Review
COVID-19 Vaccine Platforms: Challenges and Safety Contemplations

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Abstract: The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has become a pandemic as of March 2020, creating a global crisis and claiming millions of lives. To halt the pandemic and alleviate its impact on society, economy, and public health, the development of vaccines and antiviral agents against SARS-CoV-2 was a dire need. To date, various platforms have been utilized for SARS-CoV-2 vaccine development, and over 200 vaccine candidates have been produced, many of which have obtained the United States Food and Drug Administration (FDA) approval for emergency use. Despite this successful development and licensure, concerns regarding the safety and efficacy of these vaccines have arisen, given the unprecedented speed of vaccine development and the newly emerging SARS-CoV-2 strains and variants. In this review, we summarize the different platforms used for Coronavirus Disease 2019 (COVID-19) vaccine development, discuss their strengths and limitations, and highlight the major safety concerns and potential risks associated with each vaccine type.

Keywords: SARS-CoV-2; COVID-19; vaccine platforms; challenges; safety; strengths; limitations

1. Introduction

The coronavirus disease 2019 (COVID-19), caused by the novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), first reported in late 2019 in Wuhan, the capital of Hubei province in Central China, has become a global pandemic with devastating effects worldwide [1]. Since then, and until 29 June 2021, this newly emerging disease caused by the enveloped SARS-CoV-2 virus, which belongs to the Coronaviridae family and the lineage B of the betacoronavirus (β-CoV) genera, has brought over 181 million confirmed cases and claimed the lives of about 4 million people worldwide [1]. SARS-CoV-2 has a positive-sense, single-stranded genome that encodes a large non-structural polyprotein (ORF1a/b) proteolytically cleaved to generate proteins, four of which are structural proteins including spike (S), envelope (E), membrane (M), and nucleocapsid (N) (Figure 1a) [2,3]. Among these proteins, the S surface glycoprotein plays a critical role in receptor recognition and attachment to host cells [4]. The S protein also induces T-cell responses and is the main target of highly potent neutralizing antibodies (nAbs) against the virus, presenting it as the major antigenic pick out for vaccine design [5]. The structure of SARS-CoV-2 is similar to other β-CoVs, including the severe acute respiratory syndrome coronavirus (SARS-CoV) and the Middle Eastern respiratory syndrome-related coronavirus (MERS-CoV), the causative agents of SARS and MERS, two previously reported viral pneumonia disease outbreaks, respectively [6]. Compared to SARS-CoV and MERS-CoV, however, SARS-CoV-2 has higher infectivity and transmissibility due to its high-affinity binding to the host cell receptors and high viral shedding levels during the early stage of infection, contributing...
As initial measures to control the disease spread, the COVID-19 pandemic was primarily withstood through social distancing, hygiene measures, and repurposed drugs [10]. Some countries’ implemented measures were relatively emollient and particularly designated to control the disease by achieving herd immunity following natural infection [11,12].

