Landscape analysis of therapeutics as 17 February 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 |
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| **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] | Clinical trial COVID-19[6], in vitro study COVID-19[7], in vitro studies MERS-CoV[8–10], in vivo and in vitro study SARS-CoV[11], in vitro studies SARS-CoV[12,13] | COVID-19 clinical trial: hydroxychloroquine 400mg per day for 5 days | |
| 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], clinical studies SARS[22], in vitro and clinical studies SARS-CoV[23], in vivo studies MERS-CoV[24] | 500mg once, twice a day, 2 weeks | |
| 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 treatement up to 10 days. Case study: ribavirin 600mg 2x day and lopinavir + ritonavir 1000mg 1x day | |
| Darunavir (with cobicistat) (Prezista® / Prezcobix® 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 | |

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| 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 | | | | |
| 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<br>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.<br>Severe H1N1 pneumonia: 2mg 1xday | RCT for H1N1:<br>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. |

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| IFN-α / PEG-IFN-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. | | | | | 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<br><br>Clinical studies MERS: Al Ghamdi et al. BMC Infect Dis 2016;16:174 (case series ; 8 patients) - 6/8 died. | | |
| IFN-α2a (Pegasys® and others PEGylated IFN-α2a) | type I interferon made by leukocytes during viral infection | Hepatitis C (with ribavirin) and hepatitis B | 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. | Parenteral injection, for subcutaneous use | | 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-2a (Pegasys): 180 µg subcutaneously per week for 2 weeks | |

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| IFN-α2b (PegIntron®, Sylatron®, IntronA®) | type I interferon made by leukocytes during viral infection | - Hepatitis C (with ribavirin)<br>- Melanoma<br>- 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 m² 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<br>- Parenteral injection SC<br>- intramuscular, subcutaneous, intralesional, or intravenous | Yes<br><br>http://www.chictr.org.cn/showprojen.aspx?proj=48684 | Clinical trials COVID-19<br><br>Clinical study MERS:<br>Arabi et al. Clin Infect Dis. 2019. pii: ciz544 (Retrospective observational study ; 349 patients) - no decrease in mortality nor faster virus RNA clearance. | MERS:<br>Pegylated interferon alfa 2b (PEG-Intron): 1.5mcg/kg subcutaneously once per week x 2 | |

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| 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. | | |

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| 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<br><br>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 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.<br><br>Clinical studies ARDS: - In an open-label, non-randomized, 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. |

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| 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 | | In vitro study SARS-CoV: Cinatl at al. Lancet. 2003;362(9380):293-4 (Vero and Caco2 cells) - IFN-β1b > IFN-α2b or IFN-γ1b<br><br>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. | | |
| IFN-γ (Actimmune®) | type II IFNs - immune interferon activated by Interleukin-12 | Serious infections associated with Chronic Granulomatous Disease (CGD) ; severe, malignant osteopetrosis (SMO) | 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. | SC injection | | 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.<br><br>In vitro study SARS-CoV: Cinatl at al. Lancet. 2003;362(9380):293-4 (Vero and Caco2 cells)<br>Sainz et al. Virology. 2004 ; 329(1):11-7 (Vero E6 cells)<br>Spiegel et al. J Clin Virol. 2004; 30(3):211-3 (Vero cells)<br>Scagnolari et al. Antivir Ther. 2004; 9(6):1003-11 (Vero cells) - IFN-β + IFN-γ > IFN-β or IFN-γ (synergic effect) . | | |

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| IFN + Ribavirin | Combination antiviral + proteins made and released by host cells | | | | | Clinical study SARS:<br>Zhao et al. J Med Microbiol. 2003; 52: 715-720 ( IFN-α + RBV) - Inconclusive<br><br>Clinical studies MERS:<br>- Al Ghamdi et al. BMC Infect Dis 2016;16:174 (case series ; 23 patients ; IFN-α or IFN-β +/- RBV) - 18/23 died.<br>- 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.<br>- Shalhoub et al. J Antimicrob Chemother. 2015. 70(7):2129-32 (Retrospective Cohort Study ; 24 patients ; IFN-α2a 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,<br>- 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.<br>- Khalid et al. Antivir Ther. 2015. 20(1):87-91 (case | | |

