CADTH COVID-19 PANDEMIC

COVID-19 CADTH HORIZON SCAN

CADTH Emerging Health Technology for COVID-19: Virus-Neutralizing Monoclonal Antibodies Against SARS-CoV-2

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To produce this report, CADTH used a modified approach to the selection, appraisal, and synthesis of the evidence to meet decision-making needs during the COVID-19 pandemic. Care has been taken to ensure the information is accurate and complete, but it should be noted that international scientific evidence about COVID-19 is changing and growing rapidly.

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Authors: Tara Cowling, Erin Graves, Hannah Loshak

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About CADTH: CADTH is an independent, not-for-profit organization responsible for providing Canada's health care decision-makers with objective evidence to help make informed decisions about the optimal use of drugs, medical devices, diagnostics, and procedures in our health care system.

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Summary

- As of November 30, 2020, the coronavirus disease (COVID-19) pandemic has infected more than 370,000 individuals in Canada, resulting in more than 12,000 deaths.
- Studies of convalescent plasma from patients infected with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) revealed neutralizing antibodies (NAbs) specific for the S protein of SARS-CoV-2, suggesting that the development of antibodies targeting the S protein may offer a therapeutic solution to fight SARS-CoV-2 infection.
- Virus-neutralizing monoclonal antibodies prevent viral particles from replicating by blocking viral entry into the cell or preventing the release of viral genetic material. They may offer an option for the treatment of SARS-CoV-2 infection, particularly for people at high risk of progressing to severe illness or who cannot produce their own antibodies.
- Bamlanivimab was the first virus-neutralizing monoclonal antibody to be authorized with conditions in Canada, under the Interim Order by Health Canada, for individuals with mild-to-moderate COVID-19 symptoms who are at high risk of progressing to severe COVID-19 and/or hospitalization.
- As of the time of publication, there are four further virus-neutralizing monoclonal antibodies or antibody combinations being investigated in phase III clinical trials for use in treating SARS-CoV-2 infections. Each of these is also being investigated for use as preventive therapies. Forty-two others are currently in earlier phases of clinical and pre-clinical development.[1]

Purpose of Scan

The objective of this Horizon Scan Bulletin is to review the current evidence on virus-neutralizing monoclonal antibodies as potential therapies for SARS-CoV-2 infection.

The following research questions were used to guide this review:

1. What are virus-neutralizing monoclonal antibodies?

What is their mechanism of action and how are they administered?

2. Which virus-neutralizing monoclonal antibodies are in clinical development for SARS-CoV-2 infection?
3. What is the evidence to date of their efficacy and safety to treat SARS-CoV-2 infection?
4. Is there any evidence for their use as a preventive therapy?

Background

The COVID-19 pandemic has already infected more than 370,000 individuals in Canada (as of November 30, 2020), resulting in more than 12,000 deaths.[2] The disease is caused by the SARS-CoV-2 virus. This virus expresses the spike protein (also referred to as the S protein) on its outer surface, which it uses to bind to the host ACE2 receptor.[3] Studies of plasma from patients infected with SARS-CoV-2 (referred to as convalescent plasma) revealed NAbs specific for the S protein of SARS-CoV-2, suggesting that the development of monoclonal antibodies targeting the S protein may offer a therapeutic solution to fight SARS-

CoV-2 infection. Neutralizing monoclonal antibodies that target the SARS-CoV-2 virus are now in development.

Neutralizing monoclonal antibodies have been previously developed for the treatment of other viral infections, such as influenza, HIV, rabies, and Ebola. Virus-neutralizing monoclonal antibodies may prove to be an important class of drugs for the treatment of COVID-19, and be particularly beneficial to at-risk populations such as elderly people or those who have difficultly developing or maintaining NAbs against the SARS-CoV-2 virus.[4] Early evidence also suggests efficacy of virus-neutralizing monoclonal antibodies in preventing SARS-CoV-2 infection, suggesting that these treatments could be used prophylactically.[5,6]

Methods

Horizon Scan Bulletins are not systematic reviews and do not involve critical appraisal or include a detailed summary of study findings. Rather, they present an overview of the technology and currently available evidence. They are not intended to provide recommendations for or against a particular technology.

Literature Search Strategy

A limited literature search was conducted by an information specialist on key resources, including MEDLINE via OVID, the Cochrane Library, the University of York Centre for Reviews and Dissemination (CRD) databases, and the websites of Canadian and major international health technology agencies. This was supplemented by a focused internet search. The search strategy comprised both controlled vocabulary, such as the National Library of Medicine's MeSH (Medical Subject Headings), and keywords. The main search concepts were monoclonal antibodies and COVID-19. Search filters were applied to limit retrieval to randomized controlled trials, controlled clinical trials, or any other type of clinical trial, health technology assessments, systematic reviews, meta-analyses, or network meta-analyses. Where possible, retrieval was limited to the human population. The search was also limited to English language documents published between January 1, 2019 and November 10, 2020.

Study Selection

One author screened the literature search results and reviewed the full text of all potentially relevant studies. Studies were considered for inclusion if the intervention was virus-neutralizing monoclonal antibodies and were in phase II or phase III of clinical development or had results in randomized controlled trials. Conference abstracts and grey literature were included when they provided additional information to that available in the published studies. Following study selection, a recursive bibliography search and targeted web search were completed to ensure completeness of the final included information.

Peer Review

A draft version of this bulletin was reviewed by one clinical expert.

Summary of the Evidence

What Are Virus-Neutralizing Monoclonal Antibodies?

Monoclonal antibodies are lab-grown molecules that are produced from the serum of those infected with an antigen (foreign substance that is recognized by immune cells and/or antibodies).[7] Monoclonal antibodies are developed to mimic the immune system's antibody response to the specific foreign invader (pathogen) for which it has been developed (e.g., viruses, bacteria, or fungi). Monoclonal antibodies are so called for their monoclonal (singular) affinity, meaning they contain a single purified antibody that binds to a single site on the virus.[8] By contrast, polyclonal preparations contain a mixture of antibodies that bind to a variety of different sites on the virus.[9]

When virus-neutralizing monoclonal antibodies bind to a virus, they prevent the virus from infecting host cells (neutralizing the virus) and activate the desired immune response.[8] Virus-neutralizing monoclonal antibodies must bind to distinct viral proteins to prevent the virus from infecting host cells or releasing genetic material contained within the virus. Antibody cocktails (injections containing more than one monoclonal antibody) that bind to multiple SARS-CoV-2 viral protein targets (epitopes) have also shown efficacy in early studies.[10]

Virus-Neutralizing Monoclonal Antibodies in Clinical Development

One treatment, bamlanivimab, has been authorized with conditions by Health Canada under the Interim Order.[11] As of November 10, 2020, there are 22 other virus-neutralizing monoclonal antibodies in clinical development, with four that are currently in phase III (Table 1); many more are in the pre-clinical phase (Appendix 1). The vast majority of the virus-neutralizing monoclonal antibodies in clinical development target the S protein, with specificity for the receptor-binding domain.[12] Additionally, some candidate NAb preparations include multiple monoclonal antibodies in a cocktail that are able to target different S protein epitopes, with the aim to prevent waning efficacy of the antibodies as a result of viral replication.[13]

Details on all virus-neutralizing monoclonal antibodies in earlier stages of clinical and pre-clinical development are included in Appendix 1.

Table 1: Virus-Neutralizing Monoclonal Antibodies Authorized or Undergoing Phase III Clinical Trial

Antibody or antibodies	Clinical stage	Patient population	Target	Sponsor
Bamlanivimab	Authorized by Health Canada under the Interim Order	Adults and pediatric patients 12 years of age or older with mild-to moderate coronavirus disease (COVID-19), who weigh at least 40 kg and who are at high risk of progressing to severe COVID-19 illness and/or hospitalization	Receptor-binding domain[4]	Eli Lilly and Company/AbCellera Biologics Inc.

