whatsoever for any death, disability, injury, suffering, loss, damage or other prejudice of any kind that may arise from or in connection with the procurement, distribution or use of any product included in any of these landscape documents.

Landscape analysis of therapeutics as 21st March 2020

Product type and candidate	Description	Licensed for	Licensed dose	Route of administration	Currently being trialed COVID - 19?	Status of clinical development for Coronaviruses	Proposed dose for COVID-19	Status of clinical development for other relevant conditions
Lopinavir + Ritonavir + IFNβ1b	Lopinavir and ritonavir are antiretroviral protease inhibitors combination protease inhibitor and host			Lopinavir/ritonavir: tablet form (or suspension via nasogastric tube) IFN-β1b: subcutaneous injections		<p>Clinical studies MERS: NCT02845843 (MIRACLE Trial) (100 mg Lopinavir/100 mg Ritonavir PO q12 h for 14 days + INF- β1b 0.25 mg/ml SQ on alternative days for 14 days), Arabi et al. Trials. 2018 ; 19(1):81 (study protocol) Arabi at al. Trials. 2020 ; 21(1):8 (statistical analysis plan) Abbott Laboratories. Product Information: Kaletra®. https://www.accessdata.fda.gov/drugsatfda_docs/label/2010/021226s030lbl.pdf</p> <p>In vivo study MERS-CoV: Chan et al. J Infect Dis. 2015. 212(12):1904-13 - Lopinavir/ritonavir and interferon-β1b, but not MMF, improved the outcome of MERS-CoVinfected common marmosets.</p>	For MERS use was: Lopinavir /Ritonavir 400mg +100 mg / ml twice daily for 14 days and Interferon beta-1b 0.25 mg subcutaneous every alternate day for 14 days	

DISCLAIMER: These landscape documents have been prepared by the World Health Organization (WHO) for information purposes only concerning the 2019-2020 global of the novel coronavirus. Inclusion of any particular product or entity in any of these landscape documents does not constitute, and shall not be deemed or construed as, any approval or endorsement by WHO of such product or entity (or any of its businesses or activities). While WHO takes reasonable steps to verify the accuracy of the information presented in these landscape documents, WHO does not make any (and hereby disclaims all) representations and warranties regarding the accuracy, completeness, fitness for a particular purpose (including any of the aforementioned purposes), quality, safety, efficacy, merchantability and/or non-infringement of any information provided in these landscape documents and/or of any of the products referenced therein. WHO also disclaims any and all liability or responsibility whatsoever for any death, disability, injury, suffering, loss, damage or other prejudice of any kind that may arise from or in connection with the procurement, distribution or use of any product included in any of these landscape documents.

Landscape analysis of therapeutics as 21st March 2020

Product type and candidate	Description	Licensed for	Licensed dose	Route of administration	Currently being trialled COVID-19?	Status of clinical development for Coronaviruses	Proposed dose for COVID-19	Status of clinical development for other relevant conditions
Baloxavir marboxil (Xofluza)	Antiviral (endonuclease inhibitor)	In the US licensed for acute uncomplicated influenza and in Japan for all influenza	single-dose (20mg or 40mg depending on body weight)	Oral	Yes http://www.cictr.org.cn/s/howprojen.aspx?proj=49013	Clinical trials COVID-19	clinical trial: 80mg on day1, 80mg on day4; and 80mg on day 7 as necessary. No more than 3 times administration in total.	Phase II clinical trial influenza: Hayden, F. G., Sugaya, N., Hirotsu, N., Lee, N., de Jong, M. D., Hurt, A. C., ... Watanabe, A. (2018). Baloxavir Marboxil for Uncomplicated Influenza in Adults and Adolescents. <i>New England Journal of Medicine</i> , 379(10), 913–923. https://doi.org/10.1056/NEJMoa1716197 : Phase 2 trial influenza Phase III Clinical trials influenza: https://clinicaltrials.gov/ct2/show/NCT02954354 https://clinicaltrials.gov/ct2/show/NCT03653364 https://clinicaltrials.gov/ct2/show/NCT03629184 https://clinicaltrials.gov/ct2/show/NCT03684044

DISCLAIMER: These landscape documents have been prepared by the World Health Organization (WHO) for information purposes only concerning the 2019-2020 global of the novel coronavirus. Inclusion of any particular product or entity in any of these landscape documents does not constitute, and shall not be deemed or construed as, any approval or endorsement by WHO of such product or entity (or any of its businesses or activities). While WHO takes reasonable steps to verify the accuracy of the information presented in these landscape documents, WHO does not make any (and hereby disclaims all) representations and warranties regarding the accuracy, completeness, fitness for a particular purpose (including any of the aforementioned purposes), quality, safety, efficacy, merchantability and/or non-infringement of any information provided in these landscape documents and/or of any of the products referenced therein. WHO also disclaims any and all liability or responsibility whatsoever for any death, disability, injury, suffering, loss, damage or other prejudice of any kind that may arise from or in connection with the procurement, distribution or use of any product included in any of these landscape documents.

Landscape analysis of therapeutics as 21st March 2020

Product type and candidate	Description	Licensed for	Licensed dose	Route of administration	Currently being trialled COVID-19?	Status of clinical development for Coronaviruses	Proposed dose for COVID-19	Status of clinical development for other relevant conditions
Licensed in country of origin for other diseases								
Favipiravir (or T-705 or Avigan)	Experimental antiviral drug. Pyrazinecarboxamide derivative viral RNA polymerase inhibitor.	Influenza (licensed in Japan)	Day 1: 1600 mg twice daily Days 2 through 5: 600 mg twice daily	Oral	Yes http://www.chictr.org.cn/showproj.aspx?proj=49015 http://www.chictr.org.cn/showproj.aspx?proj=49013 http://www.chictr.org.cn/showproj.aspx?proj=49042 =	Clinical trials COVID-19 -- ChiCTR2000029600 Trial Experimental Treatment with Favipiravir for COVID-19: An Open-Label (unpublished). Favipiravir vs Lopinavir-Ritonavir (control arm) – Multivariable Cox regression showed that FPV was independently associated with faster viral clearance. In addition, fewer adverse reactions were found in the FPV arm than in the control arm. In this open-label nonrandomized control study, FPV. fewer adverse reactions were found in the	600 mg tid with 1600mg first loading dosage for no more than 14 days	Phase I/II and phase III Clinical trials Influenza: Phase III completed in the US: NCT02026349 ; NCT02008344 Phase I / II completed, in the US: NCT01068912 ; NCT01728753 or in China: NCT03394209 or in Japan: JPRN-JapicCTI-142657 Used in JIKI Trial (Ebola, nonrandomized): day 0: 6000 mg; day 1 to day 9: 2400 mg/d Dose escalation trial in preparation in France

DISCLAIMER: These landscape documents have been prepared by the World Health Organization (WHO) for information purposes only concerning the 2019-2020 global of the novel coronavirus. Inclusion of any particular product or entity in any of these landscape documents does not constitute, and shall not be deemed or construed as, any approval or endorsement by WHO of such product or entity (or any of its businesses or activities). While WHO takes reasonable steps to verify the accuracy of the information presented in these landscape documents, WHO does not make any (and hereby disclaims all) representations and warranties regarding the accuracy, completeness, fitness for a particular purpose (including any of the aforementioned purposes), quality, safety, efficacy, merchantability and/or non-infringement of any information provided in these landscape documents and/or of any of the products referenced therein. WHO also disclaims any and all liability or responsibility whatsoever for any death, disability, injury, suffering, loss, damage or other prejudice of any kind that may arise from or in connection with the procurement, distribution or use of any product included in any of these landscape documents.

Landscape analysis of therapeutics as 21st March 2020

						FPV arm than in the control arm.		
Enisamium iodide (Amizon)	Antiviral on the market in Ukraine							In vitro studies influenza: Boltz, D., Peng, X., Muzzio, M., Dash, P., Thomas, P. G., & Margitich, V. (2018). Activity of enisamium, an isonicotinic acid derivative, against influenza viruses in differentiated normal human bronchial epithelial cells. <i>Antiviral Chemistry and Chemotherapy</i> , 26. https://doi.org/10.1177/2040206618811416 Cocking, D., Cinatl, J., Boltz, D. A., Peng, X., Johnson, W., Muzzio, M., ... Margitich, V. (2018). Antiviral effect of a derivative of isonicotinic acid enisamium iodide (FAV00A) against influenza virus. <i>Acta Virologica</i> , 62(2), 191–195. https://doi.org/10.4149/av_2018_211

DISCLAIMER: These landscape documents have been prepared by the World Health Organization (WHO) for information purposes only concerning the 2019-2020 global of the novel coronavirus. Inclusion of any particular product or entity in any of these landscape documents does not constitute, and shall not be deemed or construed as, any approval or endorsement by WHO of such product or entity (or any of its businesses or activities). While WHO takes reasonable steps to verify the accuracy of the information presented in these landscape documents, WHO does not make any (and hereby disclaims all) representations and warranties regarding the accuracy, completeness, fitness for a particular purpose (including any of the aforementioned purposes), quality, safety, efficacy, merchantability and/or non-infringement of any information provided in these landscape documents and/or of any of the products referenced therein. WHO also disclaims any and all liability or responsibility whatsoever for any death, disability, injury, suffering, loss, damage or other prejudice of any kind that may arise from or in connection with the procurement, distribution or use of any product included in any of these landscape documents.