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| | | | | | | series ; 2 patients ; SQ PEG-INF- α-2b + RBV PO (treatment or prophylaxis)) - Complete recovery and discharge home,<br>- Khalid et al. Respir Care 2016;61:340–8 (case series ; 11 patients ; RBV + INF- α-2a) - survival of all patients,<br>- 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.<br>- 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.<br>- Malik et al. Emerg Infect Dis 2016. 2013;22 (case report ; 1 patient ; RBN and IFN-α2a day 12 from onset) - died.<br>- Khalid et al. Ann Saudi Med. 2014, 34, pp. 396-400 (case series ; 6 patients ; RBV + IFN-α2b) - 3/6 died (delayed diagnosis and treatment).<br><br>In vivo study MERS-CoV: Falzarano et al. Nat Med. 2013. 19(10):1313-7 (IFN-α2b + RBV) - improved outcome. | | |
| IFN + Ribavirin + steroids | Combination of proteins made | | | | | Clinical study SARS: Wu et al. Chin Med J (Engl) | | |

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| | and released by host cells + antiviral + steroid hormones | | | | | 2003;116(6):811-8 (IFN-α + RBV + steroids)<br><br>Clinical study MERS:<br>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:<br>- Spanakis et al. https://www.ncbi.nlm.nih.gov/pubmed/25288266<br>- Kim et al. https://www.ncbi.nlm.nih.gov/pubmed/26492219 | MERS:<br>Spanakis et al. :<br>oral (p.o.) lopinavir/ritonavir (400/100 mg twice daily), pegylated interferon (180 µg 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)<br>Kim et al.:<br>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-α2a (subcutaneous injection, 180 µg /0.5 ml) | |
| IFN-β1a + mycophenolate mofetil | combination of proteins made and released by host cells + immunosupressant | 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:<br>Al Ghamdi et al. BMC Infect Dis 2016;16:174 (case series ; 23 patients ; hydrocortisone + RBV + IFN-α or IFN-β) - Inconclusive. | | |

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| Lopinavir + Ritonavir + IFN-β1b | Lopinavir and ritonavir are antiretroviral protease inhibitors combination protease inhibitor and host | | | Lopinavir/ritonavir: tablet form (or suspension via nasogastric tube)<br>IFN-β1b: subcutaneous injections | | Clinical studies MERS: NCT02845843 (MIRACLE Trial)<br>(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),<br>Arabi et al. Trials. 2018 ; 19(1):81 (study protocol)<br>Arabi at al. Trials. 2020 ; 21(1):8 (statistical analysis plan)<br>Abbott Laboratories. Product Information: Kaletra®. https://www.accessdata.fda.gov/drugsatfda_docs/label/2010/021226s030lbl.pdf .<br><br>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-CoV-infected common marmosets. | 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 | |

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| 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<br><br>http://www.chictr.org.cn/showprojen.aspx?proj=49013 | Clinical trials COVID-19 | clinical trial:<br>80mg on day1, 80mg on day4; and 80mg on day 7 as neccessary. No more than 3 times administration in total. | Phase II clinical trial influenza:<br>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. New England Journal of Medicine, 379(10), 913–923. https://doi.org/10.1056/NEJMoa1716197: Phase 2 trial influenza<br><br>Phase III Clinical trials influenza:<br>https://clinicaltrials.gov/ct2/show/NCT02954354<br>https://clinicaltrials.gov/ct2/show/NCT03653364<br>https://clinicaltrials.gov/ct2/show/NCT03629184<br>https://clinicaltrials.gov/ct2/show/NCT03684044 |
| **Licensed in country of origin for other diseases** | | | | | | | | |