Antibody or antibodies	Clinical stage	Patient population	Target	Sponsor
REGN-COV2 (casirivimab + imdevimab)	Phase III	Children, adults, and older adults hospitalized with COVID-19	Receptor-binding domain	Regeneron Pharmaceuticals
AZD7442 (AZD8895 + AZD1061)	Phase III	Adults and older adults (18 years and older) without symptoms of COVID-19, but with exposure to laboratory-confirmed COVID-19	Receptor-binding domain	AstraZeneca
VIR-7831	Phase II/III	Adult and older adults (18 years and older) at high risk of progression of COVID-19 or ≥ 55 years old with a positive SARS-CoV-2 test, oxygen saturation ≥ 94% on room air, and ≤ 5 days from symptom onset	Spike protein and receptor-binding domain	Vir Biotechnology/GlaxoSmithKline
CT-P59	Phase II/III	Adults with SARS-CoV-2 infection and mild symptoms (oxygen saturation ≥ 94% on room air and not requiring supplemental oxygen)	SARS-CoV-2	Celltrion

SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.

Bamlanivimab (Previously LY-Cov555)

Mechanism of Action

Bamlanivimab is a monoclonal antibody that targets the receptor-binding domain of the spike protein of the SARS-CoV-2 virus, thereby blocking the virus' attachment and preventing entry into human cells.[14] It is formulated as a solution for infusion (35 mg/mL) and administered intravenously as a single 700 mg infusion by a health care provider.[15]

Clinical Trial Program

The clinical development program for bamlanivimab includes four trials: BLAZE-1 (NCT04427501), BLAZE-2 (NCT04427501), ACTIV-2 (NCT04518410), and ACTIV-3 (NCT04501978). All trials are ongoing; preliminary results are available for BLAZE-1 in a pre-print.[16] These results have not been peer-reviewed and caution is required in interpreting these results.

BLAZE-1 (NCT04427501) is an ongoing randomized, double-blind, placebo-controlled single dose phase II trial of patients recently diagnosed with mild or moderate COVID-19. A total of 452 patients meeting study inclusion criteria were randomized to receive a single intravenous infusion of bamlanivimab in one of three doses (700 mg, 2,800 mg, or 7,000 mg) or a placebo within three days of their first positive SARS-CoV-2 viral test.[16] The primary end point is the change in viral load from baseline at day 11.[16] BLAZE-1 also compares bamlanivimab to etesevimab (LY-CoV016), another virus-neutralizing monoclonal antibody in development by the sponsor.[16]

Etesevimab is currently in phase II investigation as a monotherapy (NCT04342897, Appendix 7) as well as a combination therapy when used with bamlanivimab

(NCT04634409, NCT04427501, Appendix 2).[17] In the BLAZE-1 study, bamlanivimab combined with etesevimab (N = 11; 2,800 mg of each antibody) reduced viral load, patient symptoms, and COVID-related hospital and emergency department visits, as reported in a company press release.[17]

BLAZE-2 (NCT04497987) is a phase III trial conducted in collaboration with the National Institute of Allergy and Infectious Diseases (NIAID) to evaluate the efficacy and safety of bamlanivimab in preventing SARS-CoV-2 infection and COVID-19 in skilled nursing and assisted-living facility residents and staff.[18] As of November 10, 2020, this randomized, double-blind, placebo-controlled trial is still recruiting, with a target enrolment of 2,400 participants.[19]

ACTIV-2 (NCT04518410; in outpatients with COVID-19)[20] and ACTIV-3 (NCT04501978; in hospitalized patients with COVID-19)[21] are randomized, placebo-controlled, parallel assignment, triple-blind adaptive platform trials designed to study multiple interventions. ACTIV-2 is designed to transition from phase II to phase III, with a target enrolment of 2,000 participants. The primary end points include duration of COVID-19 symptoms; post-treatment presence of SARS-CoV-2 RNA on day 3, 7, 14, 21, and 28; incidence of new adverse events (AEs) of grade 3 or higher; cumulative incidence of death from any cause or hospitalization; and the proportion of participants with new severe AEs (≥ grade 3).[22] ACTIV-3 is designed in two stages. In stage 1, safety and two intermediate pulmonary outcomes (each measured on an ordinal scale) are evaluated. Those treatments that pass the necessary thresholds are considered in stage 2, for which the primary end point is time from randomization to sustained recovery.[23] The arm of ACTIV-3 evaluating bamlanivimab in hospitalized patients stopped enrolling patients following a recommendation from the independent Data and Safety Monitoring Committee.[24]

Safety and Efficacy

Although the safety and efficacy of this investigational therapy continues to be evaluated, an interim post hoc analysis of a secondary outcome of one clinical trial (BLAZE-1) showed a reduction in COVID-19–related hospitalizations or emergency department visits within 28 days (day 29) following treatment with bamlanivimab compared to placebo.[25] Bamlanivimab treatment has not been shown to benefit patients already hospitalized due to COVID-19.[25]

Most patients in BLAZE-1, including those who received placebo treatment, demonstrated viral clearance by day 11 (primary end point). However, the 2,800 mg dose (but not the 700 mg dose or 7,000 mg dose) of bamlanivimab was associated with greater viral clearance when compared with placebo (difference –0.53; 95% confidence interval, –0.98 to –0.08, P = 0.02).[26]

At day 29 post-treatment, 1.6% (n = 5) of patients treated with bamlanivimab were hospitalized with COVID-19 compared with 6.3% (n = 9) of patients who received placebo treatment.[26] A post hoc analysis of patients considered to be at high risk for disease progression (≥ 65 years of age or those with a body mass index [BMI] ≥ 35), showed that hospitalizations occurred in 4.2% (n = 4) of bamlanivimab-treated patients compared with 14.6% (n = 48) of placebo-treated patients.[26]

Thus far, bamlanivimab has demonstrated a safety profile that is similar to placebo treatment. In BLAZE-1, preliminary results reported that 22.3% (69 of 309) of patients treated with bamlanivimab and 24.5% (35 of 143) of patients receiving placebo treatment had an AE. The most frequent AE in the bamlanivimab group was nausea (3.9%), whereas the most frequent AE in the placebo group was diarrhea (4.9%). Infusion-related reactions

were reported in 2.3% (7 of 309) of patients in the bamlanivimab group versus 1.4% (2 of 143) in the placebo group; most events (e.g., pruritus, flushing, rash, and facial swelling) were reported during infusion and were reported as mild in nature.[16] In BLAZE-1, serious adverse events (SAEs) occurred in none of the 309 patients treated with bamlanivimab compared with one of 143 patients (0.7%) who received placebo treatment.[16]

Use as a Preventive Therapy

Use of bamlanivimab as a preventive therapy will be assessed as a part of the BLAZE-2 trial which is currently recruiting participants.

REGN-COV2 (Casirivimab [Previously REGN10933] + Imdevimab [Previously REGN10987])

Mechanism of Action

REGN-COV2 is a combination of casirivimab and imdevimab, two monoclonal antibodies that target the receptor-binding domain of the spike protein on the SARS-CoV-2 virus, which block the virus' attachment and entry into human cells.[10,27] These two virus-neutralizing monoclonal antibodies, which together form REGN-COV2, work by binding non-competitively to the critical receptor-binding domain of the virus' spike protein. REGN-COV2 is administered as a single IV infusion with a 1:1 concentration of each antibody.[10]

Clinical Trial Program

REGN-COV2 is being studied in multiple trials, six of which have ongoing recruitment. These include:

- a phase I/II/III randomized, double-blind, placebo-controlled, parallel assignment outpatient trial with an estimated enrolment of 2,104 participants (NCT04425629)
- a phase I/II/III randomized, double-blind, placebo-controlled, parallel assignment trial of hospitalized COVID-19 patients with an estimated enrolment of 2,970 patients (NCT04426695)
- a phase III open-label trial (RECOVERY) of hospitalized patients in the UK (NCT04381936)
- a phase III randomized, double-blind, placebo-controlled, parallel assignment trial for the prevention of COVID-19 in household contacts of infected individuals with an estimate enrolment of 2,000 participants (NCT04452318)
- a phase III randomized, open-label, factorial assignment trial investigating multiple treatments for patients with COVID-19 with an estimated enrolment of 20,000 patients is currently recruiting (NCT04381936)
- a compassionate use access trial for those recently diagnosed with mild-to-moderate COVID-19 who are at high risk for poor outcomes (NCT04617535).

In addition, a phase I randomized, double-blind, placebo-controlled parallel assignment trial recently completed recruitment with an estimated enrolment of 974 participants and final results expected in October 2021 (NCT04519437).