Landscape analysis of therapeutics as 21st March 2020

Product type and candidate	Description	Licensed for	Licensed dose	Route of administration	Currently being trialled COVID-19?	Status of clinical development for Coronaviruses	Proposed dose for COVID-19	Status of clinical development for other relevant conditions
Arbidol (Umifenovir)	Antiviral. Russian-made small indole derivative molecule	Licensed in Russia and China for prophylaxis and treatment of influenza and other respiratory viral infections. Since 2004, ARB is patented by Masterlek™ for its medicinal use as an antiviral agent against atypical pneumonia induced by the SARS-CoV. Not approved by EMA/FDA			Yes http://www.hictr.org.cn/showproj.aspx?proj=49069 http://www.hictr.org.cn/showproj.aspx?proj=49065 https://clinicaltrials.gov/ct2/show/NCT04252885	Clinical trials COVID-19 In vitro study SARS-CoV: - Khamitov et al. Vopr Virusol. 2008 ;53(4):9-13 - (GMK-AH-1 cells) - Arbidol and arbidol mesylate were shown to have a direct antiviral effect in early viral replication in the cultured cells. (in Russian)	CT ChiCTR2000029592: not mentioned CT ChiCTR2000029573: Arbidol Tablets 200mg/ time, p.o.tid. CT NCT04252885: ordinary treatment plus a regimen of arbidol (100mg) (oral, tid, 200mg each time, taking for 7-14 days).	Review: - Kramarev et al. Lik Sprava. 2013 Mar;(2):99-106 - The treatment of influenza and acute respiratory viral infections. (in Russian) Blaising et al. Antiviral Res. 2014 Jul;107:84-94.
Novaferon, Nova	Recombinant protein produced by DNA-shuffling of IFN-α	Licensed in China hepatitis B		Atomization inhalation	Yes http://www.hictr.org.cn/showproj.aspx?proj=49065 http://www.hictr.org.cn/showproj.aspx?proj=48809	Clinical trials COVID-19	20g/ time, atomized inhalation (in one trial, in combination with Arbidol tid.Arbidol Tablets 200mg/ time, p.o.tid)	

DISCLAIMER: These landscape documents have been prepared by the World Health Organization (WHO) for information purposes only concerning the 2019-2020 global of the novel coronavirus. Inclusion of any particular product or entity in any of these landscape documents does not constitute, and shall not be deemed or construed as, any approval or endorsement by WHO of such product or entity (or any of its businesses or activities). While WHO takes reasonable steps to verify the accuracy of the information presented in these landscape documents, WHO does not make any (and hereby disclaims all) representations and warranties regarding the accuracy, completeness, fitness for a particular purpose (including any of the aforementioned purposes), quality, safety, efficacy, merchantability and/or non-infringement of any information provided in these landscape documents and/or of any of the products referenced therein. WHO also disclaims any and all liability or responsibility whatsoever for any death, disability, injury, suffering, loss, damage or other prejudice of any kind that may arise from or in connection with the procurement, distribution or use of any product included in any of these landscape documents.

Landscape analysis of therapeutics as 21st March 2020

Product type and candidate	Description	Licensed for	Licensed dose	Route of administration	Currently being trialled COVID 19?	Status of clinical development for Coronaviruses	Proposed dose for COVID-19	Status of clinical development for other relevant conditions
Licensed but removed from the market for commercial reasons								
IFN alfacon-1 + corticosteroids (Infergen®, Advaferon® - Discontinued Drugs)	Synthetic recombinant type-I interferon (IFN) developed by comparing the amino acid sequences of several natural IFN-alpha subtypes	Hepatitis C, Chronic (withdrawn from use in the European Union)		Injection		Clinical study SARS: Loutfy et al. JAMA 2003;290(24):3222-8 (case series ; 22 patients) - improved outcome, but higher doses of steroids received, so it is difficult to determine whether or not the beneficial effects were due to the interferon alfacon 1 .		
Phase 2/Phase 3/Observational								

DISCLAIMER: These landscape documents have been prepared by the World Health Organization (WHO) for information purposes only concerning the 2019-2020 global of the novel coronavirus. Inclusion of any particular product or entity in any of these landscape documents does not constitute, and shall not be deemed or construed as, any approval or endorsement by WHO of such product or entity (or any of its businesses or activities). While WHO takes reasonable steps to verify the accuracy of the information presented in these landscape documents, WHO does not make any (and hereby disclaims all) representations and warranties regarding the accuracy, completeness, fitness for a particular purpose (including any of the aforementioned purposes), quality, safety, efficacy, merchantability and/or non-infringement of any information provided in these landscape documents and/or of any of the products referenced therein. WHO also disclaims any and all liability or responsibility whatsoever for any death, disability, injury, suffering, loss, damage or other prejudice of any kind that may arise from or in connection with the procurement, distribution or use of any product included in any of these landscape documents.

Landscape analysis of therapeutics as 21st March 2020

Convalescent plasma	Human polyclonal	NA	NA	IV		<p>Clinical studies SARS: Cheng, Y. et al. (2005). Use of convalescent plasma therapy in SARS patients in Hong Kong. <i>European Journal of Clinical Microbiology and Infectious Diseases</i>, 24(1), 44–46. -</p> <p>> non-randomised treatment of 80 SARS pts with convalescent plasma. Soo, Y. O. Y. et al. (2004). Retrospective comparison of convalescent plasma with continuing high-dose methylprednisolone treatment in SARS patients. <i>Clinical Microbiology and Infection</i>, 10(7), 676–678.</p>	<p>Clinical trials influenza: Hung, I. F. N. et al. (2013). Hyperimmune IV immunoglobulin treatment: A multicenter double-blind randomized controlled trial for patients with severe 2009 influenza A(H1N1) infection. <i>Chest</i>, 144(2), 464–473. -> randomisation of 35 patients with influenza infection to hyperimmune IV immunoglobulin vs normal IV immunoglobulin. Hung, I. F. N. et al. (2011). Convalescent plasma treatment reduced mortality in patients with severe pandemic influenza A (H1N1) 2009 virus infection. <i>Clinical Infectious Diseases</i>, 52(4), 447–456. -> prospective cohort study where convalescent plasma was given to 20 critically ill H1N1pdm09 patients</p>
---------------------	------------------	----	----	----	--	---	---

DISCLAIMER: These landscape documents have been prepared by the World Health Organization (WHO) for information purposes only concerning the 2019-2020 global of the novel coronavirus. Inclusion of any particular product or entity in any of these landscape documents does not constitute, and shall not be deemed or construed as, any approval or endorsement by WHO of such product or entity (or any of its businesses or activities). While WHO takes reasonable steps to verify the accuracy of the information presented in these landscape documents, WHO does not make any (and hereby disclaims all) representations and warranties regarding the accuracy, completeness, fitness for a particular purpose (including any of the aforementioned purposes), quality, safety, efficacy, merchantability and/or non-infringement of any information provided in these landscape documents and/or of any of the products referenced therein. WHO also disclaims any and all liability or responsibility whatsoever for any death, disability, injury, suffering, loss, damage or other prejudice of any kind that may arise from or in connection with the procurement, distribution or use of any product included in any of these landscape documents.

Landscape analysis of therapeutics as 21st March 2020

Continued..						<p>non-randomised retrospective 19 SARS patients treated with convalescent plasma vs 21pulsed methylprednisolone. Wong, V. et al. (2003). Treatment of severe acute respiratory syndrome with convalescent plasma. In Hong Kong Med J (Vol. 9) > Case report of SARS patient receiving convalescent plasma (+ribavirin and corticosteroids) Yeh, K. M. et al. (2005). Experience of using convalescent plasma for severe acute respiratory syndrome among healthcare workers in a Taiwan hospital. Journal of Antimicrobial Chemotherapy, 56(5), 919–922. -> 3 SARS infected patients treated with convalescent plasma Zhou, X. et al. (2003). [Epidemiologic features, clinical diagnosis and therapy of first cluster of patients with severe acute respiratory syndrome in Beijing area]. Zhonghua Yi Xue Za Zhi, 83(12), 1018– 1022. -> 1 SARS patient treated with convalescent Plasma Systematic review SARS studies: Mair-Jenkins, J. et al. (2015). The effectiveness of convalescent plasma and hyperimmune immunoglobulin for the treatment of severe acute respiratory infections of viral etiology: A systematic review and exploratory meta-analysis. Journal of</p>		
-------------	--	--	--	--	--	--	--	--

DISCLAIMER: These landscape documents have been prepared by the World Health Organization (WHO) for information purposes only concerning the 2019-2020 global of the novel coronavirus. Inclusion of any particular product or entity in any of these landscape documents does not constitute, and shall not be deemed or construed as, any approval or endorsement by WHO of such product or entity (or any of its businesses or activities). While WHO takes reasonable steps to verify the accuracy of the information presented in these landscape documents, WHO does not make any (and hereby disclaims all) representations and warranties regarding the accuracy, completeness, fitness for a particular purpose (including any of the aforementioned purposes), quality, safety, efficacy, merchantability and/or non-infringement of any information provided in these landscape documents and/or of any of the products referenced therein. WHO also disclaims any and all liability or responsibility whatsoever for any death, disability, injury, suffering, loss, damage or other prejudice of any kind that may arise from or in connection with the procurement, distribution or use of any product included in any of these landscape documents.