Therefore, despite the taken measures and as a consequence of not implementing immediate lockdown, the COVID-19 death toll increased [13,14]. This necessitated the development of an effective and safe vaccine as an imperative solution to control the pandemic and prevent future outbreaks [13,15]. As such, and since the release of the SARS-CoV-2 genome sequence in January 2020, all efforts have been directed towards COVID-19 vaccines development [16,17]. The hope and hype placed on vaccines to prevail over the disease stand up from the success of previously developed vaccines to control other infectious diseases [13]. The route for vaccine development; however, was not always paved, and several historical attempts of vaccines production were doomed with defeats [18].
scientists are still unable to conclude the safest and most effective vaccine platform [18].
Back in time, particularly following the outbreak of SARS-CoV in 2002, vaccines against the emerging virus were also developed, a few of which reached phase I clinical trials; yet, did not achieve the final stages and obtain the United States Food and Drug Administration (FDA) approval as the virus was eradicated from the human population in 2004 [16,19–21]. Similarly, several vaccines against MERS-CoV were under development, none of which have obtained FDA approved thus far [21]. Within the same notion, and in relay for safe and effective COVID-19 vaccine production, censornous steps are currently followed in all phases of COVID-19 vaccine development, including manufacturing, dispersal, and vaccination [22]. For the time being, many of the newly developed COVID-19 vaccines are undergoing clinical evaluation and have reached phase III of clinical trials. A few of which have been approved for emergency use [13] (Figure 2a, Table 1), with the research and discovery phase being skipped [21,23]. Several approaches, including traditional platforms (inactivated and live attenuated virus vaccines), and newly established ones (replicating and non-replicating viral vector vaccines, nucleic acid (DNA and RNA) vaccines, recombinant subunit vaccines, and peptide-based/virus-like particles vaccines), have been adopted for COVID-19 vaccine development (Figure 1b–h) [16,24,25]. As of 29 June 2021, and according to the World Health Organization (WHO), out of the 293 total COVID-19 vaccine candidates, 105 are currently in the clinical phase of development and 184 are still in the pre-clinical phase (Figure 2a) [26]. Presently, and besides the FDA consideration of the possibility of booster vaccine shots, several standpoints are now advocating the notion that ‘hybrid immunity’ and “the mix and match of different vaccines strategy” could provide an even stronger immune boost, presenting such approaches, if supported by data, as plausible pandemic game-changers. In this review, we detail the different COVID-19 vaccine platforms and highlight their strengths, limitations, and major risks and safety concerns associated with each type, particularly those relevant to the fast-track pace taken for their production. We also summarize all candidate COVID-19 vaccines currently in the clinical phase of development and categorize them according to the platform used for their development.
Figure 2. Phases of COVID-19 vaccine development. (a) The total number of currently available COVID-19 vaccine candidates in the pre-clinical and clinical phases of development. (b) Number of developed COVID-19 vaccine candidates per vaccine platform. Data was retrieved from the World Health Organization (WHO) vaccine tracker and landscape website [26] on 29 June 2021. N.B. The reported numbers are subject to change with time given the current efforts and pace of COVID-19 vaccines development. EU: emergency use, FDA: food and drug administration, EUA: emergency use authorization. The figure and table were created with BioRender.com.

2. Contemporary COVID-19 Vaccine Platforms and Allied Safety and Efficacy Concerns

2.1. Inactivated Vaccine

Purified inactivated viruses have been widely used for over a century in vaccine development against various emerging infectious diseases, including influenza, polio, rabies, and hepatitis A [27–31]. Today, inactivated vaccines are typically produced by propagating the virus in cell culture systems, followed by purification, concentration, and chemical and/or physical inactivation to demolish infectivity while retaining immunogenicity (Figure 1b) [32,33]. This type of vaccine is notably featured by its highly efficient proliferation and genetic stability [34]; yet, limited by the viral yield in a cell culture setting, the requirement of a biosafety level 3 facility, and the short duration of the elicited immune response, possibly making the vaccines less effective in preventing viral entry [33,35]. Up to date, 16 inactivated SARS-CoV-2 vaccines have been developed and are currently in clinical trial phases (Figure 2b) [26]. One of which, for example, is the Sinovac’s CoronaVac vaccine candidate which has demonstrated sufficient safety and efficacy in phase III of clinical trials in Brazil, Turkey, and Indonesia and is currently in phase IV of clinical trials (Table 1) [26,34,36–39]. Another is the BBIBP-CorV vaccine candidate, which showed adequate humoral immune responses in adults aged 18 years and above and currently stands
Vaccines have been listed by the WHO for COVID-19 Emergency Use (EUL) and are presently being adopted by several countries worldwide. Despite these promising data, concerns of using inactivated virus vaccines platforms against COVID-19 still reside, some of which relate to the difficulty of confirming a complete virus inactivation status, a risk that could translate into a scenario similar to the 1955 Cutter incident where children receiving the polio vaccine were infected with the inactivated poliovirus [33,42]. Into the bargain, although several developed inactivated SARS-CoV vaccines have been reported to induce nAbs, vaccinated animals still display significant disease upon challenge, which could explain why no vaccines are currently licensed for SARS-CoV [43]. Further, previous studies on animal models have shown that immunizations with inactivated SARS-CoV and MERS-CoV vaccines are associated with hypersensitive-type lung pathology post-challenges with the infectious virus [32,44–46]. Similarly, respiratory syncytial virus (RSV) formalin-inactivated vaccine has been reported to cause enhanced pulmonary disease after live RSV infection [47,48]. In addition, it was suggested that treating the vaccine with formalin could have altered the epitopes, inducing functional antibodies, causing the immune system to produce antibodies against non-protective epitopes [33,49]. It is worth noting here that none of these concerns and/or complications of using inactivated virus vaccines have been thus far reported from the use of recently developed COVID-19 inactivated vaccines.