Safety and Efficacy

The safety and efficacy of this investigational IV therapy for the treatment of COVID-19 continues to be evaluated. The FDA issued an emergency use authorization (EUA) and, in doing so, publicized the following interim, non–peer-reviewed results. In a phase I/II/III

double-blind, placebo-controlled clinical trial (NCT04426695), 799 non-hospitalized adult patients with mild-to-moderate COVID-19 symptoms were randomized to receive a single dose of either 2.4 g or 8.0 g of REGN-COV2 or placebo within three days of a positive SARS-CoV-2 viral test.[7]

The primary end point was time-weighted average change in viral load from baseline. At day 7, patients treated with REGN-COV2 had a greater reduction in viral load than patients treated with placebo. Preliminary results cited as part of the FDA's EUA decision show that REGN-COV2 reduces COVID-19–related hospitalizations or ER visits within 28 days of treatment in patients at high risk for disease progression compared with patients receiving placebo treatment.[7] Hospitalizations and ER visits occurred in 3% of REGN-COV2–treated high-risk patients compared with 9% among high-risk patients receiving placebo.[7] Additionally, the effects on viral load and reduction in hospitalizations and emergency room visits were similar in patients receiving either of the two REGN-COV2 doses.[28]

A press release from Regeneron reporting on an earlier analysis (n = 275) from the same trial used in the FDA EUA decision (NCT04426695) stated that REGN-COV2 rapidly reduced viral load through day 7 in seronegative patients (lack of measurable antiviral antibodies).[29] Additionally, patients with higher baseline viral levels had correspondingly greater reductions in viral load at day 7 with REGN-COV2 treatment. They also noted that patients who were seronegative and/or had higher baseline viral levels also had greater benefits in terms of symptom alleviation.[30] These data suggest that REGN-COV2 may provide benefits for people who have not been able to produce their own antiviral antibodies (seronegative) to clear the virus via their own immune defences. REGN-COV2 was shown to reduce the rate of mutation of the virus better than if either drug was used alone.[10] These individuals have a higher viral load than individuals who are able to mount their own immune response (seropositive; produce antiviral antibodies) and therefore may not be able to clear the virus effectively without treatment.

According to the press release, both doses of REGN-COV2 were well-tolerated. Infusion reactions were seen in two patients receiving placebo and two patients receiving REGN-COV2; SAEs occurred in two placebo patients, one low dose REGN-COV2 patient, and no high dose REGN-COV2 patients. There were no deaths in the trial. Regeneron noted that more than 2,000 people have been enrolled across the REGN-COV2 development program so far, and no unexpected safety signals have been reported by the Independent Data Monitoring Committee.[29]

These results on REGN-COV2 have not been published in a peer-reviewed journal; therefore, detailed clinical data are lacking. Caution is required in interpreting these results.

Use as a Preventive Therapy

Use of REGN-COV2 as a preventive therapy will be assessed through a phase III prevention trial (NCT04452318), being conducted by Regeneron. This phase III randomized, double-blind, placebo-controlled trial with an estimated enrolment of 2,000 participants will investigate the prevention of COVID-19 in uninfected people who are at high risk of exposure to a COVID-19 patient (such as the patient's housemate) using subcutaneous injections (no dose reported) rather than IV administration.[31]

AZD7442 (AZD8895 + AZD1061)

Mechanism of Action

AZD7442 is a combination of two long-acting monoclonal antibodies (AZD8895+AZD1061) that target the receptor-binding domain of the spike protein, thereby preventing attachment of the virus to host cells.[32] AZD7442 has been engineered with proprietary half-life extension technology to increase the durability of the therapy for six to 12 months following a single administration. In addition to the durability of therapy, AZD7442 is designed to reduce the risk of antibody-dependent enhancement of the disease (when virus-specific antibodies promote infection), which can develop in response to antibody treatment. AZD74442 will be administered as one IV infusion (no dose reported; phase I) or two 300 mg intramuscular injections (phase III).[33]

Clinical Trial Program

As noted in a press release, AZD7442 has the potential to treat and prevent disease progression in patients who have been infected with the virus and it may also be able to be used prophylactically. A series of clinical trials have been announced that will examine the safety and efficacy of AZD7442 to prevent infection for up to 12 months in approximately 5,000 participants. There is currently one trial underway investigating AZD7442 as a treatment for patients with COVID-19. This phase I double-blind, placebo-controlled trial (NCT04507256) is evaluating the safety, tolerability, and pharmacokinetics of AZD7442 in 60 participants. The primary outcome for this trial is the number of participants with AEs and SAEs from day 1 to the last day of follow-up (day 361).[34]

Safety and Efficacy

Although no safety or efficacy data from human trials are yet available, the treatment has shown a significant reduction in viral RNA levels compared with controls in animal models.[32] In addition, mice models reportedly “developed notably less lung disease” demonstrating lung pathology that was similar to non-infected control mice. Similar results were reported in non-human primate models.[32]

At the time of this Horizon Scan, no interim results had been released.

Use as a Preventive Therapy

AZD7442 will be examined in two phase III clinical trials to evaluate post-exposure prophylaxis (for those who have come in contact with an infected person) and pre-emptive treatment in approximately 1,100 participants.[35] In STORM CHASER, a phase III randomized, double-blind, placebo-controlled multi-centre study (NCT04625972) with an estimated enrolment of 1,125 patients, AZD7442 was investigated for efficacy as a post-exposure prophylactic treatment as two intramuscular injections (300 mg).[36] PROVENT is a phase III double-blind, placebo-controlled trial (NCT04625725) focusing entirely on pre-exposure prophylaxis with an estimated enrolment of 5,000 participants (but is not yet recruiting patients; November 12, 2020) that is planning to investigate the same dosage.[34]

VIR-7831 (GSK4182136)

Mechanism of Action

VIR-7831 is a monoclonal antibody that neutralizes SARS-CoV-2 virus by recruiting immune cells to eliminate viral particles and infected cells.[3] Interestingly, this antibody does not block the virus from binding to host receptors and has broad specificity among other coronaviruses.[3] The VIR-7831 antibody treatment is administered by a single IV infusion.

Clinical Trial Program

VIR-7831 is currently under investigation via a phase II/III multi-centre, randomized, double-blind, placebo-controlled trial (COMET-ICE) (NCT04545060). On September 30, 2020, a single 500 mg IV dose of VIR-7831 was recommended by the Independent Data Monitoring Committee to continue on to phase III clinical trials following the positive evaluation of phase II data.[37] The COMET-ICE registry study will now expand globally to additional sites in North America, South America, and Europe, where the safety and efficacy of a single IV infusion of VIR-7831 will be assessed compared to placebo.[37] This study will enrol approximately 1,300 non-hospitalized participants globally. Efficacy will be assessed by the proportion of patients with mild or moderate COVID-19 who experience worsening disease, as defined by the need for hospitalization or death, within 29 days of randomization (primary efficacy end point).[38]

The clinical trial program for VIR-7831 has now expanded to include two additional trials, as described in a recent press release from the sponsor, including one for the treatment of hospitalized patients and one for the prevention of symptomatic infection.[39] At the time of publication, no additional details on these additional trials were available.

In addition to the expanded work on VIR-7831, the sponsor also plans to launch a phase Ib/IIa trial in late 2020 to evaluate a similar neutralizing monoclonal antibody, VIR-7832, which is very similar to VIR-7831 but has enhanced effector function, which may be associated with additional efficacy by stimulating a T-cell response. [40]

Safety and Efficacy

At the time of this Horizon Scan, no interim results had been released.