Landscape analysis of therapeutics as 21st March 2020

						Infectious Diseases, 211(1), 80–90. -> systematic		
--	--	--	--	--	--	---	--	--

DISCLAIMER: These landscape documents have been prepared by the World Health Organization (WHO) for information purposes only concerning the 2019-2020 global of the novel coronavirus. Inclusion of any particular product or entity in any of these landscape documents does not constitute, and shall not be deemed or construed as, any approval or endorsement by WHO of such product or entity (or any of its businesses or activities). While WHO takes reasonable steps to verify the accuracy of the information presented in these landscape documents, WHO does not make any (and hereby disclaims all) representations and warranties regarding the accuracy, completeness, fitness for a particular purpose (including any of the aforementioned purposes), quality, safety, efficacy, merchantability and/or non-infringement of any information provided in these landscape documents and/or of any of the products referenced therein. WHO also disclaims any and all liability or responsibility whatsoever for any death, disability, injury, suffering, loss, damage or other prejudice of any kind that may arise from or in connection with the procurement, distribution or use of any product included in any of these landscape documents.

Landscape analysis of therapeutics as 21st March 2020

Continued..						<p>review and exploratory meta-analysis of convalescent plasma treatment for SARS and severe influenza</p> <p>Protocol clinical study MERS: Arabi, Y. et al. (2015). Feasibility, safety, clinical, and laboratory effects of convalescent plasma therapy for patients with Middle East respiratory syndrome coronavirus infection: a study protocol. SpringerPlus, 4(1), 1–8. -> protocol for convalescent plasma study in MERS</p> <p>Clinical studies MERS: Ko, J. H. et al. (2018). Challenges of convalescent plasma infusion therapy in Middle East respiratory coronavirus infection: A single centre experience. Antiviral Therapy, 23(7), 617–622. -> 3 patients received convalescent plasma. Neutralisation activity assessed. van Doremalen, N. et al. (2017). Efficacy of antibody-based therapies against Middle East respiratory syndrome coronavirus (MERS-CoV) in common marmosets. Antiviral Research, 143, 30–37.-></p>		
-------------	--	--	--	--	--	---	--	--

DISCLAIMER: These landscape documents have been prepared by the World Health Organization (WHO) for information purposes only concerning the 2019-2020 global of the novel coronavirus. Inclusion of any particular product or entity in any of these landscape documents does not constitute, and shall not be deemed or construed as, any approval or endorsement by WHO of such product or entity (or any of its businesses or activities). While WHO takes reasonable steps to verify the accuracy of the information presented in these landscape documents, WHO does not make any (and hereby disclaims all) representations and warranties regarding the accuracy, completeness, fitness for a particular purpose (including any of the aforementioned purposes), quality, safety, efficacy, merchantability and/or non-infringement of any information provided in these landscape documents and/or of any of the products referenced therein. WHO also disclaims any and all liability or responsibility whatsoever for any death, disability, injury, suffering, loss, damage or other prejudice of any kind that may arise from or in connection with the procurement, distribution or use of any product included in any of these landscape documents.

Landscape analysis of therapeutics as 21st March 2020

Continued..						<p>MERS infected marmosets treated with high titre hyperimmune plasma vs mAb m336. Arabi, Y. M., et al. (2016). Feasibility of using convalescent plasma immunotherapy for MERSCoV infection, Saudi Arabia. Emerging Infectious Diseases, 22(9), 1554–1561. -> feasibility of collecting convalescent plasma from MERS survivors Chun, S., et al. (2016). Possible transfusionrelated acute lung injury following convalescent plasma transfusion in a patient with middle east respiratory syndrome. Annals of Laboratory Medicine, Vol. 36, pp. 393–395. -> possible acute lung injury following convalescent plasma transfusion in MERS patient</p>		
-------------	--	--	--	--	--	--	--	--

DISCLAIMER: These landscape documents have been prepared by the World Health Organization (WHO) for information purposes only concerning the 2019-2020 global of the novel coronavirus. Inclusion of any particular product or entity in any of these landscape documents does not constitute, and shall not be deemed or construed as, any approval or endorsement by WHO of such product or entity (or any of its businesses or activities). While WHO takes reasonable steps to verify the accuracy of the information presented in these landscape documents, WHO does not make any (and hereby disclaims all) representations and warranties regarding the accuracy, completeness, fitness for a particular purpose (including any of the aforementioned purposes), quality, safety, efficacy, merchantability and/or non-infringement of any information provided in these landscape documents and/or of any of the products referenced therein. WHO also disclaims any and all liability or responsibility whatsoever for any death, disability, injury, suffering, loss, damage or other prejudice of any kind that may arise from or in connection with the procurement, distribution or use of any product included in any of these landscape documents.

Landscape analysis of therapeutics as 21st March 2020

GS-5734/ Remdesivir	Nucleoside Inhibitor	NA	NA	IV	<p>Yes https://clinicaltrials.gov/ct2/show/NCT04252664?cond=COVID19&draw=2&rank=1 https://clinicaltrials.gov/ct2/show/NCT04257656?term=remdesivir&draw=2&rank=1</p>	<p><u>In vitro COVID-19:</u> Wang, M., et al. (2020). Remdesivir and chloroquine effectively inhibit the recently emerged novel coronavirus (COVID-19) in vitro. Cell Research. Holshue, M. L. et al. (2020). First Case of 2019 Novel Coronavirus in the United States. New England Journal of Medicine, NEJMoa2001191. -> 1 COVID-19 patient</p> <p><u>In vivo MERS-CoV:</u> de Wit, E. et al. (2020). Prophylactic and therapeutic remdesivir (GS-5734) treatment in the rhesus macaque model of MERS-CoV infection. Proceedings of the National Academy of Sciences, 201922083. -> Efficacy against MERS in monkeys Sheahan, T. P. et al. (2020). Comparative therapeutic efficacy of remdesivir and combination lopinavir, ritonavir, and interferon beta against MERS-CoV. Nature Communications, 11(1). -> study in MERS-CoV infected mice Jordan, R. et al. (2017). Broad-spectrum Investigational Agent GS5734 for the Treatment of Ebola, MERS Coronavirus and Other Pathogenic Viral Infections with</p>	<p>CT NCT04252664: 200 mg loading dose on day 1 is given, followed by 100 mg iv once-daily maintenance doses for 9 days.</p> <p>CT NCT04257656: 200 mg loading dose on day 1 is given, followed by 100 mg iv once-daily maintenance doses for 9 days.</p>	<p>Clinical trials Ebola: Phase II: https://clinicaltrials.gov/ct2/show/NCT02818582, Phase III: https://clinicaltrials.gov/ct2/show/NCT03719586</p>
------------------------	-------------------------	----	----	----	---	---	---	---

DISCLAIMER: These landscape documents have been prepared by the World Health Organization (WHO) for information purposes only concerning the 2019-2020 global of the novel coronavirus. Inclusion of any particular product or entity in any of these landscape documents does not constitute, and shall not be deemed or construed as, any approval or endorsement by WHO of such product or entity (or any of its businesses or activities). While WHO takes reasonable steps to verify the accuracy of the information presented in these landscape documents, WHO does not make any (and hereby disclaims all) representations and warranties regarding the accuracy, completeness, fitness for a particular purpose (including any of the aforementioned purposes), quality, safety, efficacy, merchantability and/or non-infringement of any information provided in these landscape documents and/or of any of the products referenced therein. WHO also disclaims any and all liability or responsibility whatsoever for any death, disability, injury, suffering, loss, damage or other prejudice of any kind that may arise from or in connection with the procurement, distribution or use of any product included in any of these landscape documents.

Landscape analysis of therapeutics as 21st March 2020

						High Outbreak Potential. Open Forum Infectious Diseases, 4(suppl_1), S737–S737. -> mice infected with MERSCoV		
--	--	--	--	--	--	---	--	--

DISCLAIMER: These landscape documents have been prepared by the World Health Organization (WHO) for information purposes only concerning the 2019-2020 global of the novel coronavirus. Inclusion of any particular product or entity in any of these landscape documents does not constitute, and shall not be deemed or construed as, any approval or endorsement by WHO of such product or entity (or any of its businesses or activities). While WHO takes reasonable steps to verify the accuracy of the information presented in these landscape documents, WHO does not make any (and hereby disclaims all) representations and warranties regarding the accuracy, completeness, fitness for a particular purpose (including any of the aforementioned purposes), quality, safety, efficacy, merchantability and/or non-infringement of any information provided in these landscape documents and/or of any of the products referenced therein. WHO also disclaims any and all liability or responsibility whatsoever for any death, disability, injury, suffering, loss, damage or other prejudice of any kind that may arise from or in connection with the procurement, distribution or use of any product included in any of these landscape documents.