2.2. Live Attenuated Vaccine

Live attenuated vaccines, which embody a weakened version of the live virus with reduced virulence, are considered one of the oldest and most effective immunization approaches to elicit life-long immune responses (Figure 1c) [32,50]. A remarkable advantage of such a vaccine type is its relatively low production and delivery costs, given that the attenuated virus can replicate and propagate within the host. As such, a relatively small dose of the virus can be enough to induce immunity [51]. Moreover, live attenuated vaccines can be given intranasally, allowing the attenuated virus to replicate in the mucosal tissue of the upper respiratory tract, a major portal for coronaviruses entry into the host [52]. For the time being, only six SARS-CoV-2 live attenuated virus vaccines have been developed, four of which are in the pre-clinical phase, and two are in phase I of clinical trials (Figure 2b, Table 1) [26]. Both COVI-VAC and MV-014-212 vaccines are attenuated via codon pair de-optimization, a strategy that involves synthetic recoding of the viral genome by amending the positions of synonymous codons, thereby raising the number of suboptimal codon pairs and cytosine phosphoguanine (CpG) dinucleotides in the recoded genome [25,53–55]. In parallel to live attenuated SARS-CoV-2 vaccine studies, ongoing studies on other live attenuated virus vaccines such as the RSV vaccine have shown success in using the codon pair deoptimization strategy in vaccine production evidenced by the robust humoral and cellular immune responses triggered in non-human primates [56].

Despite the aforementioned advantages and the pulled off accomplishments of using live attenuated virus vaccine in combating different infectious diseases, the overt risk of using such a type of vaccine still resides in the use of a live replicating virus, which can revert under any condition to its pathologic phenotype, causing disease after vaccination, especially in immunocompromised individuals [57,58]. Although this anticipated scenario is considered relatively rare, the degree of unpredictability regarding the virus stability and the arising safety considerations after that should never be ruled out [59]. Further, live attenuated vaccines could result in viral shedding into the environment, posing a potential risk to the unvaccinated community [60]. It also goes without saying that these highlighted disadvantages are acquainted with time consumption and technical difficulties associated with the virus modification approaches if such a vaccine platform is to be implemented [16].

2.3. Viral Vector Vaccine

Viral vector vaccines, in both replicating and non-replicating forms, utilize modified viruses such as adenoviruses or poxviruses as the vector to deliver the genetic material
coding for a viral antigen of interest into the host cell (Figure 1d) [57,61]. In self-replicating (replication-competent) viral vector-based vaccines, and through the host cell machinery used by the virus vector, new viral particles are produced in infected cells, which then infect other new cells, resulting in additional vaccine antigen production [62]. On the contrary, non-replicating (replication-incompetent or deficient) viral vector-based vaccines cannot produce new viral particles, and the host cell machinery is used to produce the vaccine antigens, after which the viral vector gets cleared [61,62]. Both viral vector vaccine forms do not cause infection from neither the loaded virus nor the viral vector as the delivered genetic material does not become integrated into the host genome [61,63]. Typically, the advantage of this type of vaccine lies in promoting the expression of viral antigens within infected host cells for efficient major histocompatibility complex (MHC) class I and class II presentation [61]. Moreover, viral vectors are characterized by their high gene transduction efficiency, high specificity of genes delivered to target cells, and the immune response they elicit with increased cellular response [64]. Further, although viral vector vaccines are generally considered less robust than traditional vaccine types, the fact that they persist as genetic material in the host, directly infect antigen-presenting cells, and possess a strong inherent adjuvant activity triggering innate and adaptive immune responses and generating high titers of nAbs, could suffice a single vaccine dose for adequate immunization as in the case of the vesicular-stomatitis virus (VSV)-based Ervebo vaccine against Ebola virus [62,63,65].