Use as a Preventive Therapy

The monoclonal antibody VIR-7831 (GSK4182136) is being examined in a phase II/III study (NCT04545060) as a therapy to prevent hospitalization for high-risk individuals currently showing mild or moderate COVID-19.[38]

CT-P59

Mechanism of Action

CT-P59 is a monoclonal antibody that targets the SARS-CoV-2 receptor-binding domain, preventing the virus from binding to human receptors.[41] Animal models of SARS-CoV-2 infection treated with CT-P59 demonstrated reduced viral load compared with untreated animals.[41] CT-P59 is administered as an IV infusion (schedule and dose information not available).[42]

Clinical Trial Program

The safety, tolerability, and pharmacokinetics of CT-P59 is being evaluated in healthy subjects through a phase I randomized, double-blind, placebo-controlled, parallel-group, single ascending dose trial in healthy subjects (NCT04525079).The safety, tolerability, and antiviral effect of CT-P59 is also being studied through a global phase I (randomized, double-blind, placebo-controlled, and parallel-group trial, NCT04593641), which enrolled 18 patients with mild symptoms of SARS-COV-2 infection.[43] The enrolment of 327 patients with mild-to-moderate symptoms of SARS-CoV-2 into a phase II clinical trial of CT-P59 has been completed and the results from the trial are expected in the coming weeks.[39] A phase II/III randomized, double-blind, placebo-controlled, parallel-group study was initiated in October 2020 to evaluate the safety and efficacy of CT-P59 in patients with mild-to-moderate symptoms. This trial is still recruiting patients.[44]

Safety and Efficacy

In the phase I study (NCT04525079), patients were randomized into three cohorts; 15 patients each received CT-P59 at 20 mg/kg, 40 mg/kg, or 80 mg/kg, respectively, and three patients received matching placebo.[43] Those treated with CT-P59 experienced a 44% reduced mean clinical recovery time compared with the average placebo recovery time, and no patients treated with CT-P59 required hospitalization or antiviral therapy as a result of COVID-19. Additionally, no treatment-emergent SAEs or clinically significant treatment-emergent adverse events (TEAEs) were reported at the interim stage.[43]

Use as a Preventive Therapy

The sponsor is also initiating a clinical trial to evaluate the preventive effect and safety of CT-P59 to investigate whether this treatment candidate can elicit a NAb response to prevent SARS-CoV-2 from infecting humans.[39] However, further details on this trial are not yet available at the time of publication.

Approval and Availability in Canada

The first coronavirus antibody treatment to be approved in Canada was recently announced. On November 20, 2020, Health Canada granted interim authorization for bamlanivimab with conditions that include monitoring of the quality of the drug and the continued generation of evidence to ascertain its safety and efficacy in the treatment of COVID-19 patients who are not yet hospitalized but are potentially at risk of developing serious illness due to age or comorbidities.[45] Eli Lilly has entered an initial agreement to provide the Government of Canada with 17,000 doses in December 2020 and with more doses by February 2021, if required.[46] A press release on November 24, 2020, notes that the Government of Canada will be working with provinces and territories to allocate the supply of bamlanivimab equitably, while acknowledging the need for flexibility based on COVID-19 activity.[46]

EUAs have also been issued by the US FDA for bamlanivimab and REGN-COV2 (Table 2).

Table 2: Approval and Availability Outside of Canada

Regulatory authority	Approval
Bamlanivimab	
FDA	On November 9, 2020, the US FDA issued an EUA for the use of bamlanivimab for the treatment of mild-to-moderate COVID-19 in adult and pediatric patients (12 years of age and older weighing at least 40 kg) with positive results of direct SARS-CoV-2 viral testing and who are at high risk for progressing to severe COVID-19 and/or hospitalization, including those who are 65 years of age or older or who have certain chronic medical conditions.[25]
EMA	As of November 19, 2020, bamlanivimab has not been reviewed for use by the EMA.
REGN-COV2 (casirivimab + imdevimab)	
FDA	On November 21, 2020, the US FDA issued an EUA for the use of REGN-COV2 for treatment of mild-to-moderate COVID-19 in adult and pediatric patients (12 years of age and older weighing at least 40 kg) with positive results of direct SARS-CoV-2 viral testing and who are at high risk for progressing to severe COVID-19, including those who are 65 years of age or older or who have certain chronic medical conditions.[28]
EMA	As of November 19, 2020, REGN-COV2 has not been reviewed for use by the EMA.

EMA = European Medicines Agency; EUA = emergency use authorization.

Considerations for Virus-Neutralizing Monoclonal Antibody Therapy Use

New evidence on the treatment of COVID-19 with virus-neutralizing monoclonal antibodies is constantly emerging. Logistical barriers to the use of these treatments are not insignificant in the Canadian health care context, including how to identify and intravenously treat high-risk patients within three to four days of diagnosis of COVID-19. Early data suggest potential but still uncertain benefits that must be considered in relation to potential risks of developing severe disease and adverse reactions to the treatment. Further evidence that will help to evaluate these considerations is key to optimize the use of these treatments in specific populations most likely to benefit.

One important consideration for use of virus-neutralizing monoclonal antibodies, including bamlanivimab, is that these treatments have not shown benefit when administered to hospitalized patients with COVID-19.[25] Further, an important caveat of NAbs is the possibility for antibody-dependent enhancement, in which binding to host cells is promoted rather than inhibited.[47]

Virus-neutralizing monoclonal antibodies can be difficult and expensive to produce making them out of reach for nations without large financial capabilities.[48] In the US, Operation Warp Speed invested $450 million to produce 300,000 doses of virus-neutralizing monoclonal antibody from Regeneron Pharmaceuticals.[48] Therefore, understanding effective mechanisms of SARS-CoV-2 NAbs in specific patient populations is vital.

Importantly, early-to-market treatments such as bamlanivimab may provide direction for the success of other antibodies against SARS-CoV-2, much like the ZMapp antibody developed for treatment of Ebola acted as a proof of concept and allowed the development of successor antibodies that improved mortality rates. For example, results for REGN-COV2 indicate that multiple antibodies specific for different locations on the spike protein may provide protection against viral mutation.[10] The diversity in antibodies being studied only

increases the chance that one (or more), used alone or in combination, will be identified as an effective therapeutic for treatment of COVID-19.

Final Remarks

The ongoing development of virus-neutralizing monoclonal antibodies may lead to promising treatment options, especially for individuals who are at high risk of developing severe COVID-19 illness. Bamlanivimab, the first virus-neutralizing monoclonal antibody to be made available in Canada, with conditions, was done so under Health Canada's Interim Order, an approval mechanism used to expedite access to drugs and vaccines for COVID-19.[46] Four more treatments of its kind are currently in late-phase clinical development, with many others in early and pre-clinical development.

These early promising results for virus-neutralizing monoclonal antibodies used for the clinical management of SARS-CoV-2 need to be considered carefully before adoption as a treatment strategy. The currently available data are preliminary and still require peer review. In addition to the efficacy and safety data described in this Horizon Scan, data on the potential development of antibody-dependent enhancement of COVID-19 must be examined as these drugs are reviewed for approval. Nevertheless, virus-neutralizing monoclonal antibodies offer a treatment strategy that may benefit individuals at high risk of severe disease and those who are unable to produce a viable immune response against SARS-CoV-2. As more virus-neutralizing monoclonal antibodies become available, further consideration of the differences between the single monoclonal antibody approach versus that of the cocktail approach will be useful to guide optimal use.

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Appendix 1: Virus-Neutralizing Monoclonal Antibodies Currently Under Development (Phase I to Phase III)

Table 3: Details of Virus-Neutralizing Monoclonal Antibodies Currently Under Clinical Development

Antibody	Sponsor	Trial ID	Clinical stage	Target
Bamlanivimab (LY3819253/LY-Cov555)	Eli Lilly and Company/AbCellera Biologics Inc.	NCT04603651 NCT04497987 NCT04501978 NCT04518410 NCT04634409 NCT04427501 NCT04411628 NCT04537910	Expanded access Phase III Phase III Phase II/III Phase II Phase II Phase I Phase I	Spike protein
REGN-COV2 (REGN10933 + REGN10987)	Regeneron Pharmaceuticals	NCT04617535 NCT04381936 NCT04452318 NCT04425629 NCT04426695 NCT04519437	Expanded access (compassionate use) Phase II/III Phase III Phase I/II/III Phase I/II/III Phase I	Receptor-binding domain
AZD7442 (AZD8895 + AZD1061)	AstraZeneca	NCT04625725 NCT04625972 NCT04507256	Phase III Phase III Phase I	Spike protein
VIR-7831	Vir Biotechnology/GlaxoSmithKline	NCT04545060	Phase II/III	SARS-CoV-2
CT-P59	Celltrion	NCT04602000 NCT04525079 NCT04593641	Phase II/III Phase I Phase I	SARS-CoV-2
LY3127804	Eli Lilly and Company	NCT04342897	Phase II	Spike protein
BGB DXP593	Beigene	NCT04551898 NCT04532294	Phase II Phase I	Spike protein
Kamada Anti-SARS-CoV-2	Kamada	NCT04550325	Phase I/II	SARS-CoV-2
DZIF-10c	University of Cologne/Boehringer Ingelheim	NCT04631705 NCT04631666	Phase I/II Phase I/II	Spike protein
COVI-AMG (STI-2020)	Sorrento Therapeutics, Inc.	NCT04584697	Phase I/II	Spike protein