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| 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<br>Days 2 through 5: 600 mg twice daily | Oral | Yes<br>http://www.chictr.org.cn/showprojen.aspx?proj=49015<br>http://www.chictr.org.cn/showprojen.aspx?proj=49013<br>http://www.chictr.org.cn/showproj.aspx?proj=49042 | Clinical trials COVID-19 | 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<br>Phase I / II completed, in the US: NCT01068912 ; NCT01728753 or in China: NCT03394209 or in Japan: JPRN-JapicCTI-142657<br><br>Used in JIKI Trial (Ebola, non-randomized): day 0: 6000 mg; day 1 to day 9: 2400 mg/d<br>Dose escalation trial in preparation in France |
| 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. Antiviral Chemistry and Chemotherapy, 26. https://doi.org/10.1177/2040206618811416<br>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. Acta Virologica, 62(2), 191–195. https://doi.org/10.4149/av_2018_211 |

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| 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.chictr.org.cn/showprojen.aspx?proj=49069 http://www.chictr.org.cn/showprojen.aspx?proj=49065 https://clinicaltrials.gov/ct2/show/NCT04252885 | Clinical trials COVID-19<br><br>In vitro study SARS-CoV:<br>- 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<br><br>CT ChiCTR2000029573: Arbidol Tablets 200mg/ time, p.o.tid.<br><br>CT NCT04252885: ordinary treatment plus a regimen of arbidol (100mg) (oral, tid, 200mg each time, taking for 7-14 days). | Review:<br>- 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.chictr.org.cn/showproj.aspx?proj=49065 http://www.chictr.org.cn/showprojen.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) | |
| **Licensed but removed from the market for commercial reasons** | | | | | | | | |

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| 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** | | | | | | | | |

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| Convalescent plasma | Human polyclonal | NA | NA | IV | | Clinical studies SARS: Cheng, Y. et al. (2005). Use of convalescent plasma therapy in SARS patients in Hong Kong. European Journal of Clinical Microbiology and Infectious Diseases, 24(1), 44–46. -> **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. Clinical Microbiology and Infection, 10(7), 676–678. -> **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** | | 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. Chest, 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. Clinical Infectious Diseases, 52(4), 447–456. -> prospective cohort study where convalescent plasma was given to 20 critically ill H1N1pdm09 patients |

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| | | | | | | **patients treated with convalescent plasma**<br>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**<br><br>Systematic review SARS studies:<br>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 Infectious Diseases, 211(1), 80–90. -> **systematic review and exploratory meta-analysis of convalescent plasma treatment for SARS and severe influenza**<br><br>Protocol clinical study MERS:<br>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** | | |

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

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| | | | | | | 395. -> possible acute lung injury following convalescent plasma transfusion in MERS patient | | |

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| GS-5734/ Remdesivir | Nucleoside Inhibitor | NA | NA | IV | Yes https://clinicaltrials.gov/ct2/show/NCT04252664?cond=COVID-19&draw=2&rank=1 https://clinicaltrials.gov/ct2/show/NCT04257656?term=remdesivir&draw=2&rank=1 | Clinical trials COVID-19<br><br>In vitro COVID-19:<br>Wang, M., et al. (2020). Remdesivir and chloroquine effectively inhibit the recently emerged novel coronavirus (COVID-19) in vitro. Cell Research.<br><br>Clinical COVID-19:<br>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<br><br>In vivo MERS-CoV:<br>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<br>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<br>Jordan, R. et al. (2017). Broad-spectrum Investigational Agent GS-5734 for the Treatment of Ebola, MERS Coronavirus | CT NCT04252664: 200 mg loading dose on day 1 is given, followed by 100 mg iv once-daily maintenance doses for 9 days.<br><br>CT NCT04257656: 200 mg loading dose on day 1 is given, followed by 100 mg iv once-daily maintenance doses for 9 days. | Clinical trials Ebola:<br>Phase II: https://clinicaltrials.gov/ct2/show/NCT02818582,<br>Phase III: https://clinicaltrials.gov/ct2/show/NCT03719586 |