Landscape analysis of therapeutics as 21st March 2020

						<p><u>In vivo and in vitro SARSCoV and MERS:</u> Agostini, M. L. et al. (2018a). Coronavirus Susceptibility to the Antiviral Remdesivir (GS5734) Is Mediated by the Viral Polymerase and the Proofreading Exoribonuclease. MBio, 9(2). -> human airway epithelial cells and animal model findings SARS and MERS</p> <p>Sheahan, T. P. et al. (2017). Broad-spectrum antiviral GS-5734 inhibits both epidemic and zoonotic coronaviruses. Science Translational Medicine, 9(396). -> in human airway epithelial cultures and animal model findings SARS and MERS</p> <p><u>In vitro coronaviruses:</u> Brown, A. J. et al. (2019). Broad spectrum antiviral remdesivir inhibits human endemic and zoonotic deltacoronaviruses with a highly divergent RNA dependent RNA polymerase. Antiviral Research, 169. -> in vitro inhibition of coronaviruses</p>		
--	--	--	--	--	--	---	--	--

DISCLAIMER: These landscape documents have been prepared by the World Health Organization (WHO) for information purposes only concerning the 2019-2020 global of the novel coronavirus. Inclusion of any particular product or entity in any of these landscape documents does not constitute, and shall not be deemed or construed as, any approval or endorsement by WHO of such product or entity (or any of its businesses or activities). While WHO takes reasonable steps to verify the accuracy of the information presented in these landscape documents, WHO does not make any (and hereby disclaims all) representations and warranties regarding the accuracy, completeness, fitness for a particular purpose (including any of the aforementioned purposes), quality, safety, efficacy, merchantability and/or non-infringement of any information provided in these landscape documents and/or of any of the products referenced therein. WHO also disclaims any and all liability or responsibility whatsoever for any death, disability, injury, suffering, loss, damage or other prejudice of any kind that may arise from or in connection with the procurement, distribution or use of any product included in any of these landscape documents.

Landscape analysis of therapeutics as 21st March 2020

Product type and candidate	Description	Licensed for	Licensed dose	Route of administration	Currently being trialled COVID - 19?	Status of clinical development for Coronaviruses	Proposed dose for COVID-19	Status of clinical development for other relevant conditions
Alferon® (IFN-α-n3)	natural, human interferon alpha protein	NA	NA	Parenteral injection of oral		<p><u>Clinical trial SARS:</u> Alferon® LDO - NCT00215826 (Phase 2) - No results posted Phase 2 - randomized dose-ranging study to evaluate the safety and activity of orally administered low dose IFNα-n3 as an antiviral and immunomodulator in asymptomatic subjects with recent exposure to a person with severe acute respiratory syndrome (SARS) or possible SARS. NO RESULTS POSTED</p> <p><u>In vivo study SARS-CoV:</u> Barnard at al. Antivir Chem Chemother.2006;17(5):275-84 - Alferon® did not reduce virus lung titres in the SARS- CoV mouse model most probably because of the well- known species barrier between human IFN-α and the mouse IFN type 1 receptor.</p>	In Phase II CT NCT00215826 SARS 650 IU vs. 1300 IU trialled	

DISCLAIMER: These landscape documents have been prepared by the World Health Organization (WHO) for information purposes only concerning the 2019-2020 global of the novel coronavirus. Inclusion of any particular product or entity in any of these landscape documents does not constitute, and shall not be deemed or construed as, any approval or endorsement by WHO of such product or entity (or any of its businesses or activities). While WHO takes reasonable steps to verify the accuracy of the information presented in these landscape documents, WHO does not make any (and hereby disclaims all) representations and warranties regarding the accuracy, completeness, fitness for a particular purpose (including any of the aforementioned purposes), quality, safety, efficacy, merchantability and/or non-infringement of any information provided in these landscape documents and/or of any of the products referenced therein. WHO also disclaims any and all liability or responsibility whatsoever for any death, disability, injury, suffering, loss, damage or other prejudice of any kind that may arise from or in connection with the procurement, distribution or use of any product included in any of these landscape documents.

Landscape analysis of therapeutics as 21st March 2020

<p>IFN-β1a solution for inhalation (SNG001)</p>	<p>IFN-β is a naturally occurring protein which orchestrates the body's antiviral defences IFN-β1a (SNG001) is a pH neutral and contains the excipient methionine, an amino acid native to the airways.</p>	<p>NA</p>	<p>NA</p>	<p>Inhalation. The delivery device (iNeb by Philips) used to date is a breath actuated mesh nebuliser</p>		<p>Unpublished data assessing IFN-β1a activity against MERS virus, generated by Heinrich Feldmann and Darryl Falzarano at NIH/NIAID in 2014</p>		<p><u>Asthma phase II trial:</u> Djukanović et al. Am J Respir Crit Care Med. 2014.190(2):145-54 ; NCT01126177 Asthma: Phase II trials (SG005 and INEXAS) in asthma, conducted by Synairgen (NCT01126177) and AstraZeneca respectively, suggest that SNG001 boosts antiviral responses in the lungs, has a beneficial effect on lung function and, in more difficult to treat patients, improves asthma control during cold infections. However, the unexpectedly low exacerbation rate (<10%) in the INEXAS trial population suggests that the economic viability of the drug in an asthma indication would be limited. (https://www.synairgen.com/programmes/ifn-%CE%B2-in-copd/) COPD phase II trial: NCT03570359 (Phase II) ; https://www.synairgen.com/programmes/ifn-%CE%B2-incopd/ COPD: Phase II Randomised, Double-blind, Placebocontrolled Study (SG015) - ongoing (https://clinicaltrials.gov/ct2/show/NCT03570359?term=N)</p>
---	---	-----------	-----------	---	--	---	--	--

DISCLAIMER: These landscape documents have been prepared by the World Health Organization (WHO) for information purposes only concerning the 2019-2020 global of the novel coronavirus. Inclusion of any particular product or entity in any of these landscape documents does not constitute, and shall not be deemed or construed as, any approval or endorsement by WHO of such product or entity (or any of its businesses or activities). While WHO takes reasonable steps to verify the accuracy of the information presented in these landscape documents, WHO does not make any (and hereby disclaims all) representations and warranties regarding the accuracy, completeness, fitness for a particular purpose (including any of the aforementioned purposes), quality, safety, efficacy, merchantability and/or non-infringement of any information provided in these landscape documents and/or of any of the products referenced therein. WHO also disclaims any and all liability or responsibility whatsoever for any death, disability, injury, suffering, loss, damage or other prejudice of any kind that may arise from or in connection with the procurement, distribution or use of any product included in any of these landscape documents.

Landscape analysis of therapeutics as 21st March 2020

								CT03570359&draw=2&rank=1)
--	--	--	--	--	--	--	--	---------------------------

DISCLAIMER: These landscape documents have been prepared by the World Health Organization (WHO) for information purposes only concerning the 2019-2020 global of the novel coronavirus. Inclusion of any particular product or entity in any of these landscape documents does not constitute, and shall not be deemed or construed as, any approval or endorsement by WHO of such product or entity (or any of its businesses or activities). While WHO takes reasonable steps to verify the accuracy of the information presented in these landscape documents, WHO does not make any (and hereby disclaims all) representations and warranties regarding the accuracy, completeness, fitness for a particular purpose (including any of the aforementioned purposes), quality, safety, efficacy, merchantability and/or non-infringement of any information provided in these landscape documents and/or of any of the products referenced therein. WHO also disclaims any and all liability or responsibility whatsoever for any death, disability, injury, suffering, loss, damage or other prejudice of any kind that may arise from or in connection with the procurement, distribution or use of any product included in any of these landscape documents.