Antibody	Sponsor	Trial ID	Clinical stage	Target
TY027	Tychan Pte. Ltd.	NCT04429529	Phase I	Spike protein
SCTA01	Sinocelltech Ltd.	NCT04483375	Phase I	SARS-CoV-2
JS016	Junshi Biosciences/Eli Lilly and Company	NCT04441918	Phase I	Receptor-binding domain
BRII-196	Brii Biosciences	NCT04479631	Phase I	Spike protein
BRII-198	Brii Biosciences	NCT04479644	Phase I	Spike protein
COVI-GUARD (STI-1499)	Sorrento Therapeutics, Inc.	NCT04454398 NCT04454398	Phase I Phase I	Spike protein
MW33	Mabwell (Shanghai) Bioscience Co., Ltd.	NCT04533048	Phase I	Spike protein
HLX70	Hengenix Biotech Inc.	NCT04561076 NCT04561076	Phase I Phase I	Spike protein
HFB30132A	HiFiBiO Therapeutics	NCT04590430	Phase I	Spike protein
ADM03820	Ology Bioservices	NCT04592549	Phase I	SARS-CoV-2

Appendix 2: Bamlanivimab (Eli Lilly and Company/AbCellera Biologics Inc.)

Table 4: Summary of Current Clinical Trial Program for Bamlanivimab (Eli Lilly and Company/AbCellera Biologics Inc.)

Study information	Study design and sample size	Population	Interventions	Primary outcomes
Expanded Access Program to Provide Bamlanivimab (LY3819253) for the Treatment of COVID-19 Sponsor: Eli Lilly and Company ClinicalTrials.gov identifier: NCT04603651 Estimated primary completion date: NR Estimated study completion date: NR	Expanded access Status: No longer available	Children and adults older than 12 years with SARS-CoV-2	Bamlanivimab	NA
A Study of LY3819253 (LY-CoV555) in Preventing SARS-CoV-2 Infection and COVID-19 in Nursing Home Residents and Staff (BLAZE-2) Sponsor: Eli Lilly and Company ClinicalTrials.gov identifier: NCT04497987 Estimated primary completion date: March 8, 2021 Estimated study completion date: June 29, 2021	Phase III randomized, double-blind, placebo-controlled, parallel assignment interventional study Estimated enrolment: N = 2,400 Status: Recruiting	Resident or facility staff in a nursing or assisted-living facility with at least one confirmed case of SARS-CoV-2	• Bamlanivimab • Placebo	• Percentage of participants with SARS-CoV-2 infection
ACTIV-3: Therapeutic for Inpatients with COVID-19 (TICO) Sponsor: National Institute of Allergy and Infectious Diseases ClinicalTrials.gov identifier: NCT04501978	Phase III randomized, double-blind, placebo-controlled, parallel assignment interventional study Estimated enrolment: N = 10,000 Status: Active, not recruiting	Adults with COVID-19 requiring hospital admission	• Bamlanivimab • Placebo • Remdesivir also administered to both treatment groups	• Pulmonary ordinal outcome (stage 1) • Pulmonary and ordinal outcome (stage 1) • Time from randomization to sustained recovery (stage 2)

Study information	Study design and sample size	Population	Interventions	Primary outcomes
Estimated primary completion date: July 2021 Estimated study completion date: July 2021 Study stopped recruiting patients for this study on 26 October 2020, due to a lack of benefit seen in people hospitalized with COVID-19.[49]				
ACTIV-2: A Study for Outpatients with | COVID-19 Sponsor: National Institute of Allergy and Infectious Diseases (NIAID) ClinicalTrials.gov identifier: NCT04518410 Estimated primary completion date: November 2020 Estimated study completion date: February 2021	Phase II/III randomized, double-blind, placebo-controlled, parallel assignment interventional study Estimated enrolment: N = 2,000 Status: Recruiting	Adults with a positive COVID-19 test	• Bamlanivimab • Placebo	• Duration of COVID-19 symptoms • Post-treatment presence of SARS-CoV-2 RNA at day 3 • Post-treatment presence of SARS-CoV-2 at day 7 • Post-treatment presence of SARS-CoV-2 at day 14 • Post-treatment presence of SARS-CoV-2 at day 21 • Post-treatment presence of SARS-CoV-2 at day 28 • Incidence of new AEs ≥ grade 3 • Cumulative incidence of death from any cause or hospitalization • Proportion of participants with new AEs ≥ grade 3
A Study of Immune System Proteins in Participants With Mild to Moderate COVID-19 Illness (BLAZE-4) Sponsor: Eli Lilly and Company ClinicalTrials.gov identifier: NCT04634409 Estimated primary completion date: December 31, 2020 Estimated study completion date: March 15, 2021	Phase II randomized, double-blind, placebo-controlled, parallel assignment interventional study Estimated enrolment: N = 500 Status: Recruiting	Adults with mild-to-moderate COVID-19 symptoms	• Bamlanivimab • Bamlanivimab + etesevimab • Placebo	• Percentage of participants with SARS-CoV-2 viral load > 5.27

Study information	Study design and sample size	Population	Interventions	Primary outcomes
A Study of LY3819253 (LY-CoV555) and LY3832479 (LY-CoV016) in Participants With Mild to Moderate COVID-19 Illness (BLAZE-1) Sponsor: Eli Lilly and Company ClinicalTrials.gov identifier: NCT04427501 Estimated primary completion date: September 20, 2020 Estimated study completion date: March 11, 2021	Phase II, randomized, double-blind, placebo-controlled, sequential assignment interventional study Estimated enrolment: N = 1,200 Status: recruiting	Patients 12 years and older with mild-to-moderate COVID-19 symptoms	• Bamlanivimab • Bamlanivimab + etesevimab • Placebo	• Change from baseline to day 11 SARS-CoV-2 viral load • Percentage of participants who experience COVID-related hospitalization or death • Percentage of participants with SARS-CoV-2 viral load greater than a pre-specified threshold
A Study of LY3819253 (LY-CoV555) in Participants Hospitalized for COVID-19 Sponsor: Eli Lilly and Company ClinicalTrials.gov identifier: NCT04411628 Estimated primary completion date: August 26, 2020 Estimated study completion date: August 26, 2020	Phase I randomized, double-blind, placebo-controlled, parallel assignment interventional study Estimated enrolment: N = 24 Status: Completed	Adults hospitalized or in the process of being admitted to hospital with COVID-19 infection	• Bamlanivimab • Placebo	• Number of participants with one or more SAEs considered by the investigator to be related to study drug administration
A Study of LY3819253 (LY-CoV555) in Healthy Participants Sponsor: Eli Lilly and Company ClinicalTrials.gov identifier: NCT04537910 Estimated primary completion date: December 22, 2020	Phase I, randomized, double-blind, placebo-controlled, parallel assignment interventional study Estimated enrolment: N = 25 Status: Active, not recruiting	Healthy adults	• Bamlanivimab • Placebo	• Pharmacokinetics: area under the concentration versus time curve (from time 0 to infinity)

Study information	Study design and sample size	Population	Interventions	Primary outcomes
Estimated study completion date: December 22, 2020				

AE = adverse event; NA = not applicable; NR = not reported; SAE = serious adverse event; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.