In COVID-19 vector-based vaccine production, replicating and non-replicating vectors have been utilized to deliver genes encoding for either the SARS-CoV-2 S glycoprotein or the receptor-binding domain (RBD) [16,26]. Thus far, vaccinia and adenovirus are the predominantly used virus vectors for vectored vaccines development [64]. The adenovirus, for example, has been previously utilized in developing SARS-CoV VectoCoV expressing the S and N proteins [32,43,66]. Currently, it is also being used for developing COVID-19 vector-based vaccines. Up to date, 4 replicating and 17 non-replicating COVID-19 vector-based vaccines have been developed, of which 2 have reached phase III clinical trials, and 3 are currently in phase IV (Table 1, Figure 2b) [26]. All five vaccines are adenovirus-based non-replicating vaccines containing the gene encoding for SARS-CoV-2 S glycoprotein [67–70]. Among these vaccines, Janssen’s (Ad26.COV2.S) vaccine has recently received the FDA EUA for use in in 18 years old and elder individuals after showing good efficacy data in phase III of clinical trials [71]. Although the Ad26.COV2.S vaccine showed around 65–66% efficacy in moderate to severe/critical and around 76–83% in severe/critical COVID-19 patients, its efficacy dropped to 52 and 64% against the Beta (B.1.351) variant in moderate to severe/critical disease conditions, respectively [69] (Table 1). Low efficacy data were also reported for AstraZeneca vaccine against the Beta variant, with an efficiency of 10.4% only reported in South Africa and 48% in Canada [72,73], contrarily to the 70.4% retained efficacy against the Alpha (B.1.1.7) variant as reported in a study conducted in the UK [74].

The other three viral vector vaccines at stages II/III–IV of clinical development are CanSino’s adenovirus type-5 (Ad5) vectored vaccine, Gamaleya Research Institute’s Gam-COVID-Vac vaccine, and ReiThera’s GRAd-COV2 (Table 1). Although clinical trials have revealed that these vaccines are tolerable and immunogenic, age and the presence of high pre-existing anti adenovirus immunity were shown to partly diminish vaccination-induced specific antibody and T-cell responses [68]. To overcome pre-existing immunity to the adenovirus in vaccinated individuals, a plausible approach could be using a heterologous recombinant vector as in the Gam-COVID-Vac (Sputnik V) vaccine, the only heterologous COVID-19 vaccine that uses both adenovirus 26 (Ad26) and adenovirus 5 (Ad5) as vectors to express the SARS-CoV-2 S protein [70,75]. Of note, the general principle of prime-boost with two distinct vectors was not exclusively used in recent COVID-19 vaccine platforms but has been largely implemented experimentally and was also previously used in developing the GamEvac-Combi Ebola virus vaccine [76].
2.4. Nucleic Acid (DNA and RNA)-Based Vaccine

In nucleic acid-based vaccines, only the genetic material (DNA or RNA), but not the recombinant/live virus, is taken up by host cells and translated into the protein to elicit an immune response (Figure 1e,f) [77]. Although various messenger RNA (mRNA) vaccines, including those against influenza, Zika, and rabies viruses, have been thus far developed, this vaccine development platform is still considered relatively new [78]. The pronounced advantage of some types of nucleic acid vaccines generally lies in the large-scale production pace and cost [16]. DNA vaccines, for example, are based on the use of highly stable plasmid DNA that can be easily propagated at a large scale in bacteria, as the plasmid DNA typically encloses mammalian expression promoters and the gene encoding the protein of interest [16]. On the other hand, presenting mRNA vaccines as promising alternatives for conventional vaccines mainly lies in the ability to produce the vaccine completely in vivo, along with their high potency, cost-effectiveness, rapid development, and safe delivery [16,78,79]. Currently, lipid nanoparticles (LNPs) are among the most commonly used in vivo RNA delivery vectors, protecting the mRNA from enzymatic degradation and facilitating endocytosis and endosomal escape [80]. Contrarily to the highlighted recognition of mRNA vaccines, the physiochemical properties of the mRNA that may impact its cellular and organ dispersal, the questioned safety and efficacy of mRNA vaccine use in humans, them being unlikely to induce strong mucosal immunity due to their intramuscular administration, and the uncertainty from what could arise with large-scale production, storage, and stability are among the alarming concerns tailored to mRNA vaccines production [16,57,80]. Likewise, potential disadvantages also relate to DNA vaccines, particularly those relevant to their low immunogenicity and to the need of DNA molecules to traverse the nuclear membrane to be transcribed, necessitating complicated delivery systems such as electroporators for better efficiency [16,57]. In addition, introducing mutation and dysregulated gene expression by the plausible stable integration of transfected DNA into the somatic or germline host cells genome is another arising concern [81] though unconventional as per relevant follow-up studies [82–85]. Up to date, 28 nucleic acids (10 DNA and 18 mRNA)-based COVID-19 vaccines have been developed and are currently in the clinical stages, and 24 mRNA vaccines are in the pre-clinical stage (Figure 2b, Table 1) [26]. Two mRNA-based vaccines, developed by Pfizer/BioNTech and Moderna, are currently in phase IV clinical trials and have received the FDA EUA for protection against COVID-19 [26,86,87]. Preliminary results showed astoundingly 94–95% efficacy for both vaccines [88,89]. Though promising, a major concern relevant to mRNA vaccines resides in their rapid pace of development and the uncertainty of potential long-term adverse effects associated with them, particularly because these are the first approved mRNA vaccines with no other FDA-approved mRNA vaccines to date [90]. Another concern is the efficacy of these vaccines against the newly emerging SARS-CoV-2 variants with mutations in the S protein, the main target in COVID-19 vaccines development [91]. As of yet, Pfizer/BioNTech COVID-19 vaccine was reported to protect against four variants of concern (VOCs), including Alpha, Beta, Gamma, and Delta (Table 1) [91–94]. Interestingly, a recent study by Zakhartchouk et al. reported that combining DNA vaccine and whole killed virus vaccines augments immune responses to SARS-CoV [95], a propitious tactic worth considering in ongoing COVID-19 vaccine development approaches [95].