Landscape analysis of therapeutics as 21st March 2020

Product type and candidate	Description	Licensed for	Licensed dose	Route of administration	Currently being trialled COVID-19?	Status of clinical development for Coronaviruses	Proposed dose for COVID-19	Status of clinical development for other relevant conditions
Part 1 Safety, Part 2 Efficacy and safety								
pegylated IFNλ1a	type III IFN	NA	NA	SC injection		Eiger BioPharmaceuticals have some initial in vitro and in vivo data with coronas.		Influenza: Sun et al. IFN-λ: A new spotlight in innate immunity against influenza virus infection. Protein Cell. 2018 Oct; 9(10): 832–837. Klinkhammer et al. IFN-λ prevents influenza virus spread from the upper airways to the lungs and limits virus transmission. eLife. 2018; 7: e33354. multiple Phase 2 and 3 Clinical trials mostly for hepatitis viruses: https://clinicaltrials.gov/ct2/results?cond=&term=interferon+lambd&cntry=&state=&city=&dist=

DISCLAIMER: These landscape documents have been prepared by the World Health Organization (WHO) for information purposes only concerning the 2019-2020 global of the novel coronavirus. Inclusion of any particular product or entity in any of these landscape documents does not constitute, and shall not be deemed or construed as, any approval or endorsement by WHO of such product or entity (or any of its businesses or activities). While WHO takes reasonable steps to verify the accuracy of the information presented in these landscape documents, WHO does not make any (and hereby disclaims all) representations and warranties regarding the accuracy, completeness, fitness for a particular purpose (including any of the aforementioned purposes), quality, safety, efficacy, merchantability and/or non-infringement of any information provided in these landscape documents and/or of any of the products referenced therein. WHO also disclaims any and all liability or responsibility whatsoever for any death, disability, injury, suffering, loss, damage or other prejudice of any kind that may arise from or in connection with the procurement, distribution or use of any product included in any of these landscape documents.

Landscape analysis of therapeutics as 21st March 2020

Polyclonal human antiMERS CoV Abs SAB 301	SAB-301 is a purified human Immune globulin G (hlgG) polyclonal antibody designed to bind to the MERSCoV spike (S) protein. The hlgG is purified from the plasma of immunized transchromoso mic (Tc) bovines that were immunized with a recombinant spike protein produced in insect cells.	NA	NA	IV		Group sequential design with multiple interim analyses to determine futility or efficacy. -Hospitalized adults with MERS CoV infection -Single 50mg/kg infusion of SAB-301 vs. placebo control -Being considered by KSA KAIMARC – P.I. Dr. Yaseen Arabi, M.D.		
--	--	----	----	----	--	---	--	--

Product type and candidate	Description	Licensed for	Licensed dose	Route of administration	Currently being trialled COVID-19?	Status of clinical development for Coronaviruses	Proposed dose for COVID-19	Status of clinical development for other relevant conditions
Phase 1								
Camostat	TMPRSS-2 inhibitor - see citation	NA	NA	Oral	NA	Role of TMPRSS2: https://www.ncbi.nlm.nih.gov/pubmed/30849247		Chronic pancreatitis: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6694471/
Sab-301	Polyclonal anti MERS-CoV (likely MERSspecific, but possible to crossreact)	NA	NA	IV	NA	<u>Clinical trial Phase 1 MERS:</u> https://clinicaltrials.gov/ct2/show/NCT02788188 <u>In vivo study MERS-CoV:</u> https://www.ncbi.nlm.nih.gov/pubmed/26888429	1 to 2 doses at 50 mg/kg	

DISCLAIMER: These landscape documents have been prepared by the World Health Organization (WHO) for information purposes only concerning the 2019-2020 global of the novel coronavirus. Inclusion of any particular product or entity in any of these landscape documents does not constitute, and shall not be deemed or construed as, any approval or endorsement by WHO of such product or entity (or any of its businesses or activities). While WHO takes reasonable steps to verify the accuracy of the information presented in these landscape documents, WHO does not make any (and hereby disclaims all) representations and warranties regarding the accuracy, completeness, fitness for a particular purpose (including any of the aforementioned purposes), quality, safety, efficacy, merchantability and/or non-infringement of any information provided in these landscape documents and/or of any of the products referenced therein. WHO also disclaims any and all liability or responsibility whatsoever for any death, disability, injury, suffering, loss, damage or other prejudice of any kind that may arise from or in connection with the procurement, distribution or use of any product included in any of these landscape documents.

Landscape analysis of therapeutics as 21st March 2020

BCX4430	Nucleoside Inhibitor	NA	NA	IV and IM formulations	NA			<p><u>Clinical trial Phase 1 Ebola Virus Disease:</u> https://clinicaltrials.gov/ct2/show/NCT02319772</p> <p><u>Clinical trial Phase 1 Yellow Fever:</u> https://clinicaltrials.gov/ct2/show/NCT03891420</p> <p><u>Clinical trial Phase 1 Marburg Virus Disease:</u> https://clinicaltrials.gov/ct2/show/NCT03800173</p>
Relacatib (SB462795)		NA	NA		NA	<p><u>Pers comm Pauline Williamns:</u> We can confirm that as well as Cathepsin-K activity, it does have good activity against CathepsinL. It has completed a first time in human study in healthy post-menopausal women, and the preclinical and clinical profile would support further studies in humans. We are collating the relevant documentation on the asset.</p>		

DISCLAIMER: These landscape documents have been prepared by the World Health Organization (WHO) for information purposes only concerning the 2019-2020 global of the novel coronavirus. Inclusion of any particular product or entity in any of these landscape documents does not constitute, and shall not be deemed or construed as, any approval or endorsement by WHO of such product or entity (or any of its businesses or activities). While WHO takes reasonable steps to verify the accuracy of the information presented in these landscape documents, WHO does not make any (and hereby disclaims all) representations and warranties regarding the accuracy, completeness, fitness for a particular purpose (including any of the aforementioned purposes), quality, safety, efficacy, merchantability and/or non-infringement of any information provided in these landscape documents and/or of any of the products referenced therein. WHO also disclaims any and all liability or responsibility whatsoever for any death, disability, injury, suffering, loss, damage or other prejudice of any kind that may arise from or in connection with the procurement, distribution or use of any product included in any of these landscape documents.

Landscape analysis of therapeutics as 21st March 2020

<p>REGN3048 and REGN3051 Antibody Cocktail</p>	<p>Biological: REGN3048 REGN3048 is a fully monoclonal antibody (mAbs) which binds to the S protein of MERS-CoV. Biological: REGN3051 REGN3051 is a fully human monoclonal antibody (mAb) which binds to the S protein of MERS-CoV. It can reduce virus titers and ameliorate MERS-CoV- induced lung pathology when given post infection.</p>	<p>NA</p>	<p>NA</p>		<p>NA</p>	<p>Clinical trial Phase I MERS: https://clinicaltrials.gov/ct2/show/NCT03301090</p>		
--	---	-----------	-----------	--	-----------	---	--	--

DISCLAIMER: These landscape documents have been prepared by the World Health Organization (WHO) for information purposes only concerning the 2019-2020 global of the novel coronavirus. Inclusion of any particular product or entity in any of these landscape documents does not constitute, and shall not be deemed or construed as, any approval or endorsement by WHO of such product or entity (or any of its businesses or activities). While WHO takes reasonable steps to verify the accuracy of the information presented in these landscape documents, WHO does not make any (and hereby disclaims all) representations and warranties regarding the accuracy, completeness, fitness for a particular purpose (including any of the aforementioned purposes), quality, safety, efficacy, merchantability and/or non-infringement of any information provided in these landscape documents and/or of any of the products referenced therein. WHO also disclaims any and all liability or responsibility whatsoever for any death, disability, injury, suffering, loss, damage or other prejudice of any kind that may arise from or in connection with the procurement, distribution or use of any product included in any of these landscape documents.

Landscape analysis of therapeutics as 21st March 2020

Product type and candidate	Description	Licensed for	Licensed dose	Route of administration	Currently being trialled COVID-19?	Status of clinical development for Coronaviruses	Proposed dose for COVID-19	Status of clinical development for other relevant conditions
Polyclonal Human Abs anti-Mers		NA	NA		NA			
Polyclonal human antiMERS CoV Abs SAB 301	SAB-301 is a purified human immune globulin G (hIgG) polyclonal antibody designed to specifically bind to the MERSCoV spike (S) protein, a component of the virion membrane that is responsible for binding of the virus to the host cell. The hIgG is purified from the plasma of immunized transchromosomal (Tc) bovines that were immunized with a recombinant spike protein produced in insect cells. SAB-301 is purified hIgG in a sterile liquid formulated in 10 mM glutamic acid monosodium salt, 262 mM Dsorbitol, 0.05 mg/mL Tween 80, pH 5.5. The drug product will be administered intravenously and will be diluted in saline per the clinical protocol.	NA	NA		NA	RCT, double blinded, single dose scalation phase II, >14 years- 160 subjects		

DISCLAIMER: These landscape documents have been prepared by the World Health Organization (WHO) for information purposes only concerning the 2019-2020 global of the novel coronavirus. Inclusion of any particular product or entity in any of these landscape documents does not constitute, and shall not be deemed or construed as, any approval or endorsement by WHO of such product or entity (or any of its businesses or activities). While WHO takes reasonable steps to verify the accuracy of the information presented in these landscape documents, WHO does not make any (and hereby disclaims all) representations and warranties regarding the accuracy, completeness, fitness for a particular purpose (including any of the aforementioned purposes), quality, safety, efficacy, merchantability and/or non-infringement of any information provided in these landscape documents and/or of any of the products referenced therein. WHO also disclaims any and all liability or responsibility whatsoever for any death, disability, injury, suffering, loss, damage or other prejudice of any kind that may arise from or in connection with the procurement, distribution or use of any product included in any of these landscape documents.