Appendix 3: REGN-COV2 (Regeneron Pharmaceuticals)

Table 5: Summary of Current Clinical Trial Program for REGN-COV2 (Regeneron Pharmaceuticals)

Study information	Study design and sample size	Population	Interventions	Primary outcomes
Compassionate Use of REGN-COV2 for the Treatment of COVID-19 Sponsor: Regeneron Pharmaceuticals ClinicalTrials.gov identifier: NCT04617535	Expanded access Expanded access Type: Individual patients Status: Available	Compassionate use requests are only being considered in response to individual patient Investigational New Drug applications	REGN-COV2	NA
Randomised Evaluation of COVID-19 Therapy (RECOVERY) Sponsor: University of Oxford ClinicalTrials.gov identifier: NCT04381936 Estimated primary completion date: December 2021 Estimated study completion date: December 2021	Phase II/III randomized, open-label, factorial assignment interventional study Estimated enrolment: N = 20,000 Status: Recruiting	Patients (children or adults) hospitalized, with SARS-CoV-2 infection	• Lopinavir-Ritonavir • Corticosteroid • Hydroxychloroquine • Azithromycin • Convalescent plasma • Tocilizumab • Immunoglobulin • Synthetic NAbs • Aspirin • Colchicine	• All-cause mortality
Study Assessing the Efficacy and Safety of Anti-Spike SARS CoV-2 Monoclonal Antibodies for Prevention of SARS-CoV-2 Infection Asymptomatic in Healthy Adults and Adolescents Who Are Household Contacts to an Individual with a Positive SARS-CoV-2-OCR Assay Sponsor: Regeneron Pharmaceuticals ClinicalTrials.gov identifier: NCT04452318 Estimated primary completion date: June 15, 2021	Phase III randomized, double-blind, placebo-controlled, parallel assignment interventional study Estimated enrolment: N = 2,000 Status: Recruiting	Healthy adults with an asymptomatic household contact to an individual diagnosed with SARS-CoV-2 infection	• REGN-COV2 • Placebo	• Proportion of participants who have a positive SARS-CoV-2 RT-qPCR (based on central lab test) and signs and symptoms (strict term) of SARS-CoV-2 infection during the efficacy assessment period • Proportion of participants who have an RT-qPCR–confirmed SARS-CoV-2 infection (either symptomatic or asymptomatic) during the efficacy assessment period • Proportion of participants with TEAEs and severity of TEAEs

Study information	Study design and sample size	Population	Interventions	Primary outcomes
Estimated study completion date: August 15, 2021				
Safety, Tolerability, and Efficacy of Anti-Spike (S) SARS-CoV-2 Monoclonal Antibodies for the Treatment of Ambulatory Adult Patients With COVID-19 Sponsor: Regeneron Pharmaceuticals ClinicalTrials.gov identifier: NCT04425629 Estimated primary completion date: December 19, 2020 Estimated study completion date: December 19, 2020	Phase I/II/III randomized, double-blind, placebo-controlled, parallel assignment interventional study Estimated enrolment: N = 2,104 Status: Recruiting	Adults with SARS-CoV-2 who are symptomatic or asymptomatic	• REGN-COV2 • Placebo	• Proportion of patients with treatment-emergent AEs • Proportion of patients with treatment-emergent SAEs • Proportion of patients with hypersensitivity reactions • Time-weighted average change from baseline in viral shedding as measured by RT-qPCR in nasopharyngeal swab samples • Proportion of patients with at least one COVID-19–related medically attended visit
Safety, Tolerability, and Efficacy of anti-Spike (S) SARS-CoV-2 Monoclonal Antibodies for Hospitalized Adult Patients with COVID-19 Sponsor: Regeneron Pharmaceuticals ClinicalTrials.gov identifier: NCT04426695 Estimated primary completion date: January 25, 2021 Estimated study completion date: January 25, 2021	Phase I/II randomized, double-blind, placebo-controlled, parallel assignment interventional study Estimated enrolment: N = 2,970 Status: Recruiting	Adults with a diagnosis of SARS-CoV-2 and hospitalized with COVID-19 illness	• REGN-COV2 • Placebo	• Proportion of patients with treatment-emergent SAEs • Proportion of patients with infusion-related reactions • Proportion of patients with hypersensitivity reactions • Time-weighted average change from baseline in viral shedding as measured by RT-qPCR in nasopharyngeal swab samples • Proportion of patients with at least 1-point improvement on a 7-point ordinal scale in clinical status
Study Assessing the Safety, Tolerability, Pharmacokinetics, and Immunogenicity of Repeated Subcutaneous Doses of Anti-Spike (S) SARS-CoV-2 Monoclonal Antibodies (REGN10933+REGN10987) in Adult Volunteers as Related to COVID-19	Phase I randomized, double-blind, placebo-controlled parallel assignment interventional study	Healthy adults	• REGN-COV2 • Placebo	• Incidence of AEs of special interest that occur within 4 days of study drug administration

Study information	Study design and sample size	Population	Interventions	Primary outcomes
Sponsor: Regeneron Pharmaceuticals ClinicalTrials.gov identifier: NCT04519437 Estimated primary completion date: October 25, 2021 Estimated study completion date: October 25, 2021	Estimated enrolment: N = 974 Status: Active, not recruiting			

AE = adverse event; NAb = neutralizing antibody; RT-qPCR = reverse transcription quantitative polymerase chain reaction; SAE = serious adverse event; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2; TEAE = treatment-emergent adverse event.

Appendix 4: AZD7442 (AstraZeneca)

Table 6: Summary of Current Clinical Trial Program for AZD7442 (AstraZeneca)

Study information	Study design and sample size	Population	Interventions	Primary outcomes
Phase III Double-blind, Placebo-controlled Study of AZD7442 for Pre-exposure Prophylaxis of COVID-19 in Adult. (PROVENT) Sponsor: AstraZeneca ClinicalTrials.gov identifier: NCT04625725 Estimated primary completion date: July 31, 2021 Estimated study completion date: December 14, 2021	Phase III randomized, double-blind, placebo-controlled, parallel assignment interventional study Estimated enrolment: N = 5,000 Status: Not yet recruiting	Adults who can benefit from passive immunization with antibodies and are medically stable	• AZD7442 • Placebo	• The incidence of the first case of SARS-CoV-2 RT PCR positive symptomatic illness • AEs, SAEs, MAAEs, and AESIs through 365 days post dose of intervention
Phase III Double-blind, Placebo-controlled Study of AZD7442 for Post-Exposure Prophylaxis of COVID-19 in Adults (STORM CHASER) Sponsor: AstraZeneca ClinicalTrials.gov identifier: NCT04625972 Estimated primary completion date: June 16, 2021 Estimated study completion date: December 16, 2021	Phase III randomized, double-blind, placebo-controlled, parallel assignment interventional study Estimated enrolment: N = 1,125 Status: Not yet recruiting	Adults with potential exposure within 8 days to a specific identified individual with SARS-CoV-2 infection	• AZD7442 • Placebo	• The incidence of the first case of SARS-CoV-2 RT PCR positive symptomatic illness • AEs, SAEs, MAAEs, and AESIs through 365 days post dose of intervention

Study information	Study design and sample size	Population	Interventions	Primary outcomes
AZD7442 – A Potential Combination Therapy for the Prevention and Treatment of COVID-19 Sponsor: AstraZeneca ClinicalTrials.gov identifier: NCT04507256 Estimated primary completion date: October 25, 2021 Estimated study completion date: October 25, 2021	Phase I randomized, double-blind, placebo-controlled, sequential assignment interventional study N = 60 Status: Active, not recruiting	Healthy adults who do not have SARS-CoV-2 at randomization	• AZD7442 • Placebo	• Number of participants with AEs and SAEs

AE = adverse event; AESI = adverse event of special interest; MAAE = medically attended adverse event; SAE = serious adverse event; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.

Appendix 5: VIR-7831 (Vir Biotechnology/GlaxoSmithKline)

Table 7: Summary of Current Clinical Trial Program for VIR-7831 (Vir Biotechnology/GlaxoSmithKline)

Study information	Study design and sample size	Population	Interventions	Primary outcomes
VIR-7831 for the Early Treatment of COVID-19 in Outpatients (COMET-ICE) Sponsor: Vir Biotechnology, Inc. ClinicalTrials.gov identifier: NCT04545060 Estimated primary completion date: January 2021 Estimated study completion date: July 2021	Phase II/III randomized, double-blind, placebo-controlled, parallel assignment interventional study Estimated enrolment: N = 1,360 Status: Recruiting	Adults with SARS-CoV-2 and a high risk of progression to COVID-19 or adults with SARS-CoV-2 who are older than 55 years	• VIR-7831 • Placebo	• Proportion of participants who have progression of COVID-19 through day 29

SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.