2.5. Protein Subunit and Virus-Like Particles Vaccine

As compared to the whole-pathogen vaccine platform, a protein subunit vaccine is composed of in vitro harvested and highly purified viral protein antigens carefully chosen for their ability to elicit an immune response (Figure 1g) [96]. Being incapable of causing disease, the protein subunit vaccine platform is considered safer than the whole-virus (live attenuated and inactivated) platforms [97]. Not displaying the full antigenic complexity of the virus and enclosing small antigens deficient of pathogen-associated molecular patterns (PAMPs); however, it may promote skewed immune responses, bringing the immunogenicity potential and protective efficacy of protein subunit vaccines into question [57,97].
Subunit vaccine design and production could be also costly and might necessitate specific adjuvants to boost the immune response [98], in addition to the potential occurrence of antigen denaturation, which could lead to non-specific binding [99]. Examples of developed subunit vaccines include the recombinant RBD subunit vaccine, which was reported to elicit partial protective immunity in rhesus macaques against MERS-CoV challenge [100], and S protein-based subunit vaccines against SARS-CoV infection with potency to induce nAbs and protect against SARS-CoV intranasal infection in mice [32,101]. Up to date, 33 COVID-19 protein subunit vaccines based on the S protein or the RBD have been developed and are in the clinical stages. Of which, 10 vaccines, including Novavax’s (NVX-CoV2373) are in phase III [26,102]. Recent reports showed that a two-dose regimen of the NVX-CoV2373 vaccine exhibited 89.7% efficacy against SARS-CoV-2 infection, with high efficacy against the Alpha, Beta, and other VOCs [102,103] (Table 1). Virus-like particles (VLPs) vaccine is another type of protein-based vaccine composed of proteins from the viral capsid only with no viral genetic material (Figure 1h) [57,104]. In addition to being safe, VLPs elicit potent immune responses due to their repetitive structures [104]. VLP vaccines against many viruses, including Hepatitis B virus, Human papillomaviruses, and Influenza A virus, do exist [104–107]. Likewise, VLP vaccines against MERS-CoV and SARS-CoV infection have been also developed, with eosinophilic pulmonary immunopathology detected after viral challenge in some cases [21,46,108]. For the COVID-19 status quo particularly, five VLPs vaccines in different phases of clinical trials are thus far available (Figure 2b, Table 1) [26].
| Platform/Vaccine Type | No. | Vaccine Name       | Number of Doses (Dosage) | Dosing Schedule | Route of Administration | Developer/Manufacturer                                                                 | Current Stage of Clinical Trial (Recruitment Status)                     | Efficacy *                                                                 | Current Approvals/Authorizations                          | Reference |
|-----------------------|-----|--------------------|--------------------------|-----------------|-------------------------|----------------------------------------------------------------------------------------|--------------------------------------------------------------------------|-------------------------------------------------------------------------|---------------------------------------------|-----------|