Landscape analysis of therapeutics as 21st March 2020

Product type and candidate	Description	Licensed for	Licensed dose	Route of administration	Currently being trialled COVID-19?	Status of clinical development for Coronaviruses	Proposed dose for COVID-19	Status of clinical development for other relevant conditions
Pre-clinical								
Lycorine	Inhibits cell division, antineoplastic, antiviral	NA	NA	NA	NA	Shen 2019 JV 93:e0002319		
UDA	Lectin	NA	NA	NA	NA	In vivo and in vitro influenza: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3216401/		
SSYA10-001	SARS/MERS nsp13 Helicase inhibitor	NA	NA	NA	NA	In vitro MERS-CoV and MHV: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4136041/		
Hiltonol PolyIC:LC	Host	NA	NA	intranasal doses	NA	In vivo SARS-CoV: https://www.ncbi.nlm.nih.gov/pubmed/27956136		
RTD-1 peptide	Immunomodulator	NA	NA	intranasal doses	NA	In vivo SARS-CoV: https://www.ncbi.nlm.nih.gov/pubmed/19710146		
NHC (EIDD1931)	β -D-N4 hydroxycytidine, ribonucleoside analogue, inhibit viral replication	NA	NA	NA	NA	In vitro MERS-CoV and SARS-CoV https://jvi.asm.org/content/93/24/e01348-19.long		
rHu-IFN- α B/D		NA	NA	NA	NA	In vivo SARS-CoV: https://www.ncbi.nlm.nih.gov/pubmed/17176632		

DISCLAIMER: These landscape documents have been prepared by the World Health Organization (WHO) for information purposes only concerning the 2019-2020 global of the novel coronavirus. Inclusion of any particular product or entity in any of these landscape documents does not constitute, and shall not be deemed or construed as, any approval or endorsement by WHO of such product or entity (or any of its businesses or activities). While WHO takes reasonable steps to verify the accuracy of the information presented in these landscape documents, WHO does not make any (and hereby disclaims all) representations and warranties regarding the accuracy, completeness, fitness for a particular purpose (including any of the aforementioned purposes), quality, safety, efficacy, merchantability and/or non-infringement of any information provided in these landscape documents and/or of any of the products referenced therein. WHO also disclaims any and all liability or responsibility whatsoever for any death, disability, injury, suffering, loss, damage or other prejudice of any kind that may arise from or in connection with the procurement, distribution or use of any product included in any of these landscape documents.

Landscape analysis of therapeutics as 21st March 2020

Product type and candidate	Description	Licensed for	Licensed dose	Route of administration	Currently being trialed COVID-19?	Status of clinical development for Coronaviruses	Proposed dose for COVID-19	Status of clinical development for other relevant conditions
Asterivir	Highly sulfonated chemicals attached to a U.S. FDA-approved Cyclodextrin scaffold	NA	NA	NA	NA	https://www.ncbi.nlm.nih.gov/pubmed/29251725 https://advances.sciencemag.org/content/6/5/eaax9318 The macromolecules are broad-spectrum, biocompatible, and virucidal at micromolar concentrations in vitro against many viruses [including herpes simplex virus (HSV), respiratory syncytial virus (RSV), dengue virus, and Zika virus]. They are effective ex vivo against both laboratory and clinical strains of RSV and HSV-2 in respiratory and vaginal tissue culture models, respectively. Additionally, they are effective when administered in mice before intravaginal HSV-2 inoculation.		
GD27	Human mAbs/ Fab-RBD	NA	NA	NA	NA	In vivo MERS-CoV: https://www.ncbi.nlm.nih.gov/pubmed/30091015		
Gd33	Human mAbs/ Fab-RBD	NA	NA	NA	NA	In vitro MERS-CoV: https://academic.oup.com/jid/article/218/8/1249/5017222		
MCA1	Human mAbs/ Fab-RBD	NA	NA	NA	NA	In vivo MERS-CoV: https://www.ncbi.nlm.nih.gov/pubmed/28472421		

DISCLAIMER: These landscape documents have been prepared by the World Health Organization (WHO) for information purposes only concerning the 2019-2020 global of the novel coronavirus. Inclusion of any particular product or entity in any of these landscape documents does not constitute, and shall not be deemed or construed as, any approval or endorsement by WHO of such product or entity (or any of its businesses or activities). While WHO takes reasonable steps to verify the accuracy of the information presented in these landscape documents, WHO does not make any (and hereby disclaims all) representations and warranties regarding the accuracy, completeness, fitness for a particular purpose (including any of the aforementioned purposes), quality, safety, efficacy, merchantability and/or non-infringement of any information provided in these landscape documents and/or of any of the products referenced therein. WHO also disclaims any and all liability or responsibility whatsoever for any death, disability, injury, suffering, loss, damage or other prejudice of any kind that may arise from or in connection with the procurement, distribution or use of any product included in any of these landscape documents.

Landscape analysis of therapeutics as 21st March 2020

JC57-14	Macaque mAbs/ Fab-RBD	NA	NA	NA	NA	In vitro MERS-CoV: https://www.ncbi.nlm.nih.gov/pubmed/29514901		
MERS-4	Human mAbs/ Fab-RBD	NA	NA	NA	NA	In vitro MERS-CoV: https://www.ncbi.nlm.nih.gov/pubmed/29996104		

Product type and candidate	Description	Licensed for	Licensed dose	Route of administration	Currently being trialled COVID-19?	Status of clinical development for Coronaviruses	Proposed dose for COVID-19	Status of clinical development for other relevant conditions
CDC2-C2	Human mAbs/ Fab-RBD	NA	NA	NA	NA	In vitro MERS-CoV: https://www.ncbi.nlm.nih.gov/pubmed/29514901		
VHH-83,	Dromedary VHHs	NA	NA	NA	NA	In vitro MERS-CoV: https://www.ncbi.nlm.nih.gov/pubmed/30101189		
HCAb-83	Dromedary VHHs	NA	NA	NA	NA			
CVHHs	Dromedary VHHs	NA	NA	NA	NA			
NbMs10	Llama VHHs	NA	NA	NA	NA	In vitro and in vivo MERSCoV: https://www.ncbi.nlm.nih.gov/pubmed/29950421		
NbM10-Fc	Llama VHHs	NA	NA	NA	NA			
LCA60	Human survivor, RBD	NA	NA	NA	NA			

DISCLAIMER: These landscape documents have been prepared by the World Health Organization (WHO) for information purposes only concerning the 2019-2020 global of the novel coronavirus. Inclusion of any particular product or entity in any of these landscape documents does not constitute, and shall not be deemed or construed as, any approval or endorsement by WHO of such product or entity (or any of its businesses or activities). While WHO takes reasonable steps to verify the accuracy of the information presented in these landscape documents, WHO does not make any (and hereby disclaims all) representations and warranties regarding the accuracy, completeness, fitness for a particular purpose (including any of the aforementioned purposes), quality, safety, efficacy, merchantability and/or non-infringement of any information provided in these landscape documents and/or of any of the products referenced therein. WHO also disclaims any and all liability or responsibility whatsoever for any death, disability, injury, suffering, loss, damage or other prejudice of any kind that may arise from or in connection with the procurement, distribution or use of any product included in any of these landscape documents.

Landscape analysis of therapeutics as 21st March 2020

Unnamed	New unpublished panel of human mAbs against SARS derived from a human survivor of the 2003 SARS outbreak in Hong Kong. The mAbs bind a variety of sites including RBD, NTD, and stem.	NA	NA	NA	NA	unpublished		
S3.1	human mAb	NA	NA	NA	NA	In vivo and in vitro SARSCoV: https://www.ncbi.nlm.nih.gov/pubmed/15247913		
S230.15	human mAb	NA	NA	NA	NA	In vivo and in vitro SARSCoV: https://www.ncbi.nlm.nih.gov/pubmed/17620608		

Product type and candidate	Description	Licensed for	Licensed dose	Route of administration	Currently being trialled COVID-19?	Status of clinical development for Coronaviruses	Proposed dose for COVID-19	Status of clinical development for other relevant conditions
m396	human mAb	NA	NA	NA	NA	<u>In vitro SARS-CoV:</u> https://www.ncbi.nlm.nih.gov/pubmed/?term=Structure+of+severe+acute+respiratory+syndrome+coronavirus+receptorbinding+domain+complexed+with+neutralizing+antibody		
mAb F26G18 (Chimeric)	chimeric human mouse mAb	NA	NA	NA	NA	<u>In vitro SARS-CoV:</u> https://www.ncbi.nlm.nih.gov/pubmed/20168090		
mAb F26G19	chimeric human mouse mAb	NA	NA	NA	NA	<u>In vitro SARS-CoV:</u> https://www.ncbi.nlm.nih.gov/pubmed/20168090		

DISCLAIMER: These landscape documents have been prepared by the World Health Organization (WHO) for information purposes only concerning the 2019-2020 global of the novel coronavirus. Inclusion of any particular product or entity in any of these landscape documents does not constitute, and shall not be deemed or construed as, any approval or endorsement by WHO of such product or entity (or any of its businesses or activities). While WHO takes reasonable steps to verify the accuracy of the information presented in these landscape documents, WHO does not make any (and hereby disclaims all) representations and warranties regarding the accuracy, completeness, fitness for a particular purpose (including any of the aforementioned purposes), quality, safety, efficacy, merchantability and/or non-infringement of any information provided in these landscape documents and/or of any of the products referenced therein. WHO also disclaims any and all liability or responsibility whatsoever for any death, disability, injury, suffering, loss, damage or other prejudice of any kind that may arise from or in connection with the procurement, distribution or use of any product included in any of these landscape documents.