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|---|---|---|---|---|---|---|---|---|
| | | | | | | and Other Pathogenic Viral Infections with High Outbreak Potential. Open Forum Infectious Diseases, 4(suppl_1), S737–S737. -> mice infected with MERS-CoV<br><br>In vivo and in vitro SARS-CoV and MERS:<br>Agostini, M. L. et al.. (2018a). Coronavirus Susceptibility to the Antiviral Remdesivir (GS-5734) Is Mediated by the Viral Polymerase and the Proofreading Exoribonuclease. MBio, 9(2). -> human airway epithelial cells and animal model findings SARS and MERS<br>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<br><br>In vitro coronaviruses:<br>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 | | |

| 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 | | Clinical trial SARS: 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 IFN-α-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<br><br>In vivo study SARS-CoV: 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. | In Phase II CT NCT00215826 SARS 650 IU vs. 1300 IU trialled | |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| IFN-β1a solution for inhalation (SNG001) | 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. | NA | NA | Inhalation. The delivery device (iNeb by Philips) used to date is a breath actuated mesh nebuliser | | Unpublished data assessing IFN-β1a activity agaisnt MERS virus, generated by Heinrich Feldmann and Darryl Falzarano at NIH/NIAID in 2014 | | Asthma phase II trial: Djukanović et al. Am J Respir Crit Care Med. 2014.190(2):145-54 ; NCT01126177<br>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/)<br><br>COPD phase II trial: NCT03570359 (Phase II) ; https://www.synairgen.com/programmes/ifn-%CE%B2-in-copd/<br>COPD: Phase II Randomised, Double-blind, Placebo-controlled Study (SG015) - ongoing (https://clinicaltrials.gov/ct2/show/NCT03570359?term=NCT03570359&draw=2&rank=1) |

| 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 IFN-λ1a | type III IFN | NA | NA | SC injection | | Eiger BioPharmaceuticals have some initial in vitro and in vivo data with coronas. | | Influenza:<br>Sun et al. IFN-λ: A new spotlight in innate immunity against influenza virus infection. Protein Cell. 2018 Oct; 9(10): 832–837.<br>Klinkhammer et al. IFN-λ prevents influenza virus spread from the upper airways to the lungs and limits virus transmission. eLife. 2018; 7: e33354.<br><br>multiple Phase 2 and 3 Clinical trials mostly for hepatitis viruses: https://clinicaltrials.gov/ct2/results?cond=&term=interferon+lambda&cntry=&state=&city=&dist= |

| 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 anti-MERS CoV Abs SAB 301 | SAB-301 is a purified human immune globulin G (hIgG) polyclonal antibody designed to specifically bind to the MERS-CoV 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 transchromosomic (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.<br>• Hospitalized adults with MERS CoV infection<br>• Single 50mg/kg infusion of SAB-301 vs. placebo control<br>• Being considered by KSA KAIMARC – P.I. Dr. Yaseen Arabi, M.D. | | |
| **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/ |

| 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 |
|---|---|---|---|---|---|---|---|---|
| Sab-301 | Polyclonal anti MERS-CoV (likely MERS-specific, but possible to crossreact) | NA | NA | IV | NA | Clinical trial Phase 1 MERS: https://clinicaltrials.gov/ct2/show/NCT02788188<br><br>In vivo study MERS-CoV: https://www.ncbi.nlm.nih.gov/pubmed/26888429 | 1 to 2 doses at 50 mg/kg | |
| BCX4430 | Nucleoside Inhibitor | NA | NA | IV and IM formulations | NA | | | Clinical trial Phase 1 Ebola Virus Disease: https://clinicaltrials.gov/ct2/show/NCT02319772<br><br>Clinical trial Phase 1 Yellow Fever: https://clinicaltrials.gov/ct2/show/NCT03891420<br><br>Clinical trial Phase 1 Marburg Virus Disease: https://clinicaltrials.gov/ct2/show/NCT03800173 |
| Relacatib (SB462795) | | NA | NA | | NA | Pers comm Pauline Williamns: We can confirm that as well as Cathepsin-K activity, it does have good activity against Cathepsin-L. 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. | | |

| 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 |
|---|---|---|---|---|---|---|---|---|
| REGN3048 and REGN3051 Antibody Cocktail | Biological: REGN3048 REGN3048 is a fully monoclonal antibody (mAbs) which binds to the S protein of MERS-CoV.<br><br>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. | NA | NA | | NA | Clinical trial Phase I MERS: https://clinicaltrials.gov/ct2/show/NCT03301090 | | |