Appendix 6: CT-P59 (Celltrion)

Table 8: Summary of Current Clinical Trial Program for CT-P59 (Celltrion)

Study information	Study design and sample size	Population	Interventions	Primary outcomes
To Evaluate the Safety and Efficacy of CT-P59 in Patients with Mild to Moderate Symptoms of Severe Acute Respiratory Syndrome COVID-19 Sponsor: Celltrion ClinicalTrials.gov identifier: NCT04602000 Estimated primary completion date: December 2020 Estimated study completion date: September 2021	Phase II/III randomized, double-blind, placebo-controlled, parallel assignment interventional study Estimated enrolment: N = 1,020 Status: recruiting	Adults with SARS-CoV-2 infection and mild conditions (oxygen saturation ≥ 94% on room air and not requiring supplemental oxygen)	• CT-P59 • Placebo	• Evaluate the therapeutic efficacy of CT-P59 for part 1 (phase II) • Evaluate the therapeutic efficacy of CT-P59 for part 2 (phase III)
A Pilot Phase 1, Randomized, Double-blind, Placebo-controlled, Parallel Group, Single Ascending Dose Study to Evaluate the Safety, Tolerability and Virology of CT-P59 in Patient With Mild Symptoms of SARS-CoV-2 Infection Sponsor: Celltrion ClinicalTrials.gov Identifier: NCT04593641 Estimated primary completion date: October 2020 Estimated study completion date: December 2020	Pilot phase I, randomized, double-blind, placebo-controlled, sequential assignment, single ascending dose interventional study Estimated enrolment: N = 18 Status: Active, not recruiting	Adults with laboratory-confirmed COVID-19	• CT-P59 • Placebo	• Proportion of patients with TEAEs • Proportion of patients with TEAEs of special interest • Proportion of patients with potential effects on the incidence of antibody-dependent enhancement

Study information	Study design and sample size	Population	Interventions	Primary outcomes
To Evaluate the Safety, Tolerability and Pharmacokinetics of CT-P59 in Healthy Subjects Sponsor: Celltrion ClinicalTrials.gov identifier: NCT04525079 Estimated primary completion date: August 31, 2020 Estimated study completion date: November 30, 2020	Phase I randomized, double-blind, placebo-controlled, sequential assignment, single ascending dose escalation interventional study Estimated enrolment: N = 32 Status: Recruiting	Healthy adults (aged 18 years to 55 years) with a BMI 18.0 kg/m^2 to 29.9 kg/m^2 and a body weight of ≥ 50 kg	• CT-P59 • Placebo	• Proportion of patients with TEAEs • Proportion of patients with TEAEs of special interest

BMI = body mass index; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2; TEAE = treatment-emergent adverse event.

Appendix 7: Other Virus-Neutralizing Monoclonal Antibodies Under Clinical Development

Table 9: Clinical Trials for Virus-Neutralizing Monoclonal Antibodies in Earlier Stages of Development

Study information	Study design and sample size	Population	Interventions	Primary outcomes
Tolerability, Safety, Pharmacokinetic Profile and Immunogenicity of a Recombinant Humanized Anti-SARS-CoV-2 Monoclonal Antibody (JS016) for Injection in Chinese Healthy Subjects Sponsor: Shanghai Junshi Bioscience Co., Ltd. ClinicalTrials.gov identifier: NCT04441918 Estimated primary completion date: December 11, 2020 Estimated study completion date: December 11, 2020	Phase I randomized, double-blind, placebo-controlled, sequential assignment interventional study Estimated enrolment: N = 40 Status: Recruiting	Healthy adults (aged 15 years to 45 years) without SARS-CoV-2 infection	• JS016 • Placebo	• Correlation of AEs with the investigational product
Safety, Tolerability, and Pharmacokinetics Study of Human Monoclonal Antibody BRII-196 Sponsor: Brii Biosciences Limited ClinicalTrials.gov identifier: NCT04479631 Estimated primary completion date: March 2021 Estimated study completion date: March 2021	Phase I randomized, single blind, placebo-controlled, parallel assignment, single ascending dose escalation interventional study Estimated enrolment: N = 12 Status: Active, not recruiting	Healthy adults (aged 18 years to 49 years) with a BMI 19.0 kg/m^2 to 24.0 kg/m^2	• BRII-196 • Placebo	• Incidence of AEs • Proportion of participants with SAEs • Proportion of participants with infusion-related reactions • Proportion of participants with hypersensitivity reactions
Safety, Tolerability, and Pharmacokinetics Study of Human Monoclonal Antibody BRII-198 Sponsor: Brii Biosciences Limited ClinicalTrials.gov identifier: NCT04479631 Estimated primary completion date: March 2021 Estimated study completion date: March 2021	Phase I randomized, single blind, placebo-controlled, parallel assignment, single ascending dose escalation interventional study Estimated enrolment: N = 12 Status: Active, not recruiting	Healthy adults (aged 18 years to 49 years) with a BMI 19.0 kg/m^2 to 24.0 kg/m^2	• BRII-198 • Placebo	• Incidence of AEs • Proportion of participants with SAEs • Proportion of participants with infusion-related reactions • Proportion of participants with hypersensitivity reactions

Study information	Study design and sample size	Population	Interventions	Primary outcomes
A randomized, double-blind, placebo-controlled, clinical trial of LY3127804 in participants who are hospitalized with pneumonia and presumed or confirmed COVID-19. The study may last up to 9 weeks and include daily visits up to day 28, and follow-up visits by phone. Sponsor: Eli Lilly and Company ClinicalTrials.gov identifier: NCT04342897 Actual primary completion date: October 2020 Actual study completion date: October 2020 Note: Project has been terminated.	Phase II randomized, double-blind, placebo-controlled parallel assignment, interventional study Estimated enrolment: N = 200 Actual enrolment N = 95 Status: Terminated (for futility)	Adults 18 years and older and are hospitalized with pneumonia and presumed or confirmed COVID-19	• LY3127804 • Placebo	• Number of ventilator-free days
A Phase 2, Randomized, Double-Blind, Placebo-Controlled Study to Evaluate the Efficacy and Safety of SARS-CoV-2 Neutralizing Antibody BGB-DXP593 in Patients With Mild-to-Moderate COVID-19 Sponsor: BeiGene ClinicalTrials.gov identifier: NCT04551898 Estimated primary completion date: December 2020 Estimated study completion date: February 2021	Phase II randomized, double-blind, placebo-controlled, parallel assignment, interventional study Estimated enrolment: N = 180 Status: Not yet recruiting	Adults 18 years to 65 years and laboratory-confirmed COVID-19	• BGB-DXP593 • Placebo	• Change from baseline to day 8 in SARS-CoV-2 viral shedding as measured by RT-qPCR in nasopharyngeal swab samples
A First-in-Human, Randomized, Double-Blind, Placebo Controlled, Single Dose Escalation Study to Evaluate the Safety, Tolerability, Pharmacokinetics, and Immunogenicity of SARS-CoV-2 Neutralizing Antibody BGB-DXP593 in Healthy Subjects	Phase I randomized, double-blind, placebo-controlled, parallel assignment, single dose escalation interventional study Estimated enrolment: N = 30	Adults 18 years to 60 years and in good general health as determined by the investigator or medically qualified designee based on a medical evaluation including medical history,	• BGB DXP593 • Placebo	• Number of participants experiencing TEAEs • Number of participants experiencing SAEs