Landscape analysis of therapeutics as 21st March 2020

Unnamed	purified mAbs to SARS	NA	NA	NA	NA	unpublished		
80R	human mAb	NA	NA	NA	NA	<u>In vitro SARS-CoV:</u> Rani et al 2012; doi: 10.1128/JVI.00233-12		
80R	human mAb	NA	NA	NA	NA	<u>In vitro SARS-CoV:</u> https://www.ncbi.nlm.nih.gov/pubmed/14983044		
CR3014	human mAb	NA	NA	NA	NA	<u>In vitro SARS-CoV:</u> https://www.ncbi.nlm.nih.gov/pubmed/15650189		
CR3022	human mAb	NA	NA	NA	NA	<u>In vitro SARS-CoV:</u> https://www.ncbi.nlm.nih.gov/pubmed/15650189		
CR3022		NA	NA	NA	NA			
B1	human mAb	NA	NA	NA	NA	<u>In vitro and in vivo SARSCoV:</u> https://www.ncbi.nlm.nih.gov/pubmed/15939399		

DISCLAIMER: These landscape documents have been prepared by the World Health Organization (WHO) for information purposes only concerning the 2019-2020 global of the novel coronavirus. Inclusion of any particular product or entity in any of these landscape documents does not constitute, and shall not be deemed or construed as, any approval or endorsement by WHO of such product or entity (or any of its businesses or activities). While WHO takes reasonable steps to verify the accuracy of the information presented in these landscape documents, WHO does not make any (and hereby disclaims all) representations and warranties regarding the accuracy, completeness, fitness for a particular purpose (including any of the aforementioned purposes), quality, safety, efficacy, merchantability and/or non-infringement of any information provided in these landscape documents and/or of any of the products referenced therein. WHO also disclaims any and all liability or responsibility whatsoever for any death, disability, injury, suffering, loss, damage or other prejudice of any kind that may arise from or in connection with the procurement, distribution or use of any product included in any of these landscape documents.

Landscape analysis of therapeutics as 21st March 2020

Product type and candidate	Description	Licensed for	Licensed dose	Route of administration	Currently being trialled COVID-19?	Status of clinical development for Coronaviruses	Proposed dose for COVID-19	Status of clinical development for other relevant conditions
201	human mAb	NA	NA	NA	NA	In vivo SARS-CoV: https://www.ncbi.nlm.nih.gov/pubmed/?term=Development+and+characterization+of+a+severe+acute+respiratory+syndrome+associated+coronavirusneutralizing+human+monoclonal+antibody+that+provides+effective+immunoprophylaxis+in+mice		
68	human mAb	NA	NA	NA	NA	In vivo SARS-CoV: https://www.ncbi.nlm.nih.gov/pubmed/?term=Development+and+characterization+of+a+severe+acute+respiratory+syndrome+associated+coronavirusneutralizing+human+monoclonal+antibody+that+provides+effective+immunoprophylaxis+in+mice		

DISCLAIMER: These landscape documents have been prepared by the World Health Organization (WHO) for information purposes only concerning the 2019-2020 global of the novel coronavirus. Inclusion of any particular product or entity in any of these landscape documents does not constitute, and shall not be deemed or construed as, any approval or endorsement by WHO of such product or entity (or any of its businesses or activities). While WHO takes reasonable steps to verify the accuracy of the information presented in these landscape documents, WHO does not make any (and hereby disclaims all) representations and warranties regarding the accuracy, completeness, fitness for a particular purpose (including any of the aforementioned purposes), quality, safety, efficacy, merchantability and/or non-infringement of any information provided in these landscape documents and/or of any of the products referenced therein. WHO also disclaims any and all liability or responsibility whatsoever for any death, disability, injury, suffering, loss, damage or other prejudice of any kind that may arise from or in connection with the procurement, distribution or use of any product included in any of these landscape documents.

Landscape analysis of therapeutics as 21st March 2020

Unnamed	Located frozen stock of other ~10 SARS specific mAb. These mAbs were identified together with mAb 201, with binding activities with various S protein domains. They are working on preparing these mAbs for testing.	NA	NA	NA	NA	unpublished		
Unnamed		NA	NA	NA	NA			
Product type and candidate	Description	Licensed for	Licensed dose	Route of administration	Currently being trialled COVID-19?	Status of clinical development for Coronaviruses	Proposed dose for COVID-19	Status of clinical development for other relevant conditions
Unnamed	working on nCoV Tx - no more information at the moment	NA	NA	NA	NA			

DISCLAIMER: These landscape documents have been prepared by the World Health Organization (WHO) for information purposes only concerning the 2019-2020 global of the novel coronavirus. Inclusion of any particular product or entity in any of these landscape documents does not constitute, and shall not be deemed or construed as, any approval or endorsement by WHO of such product or entity (or any of its businesses or activities). While WHO takes reasonable steps to verify the accuracy of the information presented in these landscape documents, WHO does not make any (and hereby disclaims all) representations and warranties regarding the accuracy, completeness, fitness for a particular purpose (including any of the aforementioned purposes), quality, safety, efficacy, merchantability and/or non-infringement of any information provided in these landscape documents and/or of any of the products referenced therein. WHO also disclaims any and all liability or responsibility whatsoever for any death, disability, injury, suffering, loss, damage or other prejudice of any kind that may arise from or in connection with the procurement, distribution or use of any product included in any of these landscape documents.

Bibliography:

- 1 Glucocorticoid Therapy for Novel Coronavirus Critically Ill Patients With Severe Acute Respiratory Failure - Full Text View - ClinicalTrials.gov.
<https://clinicaltrials.gov/ct2/show/NCT04244591?draw=3> (accessed Feb 14, 2020).
- 2 Auyeung TW, Lee JSW, Lai WK, *et al.* The use of corticosteroid as treatment in SARS was associated with adverse outcomes: A retrospective cohort study. *J Infect* 2005; **51**: 98–102.
- 3 Lee N, Allen Chan KC, Hui DS, *et al.* Effects of early corticosteroid treatment on plasma SARS-associated Coronavirus RNA concentrations in adult patients. *J Clin Virol* 2004; **31**: 304–9.
- 4 Arabi YM, Mandourah Y, Al-Hameed F, *et al.* Corticosteroid therapy for critically ill patients with middle east respiratory syndrome. *Am J Respir Crit Care Med* 2018; **197**: 757–67.
- 5 Low Doses Corticosteroids as Adjuvant Therapy for the Treatment of Severe H1N1 Flu - Full Text View - ClinicalTrials.gov.
<https://clinicaltrials.gov/ct2/show/NCT01014364> (accessed Feb 14, 2020).
- 6 Efficacy and Safety of Hydroxychloroquine for Treatment of Pneumonia Caused by 2019-nCoV (HC-nCoV) - Full Text View - ClinicalTrials.gov. <https://clinicaltrials.gov/ct2/show/NCT04261517?cond=SARS+%28Severe+Acute+Respiratory+Syndrome%29&draw=5> (accessed Feb 14, 2020).
- 7 Wang M, Cao R, Zhang L, *et al.* Remdesivir and chloroquine effectively inhibit the recently emerged novel coronavirus (2019-nCoV) in vitro. *Cell Res* 2020; published online Feb 4. DOI:10.1038/s41422-020-0282-0.
- 8 Cong Y, Hart BJ, Gross R, *et al.* MERS-CoV pathogenesis and antiviral efficacy of licensed drugs in human monocyte-derived antigen-presenting cells. *PLoS One* 2018; **13**: e0194868.
- 9 Coleman CM, Sisk JM, Mingo RM, Nelson EA, White JM, Frieman MB. Abelson Kinase Inhibitors Are Potent Inhibitors of Severe Acute Respiratory Syndrome Coronavirus and Middle East Respiratory Syndrome Coronavirus Fusion. *J Virol* 2016; **90**: 8924–33.
- 10 De Wilde AH, Jochmans D, Posthuma CC, *et al.* Screening of an FDA-approved compound library identifies four small-molecule inhibitors of Middle East respiratory syndrome coronavirus replication in cell culture. *Antimicrob Agents Chemother* 2014; **58**: 4875–84.
- 11 Barnard DL, Day CW, Bailey K, *et al.* Evaluation of immunomodulators, interferons and known in vitro SARS-CoV inhibitors for inhibition of SARS-CoV replication in BALB/c mice. *Antivir Chem Chemother* 2006; **17**: 275–84.