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|---|---|---|---|---|---|---|---|---|
| Polyclonal human anti-MERS CoV Abs SAB 301 | SAB-301 is a purified human immune globulin G (hIgG) polyclonal antibody designed to specifically bind to the MERS-CoV 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 transchromoso mic (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 D-sorbitol, 0.05 mg/mL Tween 80, pH 5.5. The drug product will be administered intravenously | NA | NA | | NA | RCT, double blinded, single dose scalation phase II, >14 years- 160 subjects | | |

| 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 will be diluted in saline per the clinical protocol. | | | | | | | |
| Polyclonal Human Abs anti-Mers | | NA | NA | | NA | | | |
| **Pre-clinical** | | | | | | | | |
| Lycorine | Inhibits cell division, antineoplastic, antiviral | NA | NA | NA | NA | Shen 2019 JV 93:e00023-19 | | |
| 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 Poly-IC: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 (EIDD-1931) | β-D-N4 -hydroxycytidine, ribonulcoside analogue, inhibit viral replication | NA | NA | NA | NA | In vitro MERS-CoV and MERS-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 | | |

| 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 |
|---|---|---|---|---|---|---|---|---|
| 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 administrated 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 | | |
| 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 MERS-CoV: https://www.ncbi.nlm.nih.gov/pubmed/29950421 | | |
| NbM10-Fc | Llama VHHs | NA | NA | NA | NA | | | |
| LCA60 | Human survivor, RBD | NA | NA | NA | NA | | | |
| 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 SARS-CoV: https://www.ncbi.nlm.nih.gov/pubmed/15247913 | | |
| S230.15 | human mAb | NA | NA | NA | NA | In vivo and in vitro SARS-CoV: 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 | In vitro SARS-CoV: https://www.ncbi.nlm.nih.gov/pubmed/?term=Structure+of+severe+acute+respiratory+syndrome+coronavirus+receptor-binding+domain+complexed+with+neutralizing+antibody | | |
| mAb F26G18 (Chimeric) | chimeric human mouse mAb | NA | NA | NA | NA | In vitro SARS-CoV: https://www.ncbi.nlm.nih.gov/pubmed/20168090 | | |
| mAb F26G19 | chimeric human mouse mAb | NA | NA | NA | NA | In vitro SARS-CoV: https://www.ncbi.nlm.nih.gov/pubmed/20168090 | | |
| Unnamed | purified mAbs to SARS | NA | NA | NA | NA | unpublished | | |
| 80R | human mAb | NA | NA | NA | NA | In vitro SARS-CoV: https://www.ncbi.nlm.nih.gov/pubmed/?term=Increased+antibody+affinity+confers+broad+in+vitro+protection+against+escape+mutants+of+severe+acute+respiratory+syndrome+coronavirus | | |
| 80R | human mAb | NA | NA | NA | NA | In vitro SARS-CoV: https://www.ncbi.nlm.nih.gov/pubmed/14983044 | | |
| CR3014 | human mAb | NA | NA | NA | NA | In vitro SARS-CoV: https://www.ncbi.nlm.nih.gov/pubmed/15650189 | | |
| CR3022 | human mAb | NA | NA | NA | NA | In vitro SARS-CoV: https://www.ncbi.nlm.nih.gov/pubmed/15650189 | | |
| CR3022 | | NA | NA | NA | NA | | | |
| B1 | human mAb | NA | NA | NA | NA | In vitro and in vivo SARS-CoV: https://www.ncbi.nlm.nih.gov/pubmed/15939399 | | |

| 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+coronavirus-neutralizing+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+coronavirus-neutralizing+human+monoclonal+antibody+that+provides+effective+immunoprophylaxis+in+mice | | |
| 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 | | | |



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