Study information	Study design and sample size	Population	Interventions	Primary outcomes
Sponsor: BeiGene ClinicalTrials.gov Identifier: NCT04532294 Estimated primary completion date: February 2021 Estimated study completion date: June 2021	Status: Recruiting	physical examination, laboratory tests, and cardiac monitoring		
A Phase 1/2 Open Label, Multicenter, Single Arm Study to Evaluate the Safety, Pharmacokinetics and Pharmacodynamics of Single Dose Kamada Anti-SARS-CoV-2 in COVID-19 Hospitalized Patients With Pneumonia Sponsor: Kamada, Ltd. ClinicalTrials.gov Identifier: NCT04550325 Estimated primary completion date: December 2021 Estimated study completion date: February 2021	Phase I/II open-label, single arm interventional study Estimated enrolment: N = 12 Status: recruiting	Adults 18 years of age and older who are hospitalized with laboratory-confirmed SARS-CoV-2 infection	• Kamada Anti-SARS-CoV-2	• AEs, SAEs, and deaths
A Phase 1/2a Trial of the Inhaled Administration of the SARS-CoV-2-Neutralizing Monoclonal Antibody DZIF-10c in SARS-CoV-2-Infected and -Uninfected Individuals Sponsor: University of Cologne ClinicalTrials.gov Identifier: NCT04631705 Estimated primary completion date: June 2021 Estimated study completion date: June 2021	Phase I/IIa open-label, randomized, double-blind, placebo-controlled, sequential assignment, dose escalation interventional study Estimated enrolment: N = 69 Status: Not yet recruiting	18 years to 70 years of age including both infected and non-infected COVID-19 patients	• DZIF-10c • Placebo	• Incidence of TEAEs • Incidence of reactogenicity AEs

Study information	Study design and sample size	Population	Interventions	Primary outcomes
A Phase 1/2a Trial of the Intravenous Administration of the SARS-CoV-2-Neutralizing Monoclonal Antibody DZIF-10c in SARS-CoV-2-Infected and -Uninfected Individuals Sponsor: University of Cologne ClinicalTrials.gov Identifier: NCT04631666 Estimated primary completion date: June 2021 Estimated study completion date: June 2021	Phase I/IIa randomized, double-blind, placebo-controlled sequential assignment, dose escalation interventional study Estimated enrolment: N = 69 Status: Not yet recruiting	18 to 70 years of age including both infected and non-infected COVID-19 patients	• DZIF-10c • Placebo	• Incidence of TEAEs • Incidence of reactogenicity AEs
A Randomized, Placebo-controlled Study to Evaluate the Safety, Pharmacokinetics and Efficacy of a Single Dose of STI-2020 (COVI-AMG™) in Outpatients With COVID-19 Who Are Asymptomatic or Have Mild Symptoms Sponsor: Sorrento Therapeutics, Inc. ClinicalTrials.gov Identifier: NCT04584697 Estimated primary completion date: April 2021 Estimated study completion date: April 2021	Phase I/II randomized, double-blind, placebo-controlled, sequential assignment, interventional study Estimated enrolment: N = 50 Status: Not yet recruiting	18 years of age and older outpatients with COVID-19 who are asymptomatic or have mild symptoms	• COVI-AMG • Placebo	• Incidence of AEs by type, frequency, severity, and causality • Incidence of TEAEs by type, frequency, severity, and causality • Incidence of SAEs by type, frequency, severity, and causality • Incidence of dose-limiting toxicities • Incidence of clinically meaningful laboratory abnormalities • Viral load as assessed using plasma and salivary samples at various timepoints • Time from onset of COVID-19 symptoms to treatment (day 1) • Presence and levels of anti-drug antibodies directed to COVI-AMG • Cytokine levels post-treatment

Study information	Study design and sample size	Population	Interventions	Primary outcomes
Safety of TY027, a Treatment for COBID-19, in Humans Sponsor: Tychan Pte Ltd. ClinicalTrials.gov identifier: NCT04429529 Estimated primary completion date: November 2020 Estimated study completion date: February 2021	Phase I randomized, double-blind, placebo-controlled, parallel assignment, single ascending dose interventional study Estimated enrolment: N = 32 Status: Active, not recruiting	Healthy adult volunteers	• TY027 • Placebo	• Number of participants with treatment-related AEs
Safety, Tolerability and Pharmacokinetics of SCTA01, an Anti-SARS-CoV-2 Monoclonal Antibody, in Healthy Chinese Subjects Sponsor: Sinocelltech Ltd. ClinicalTrials.gov identifier: NCT04483375 Estimated primary completion date: November 20, 2020 Estimated study completion date: January 15, 2021	Phase I randomized, double-blind, placebo-controlled, parallel assignment, interventional study Estimated enrolment: N = 22 Status: Recruiting	Healthy adult volunteers	• SCTA01 • Placebo	• Dose-limiting toxicity • Maximal tolerable dose
A Randomized, Placebo-controlled Study to Evaluate the Safety, Pharmacokinetics and Efficacy of a Single Dose of STI-1499 (COVI-GUARD™) in Hospitalized Patients With Moderate COVID-19 Sponsor: Sorrento Therapeutics, Inc. ClinicalTrials.gov Identifier: NCT04454398 Estimated primary completion date: February 2021	Phase I randomized, double-blind, placebo-controlled, parallel assignment, interventional study Estimated enrolment: N = 33 Status: Recruiting	Hospitalized adults with moderate COVID-19	• COVI-GUARD • Placebo	• Incidence of AEs • Incidence of TEAEs • Incidence of SAEs • All-cause mortality at 29 and 60 days • Incidence of dose-limiting toxicities • Incidence of laboratory abnormalities • SARS-CoV-2 viral load as assessed using various sample types

Study information	Study design and sample size	Population	Interventions	Primary outcomes
Estimated study completion date: February 2021				• Time to hospitalization, treatment, ICU admission, and discharge from ICU and/or hospital • Anti-drug antibodies • Cytokine levels
A Phase I Clinical Study to Evaluate the Safety, Tolerability, Pharmacokinetic Characteristics and Immunogenicity of a Single Dose of MW33 Injection in Healthy Subjects Sponsor: Mabwell (Shanghai) Bioscience Co., Ltd. ClinicalTrials.gov Identifier: NCT04533048 Estimated primary completion date: December 2020 Estimated study completion date: December 2020	Phase I randomized, double-blind, placebo-controlled, sequential assignment, interventional study Estimated enrolment: N = 32 Status: Active, not recruiting	Healthy adults	• MW33 • Placebo	• AEs • SAEs
A Randomized, Double-Blind, Placebo-Controlled, Dose Escalation Phase I Clinical Study to Evaluate Safety and Pharmacokinetics of HLX70 in Healthy Adult Volunteers Sponsor: Hengenix Biotech Inc. ClinicalTrials.gov Identifier: NCT04561076 Estimated primary completion date: September 2021 Estimated study completion date: September 2021	Phase I randomized, double-blind, placebo-controlled, sequential assignment, interventional study Estimated enrolment: N = 24 Status: Not yet recruiting	Healthy adult volunteers	• HLX70 • Placebo	• Number of participants with AEs, SAEs, and infusion-related reactions

Study information	Study design and sample size	Population	Interventions	Primary outcomes
A Randomized, Double-Blind, Placebo-Controlled, Single Ascending Dose First-in-Human Study Investigating the Safety, Tolerability, and Pharmacokinetics of Intravenously Administered HFB30132A, a Monoclonal Antibody Directed Against SARS-CoV-2, in Healthy Adult Subjects Sponsor: HiFiBiO Therapeutics ClinicalTrials.gov Identifier: NCT04590430 Estimated primary completion date: December 2020 Estimated study completion date: July 2021	Phase I randomized, double-blind, placebo-controlled, parallel assignment, single ascending dose interventional study Estimated enrolment: N = 24 Status: Recruiting	Healthy adult volunteers	• HFB30132A • Placebo	• Number of participants with treatment-emergent SAEs • Number of participants with TEAEs of special interest • Number of participants with TEAEs
A Phase 1, Randomized, Double-Blind, Placebo-Controlled, Dose Escalation Study to Evaluate the Safety, Pharmacokinetics, and Immunogenicity of ADM03820 in Adults Sponsor: Ology Bioservices ClinicalTrials.gov Identifier: NCT04592549 Estimated primary completion date: August 2021 Estimated study completion date: August 2021	Phase I randomized, double-blind, placebo-controlled, sequential assignment, dose escalation interventional study Estimated enrolment: N = 40 Status: Not yet recruiting	Healthy adults	• ADM03820 • Placebo	• The number of participants with SAEs

AE = adverse event; BMI = body mass index; ICU = intensive care unit; RT-qPCR = reverse transcription quantitative polymerase chain reaction; SAE = serious adverse event; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2; TEAE = treatment-emergent adverse event.