DISCLAIMER: These landscape documents have been prepared by the World Health Organization (WHO) for information purposes only concerning the 2019-2020 global of the novel coronavirus. Inclusion of any particular product or entity in any of these landscape documents does not constitute, and shall not be deemed or construed as, any approval or endorsement by WHO of such product or entity (or any of its businesses or activities). While WHO takes reasonable steps to verify the accuracy of the information presented in these landscape documents, WHO does not make any (and hereby disclaims all) representations and warranties regarding the accuracy, completeness, fitness for a particular purpose (including any of the aforementioned purposes), quality, safety, efficacy, merchantability and/or non-infringement of any information provided in these landscape documents and/or of any of the products referenced therein. WHO also disclaims any and all liability or responsibility whatsoever for any death, disability, injury, suffering, loss, damage or other prejudice of any kind that may arise from or in connection with the procurement, distribution or use of any product included in any of these landscape documents.

Landscape analysis of therapeutics as 21st March 2020

- 12 Vincent MJ, Bergeron E, Benjannet S, *et al.* Chloroquine is a potent inhibitor of SARS coronavirus infection and spread. *Virology* 2005; **2**. DOI:10.1186/1743-422X-2-69.
- 13 Keyaerts E, Vijgen L, Maes P, Neyts J, Ranst M Van. In vitro inhibition of severe acute respiratory syndrome coronavirus by chloroquine. *Biochem Biophys Res Commun* 2004; **323**: 264–8.
- 14 A Prospective, Randomized Controlled Clinical Study of Antiviral Therapy in the 2019-nCoV Pneumonia - Full Text View - ClinicalTrials.gov. <https://clinicaltrials.gov/ct2/show/NCT04255017?draw=2> (accessed Feb 14, 2020).
- 15 Chinese Clinical Trial Register (ChiCTR) - The world health organization international clinical trials registered organization registered platform. <http://www.chictr.org.cn/showprojen.aspx?proj=48824> (accessed Feb 14, 2020).
- 16 Chinese Clinical Trial Register (ChiCTR) - The world health organization international clinical trials registered organization registered platform. <http://www.chictr.org.cn/showprojen.aspx?proj=48919> (accessed Feb 14, 2020).
- 17 Chinese Clinical Trial Register (ChiCTR) - The world health organization international clinical trials registered organization registered platform. <http://www.chictr.org.cn/showprojen.aspx?proj=48809> (accessed Feb 14, 2020).
- 18 Chinese Clinical Trial Register (ChiCTR) - The world health organization international clinical trials registered organization registered platform. <http://www.chictr.org.cn/showprojen.aspx?proj=48991> (accessed Feb 14, 2020).
- 19 Chinese Clinical Trial Register (ChiCTR) - The world health organization international clinical trials registered organization registered platform. <http://www.chictr.org.cn/showprojen.aspx?proj=48992> (accessed Feb 14, 2020).
- 20 Chinese Clinical Trial Register (ChiCTR) - The world health organization international clinical trials registered organization registered platform. <http://www.chictr.org.cn/showprojen.aspx?proj=49015> (accessed Feb 14, 2020).
- 21 Chinese Clinical Trial Register (ChiCTR) - The world health organization international clinical trials registered organization registered platform. <http://www.chictr.org.cn/showprojen.aspx?proj=49065> (accessed Feb 14, 2020).
- 22 Chan KS, Lai ST, Chu CM, *et al.* Treatment of severe acute respiratory syndrome with lopinavir/ritonavir: a multicentre retrospective matched cohort study. *Hong Kong Med J = Xianggang yi xue za zhi* 2003; **9**: 399–406.
- 23 Chu CM, Cheng VCC, Hung IFN, *et al.* Role of lopinavir/ritonavir in the treatment of SARS: Initial virological and clinical findings. *Thorax* 2004; **59**: 252–6.
- 24 Sheahan TP, Sims AC, Leist SR, *et al.* Comparative therapeutic efficacy of remdesivir and combination lopinavir, ritonavir, and interferon beta against MERS-CoV. *Nat Commun* 2020; **11**. DOI:10.1038/s41467-019-13940-6.

DISCLAIMER: These landscape documents have been prepared by the World Health Organization (WHO) for information purposes only concerning the 2019-2020 global of the novel coronavirus. Inclusion of any particular product or entity in any of these landscape documents does not constitute, and shall not be deemed or construed as, any approval or endorsement by WHO of such product or entity (or any of its businesses or activities). While WHO takes reasonable steps to verify the accuracy of the information presented in these landscape documents, WHO does not make any (and hereby disclaims all) representations and warranties regarding the accuracy, completeness, fitness for a particular purpose (including any of the aforementioned purposes), quality, safety, efficacy, merchantability and/or non-infringement of any information provided in these landscape documents and/or of any of the products referenced therein. WHO also disclaims any and all liability or responsibility whatsoever for any death, disability, injury, suffering, loss, damage or other prejudice of any kind that may arise from or in connection with the procurement, distribution or use of any product included in any of these landscape documents.

Landscape analysis of therapeutics as 21st March 2020

- 25 A Multi-centre, Double-blinded, Randomized, Placebo-controlled Trial on the Efficacy and Safety of Lopinavir / Ritonavir Plus Ribavirin in the Treatment of Severe Acute Respiratory Syndrome - Full Text View - ClinicalTrials.gov.
<https://clinicaltrials.gov/ct2/show/NCT00578825> (accessed Feb 14, 2020).
- 26 Chau T-N, Lee K-C, Yao H, *et al.* SARS-associated viral hepatitis caused by a novel coronavirus: Report of three cases. *Hepatology* 2004; **39**: 302–10.
- 27 Efficacy and Safety of Darunavir and Cobicistat for Treatment of Pneumonia Caused by 2019-nCoV - Full Text View - ClinicalTrials.gov.
<https://clinicaltrials.gov/ct2/show/NCT04252274> (accessed Feb 14, 2020).
- 28 Chinese Clinical Trial Register (ChiCTR) - The world health organization international clinical trials registered organization registered platform.
<http://www.chictr.org.cn/showprojen.aspx?proj=49088> (accessed Feb 14, 2020).
- 29 Gao J, Tian Z, Yang X, Breakthrough: Chloroquine phosphate has shown apparent efficacy in treatment of COVID-19 associated pneumonia in clinical studies. *Bioscience Trends*. Advanced publication. 2020, DOI: 10.5582/bst.2020.01047
- 30 De Wilde AH, Jochmans D, Posthuma CC, *et al*, Screening of an FDA-approved compound library identified four small-molecule inhibitors of Middle East Respiratory Syndrome Coronavirus replication in cell culture. *Antimicrobial Agents Chemother.* 2014;58(8):4875-84. DOI: 10.1128/AAC.03011-14
- 31 Shen L, Yang Y, Ye F, *et al*, Safe and Sensitive Antiviral Screening Platform Based on Recombinant Human Coronavirus OC43 Expressing the Luciferase Reporter Gene. *Antimicrobial Agents Chemother.* 2016;60(9);5492-5503. PMID: 27381385
- 32 Keyaerts E, Li S, Vijgen L *et al*, Antiviral Activity of Chloroquine against Human Coronavirus OC43 Infection in Newborn Mice. *Antimicrobial Agents Chemother.* 2009;53(8): 3416-3421. DOI: 10.1128/AAC.01509-08
- 33 Chu CM, Cheng VCC, Hung IFN, *et al*, Role of lopinavir/ritonavir in the treatment of SARS: initial virological and clinical findings. *Thorax* 2004;59:252-256
- 34 Deng L, Li C, Zeng Q, *et al*, Arbidol combined with LPV/r versus LPV/r alone against Corona Virus Disease 2019: A retrospective cohort study. *Journal of Infection.* 2020: DOI: <https://doi.org/10.1016/j.jinf.2020.03.002>
- 35 Tang B, Li S, Xiong Y, Coronavirus Disease 2019 (COVID-19) Pneumonia in a Hemodialysis Patient. *Kidney Medicine.* 2020, DOI: <https://doi.org/10.1016/j.xkme.2020.03.001>

DISCLAIMER: These landscape documents have been prepared by the World Health Organization (WHO) for information purposes only concerning the 2019-2020 global of the novel coronavirus. Inclusion of any particular product or entity in any of these landscape documents does not constitute, and shall not be deemed or construed as, any approval or endorsement by WHO of such product or entity (or any of its businesses or activities). While WHO takes reasonable steps to verify the accuracy of the information presented in these landscape documents, WHO does not make any (and hereby disclaims all) representations and warranties regarding the accuracy, completeness, fitness for a particular purpose (including any of the aforementioned purposes), quality, safety, efficacy, merchantability and/or non-infringement of any information provided in these landscape documents and/or of any of the products referenced therein. WHO also disclaims any and all liability or responsibility whatsoever for any death, disability, injury, suffering, loss, damage or other prejudice of any kind that may arise from or in connection with the procurement, distribution or use of any product included in any of these landscape documents.