| Inactivated virus     | 1   | CoronaVac          | 2 doses (3 µg)           | Day 0 + 14      | IM                      | Sinovac Research and Development Co., Ltd. Whole inactivated SARS-CoV-2 with aluminum hydroxide adjuvant | Phase IV (Not yet recruiting)                                           | Efficacy from clinical trials: Brazil: 50.7% against symptomatic disease ≥14 d after 2 doses. Turkey: 83.5% against symptomatic disease ≥14 d after 2 doses. Indonesia: 65.3% against symptomatic disease ≥14 d after 2 doses. Efficacy/effectiveness against variants: Chile (predominant circulation of P.1 and B.1.1.7.): 67% against symptomatic disease ≥28 d after 2 doses. Brazil (predominant circulation of P.2 and P.1 lineages): 50.7% and 36.8% against symptomatic disease ≥14 d after 2 doses, respectively. | WHO EUL Approved in 37 countries 1 [26,36–38,109–112] |
| Inactivated virus     | 2   | BBIBP-CorV         | 2 doses (4 µg)           | Day 0 + 21      | IM                      | Sinopharm + China National Biotec Group Co + Beijing Institute of Biological Products Whole inactivated SARS-CoV-2 | Phase IV (Recruiting)                                                  | Efficacy from clinical trials in UAE, Bahrain, Egypt, and Jordan: 78.1% against symptomatic disease ≥14 d after 2 doses, and 79% against hospitalization. | WHO EUL Approved in 56 countries 2 [26,34,39,41,110,113] |
| Inactivated virus     | 3   | Inactivated SARS-CoV-2 vaccine (Vero cell) | 2–3 doses (5 µg) | Day 0 + 21 + 42 or 111 or 171 | IM                      | Sinopharm + China National Biotec Group Co + Wuhan Institute of Biological Products Whole inactivated SARS-CoV-2 with aluminum hydroxide adjuvant | Phase III (Completed)                                                   | Efficacy from clinical trials in UAE, Bahrain, Egypt, and Jordan: 72.8% against symptomatic disease ≥14 d after 2 doses, and 79% against hospitalization. | WHO EUL (Approval pending China) [26,40,110,114,115] |
| Platform/Vaccine Type | No. | Vaccine Name | Number of Doses (Dosage) | Dosing Schedule | Route of Administration | Developer/Manufacturer | Construct and/or Targeted SARS-CoV-2 Protein | Current Stage of Clinical Trial (Recruitment Status) | Efficacy * | Current Approvals/Authorizations | Reference |
|-----------------------|-----|--------------|-------------------------|-----------------|-------------------------|-----------------------|---------------------------------------------|-----------------------------------------------|--------|--------------------------------|----------|
| Inactivated virus     | 4   | Inactivated SARS-CoV-2 vaccine (Vero cell) | 2 doses (50, 100, or 150 EU) | Day 0 + 14 | IM | Institute of Medical Biology + Chinese Academy of Medical Sciences | Whole inactivated SARS-CoV-2 with Al(OH)3 adjuvant | Phase III (Enrolling by invitation) | NR | Not yet approved in any country | [26,116,117] |
| Inactivated virus     | 5   | QazCovid-in | 2 doses | Day 0 + 21 | IM | Research Institute for Biological Safety Problems, Rep of Kazakhstan | Whole inactivated SARS-CoV-2 | Phase III (Active, not recruiting) | Efficacy from clinical trials in the Republic of Kazakhstan: 96% | Republic of Kazakhstan | [26,118,119] |
| Inactivated virus     | 6   | BBV152 (COV-AXIN) | 2 doses (3 or 6 µg) | Day 0 + 14 | IM | Bharat Biotech International Limited | Whole inactivated SARS-CoV-2 with Algel-IMDG adjuvant | Phase III (Active, not recruiting) | Efficacy from clinical trials: 77.8% against symptomatic disease, 93.4% against severe disease, 63.6% against asymptomatic disease. Efficacy/effectiveness against variants: 65.2% against disease caused by Delta (B.617.2) variant. | WHO EUL (Approval pending) Approved in 9 countries | [26,110,120–123] |
| Inactivated virus     | 7   | Inactivated SARS-CoV-2 vaccine (Vero cell) | 2 doses | Day 0 + 28 | IM | Shenzhen Kangtai Biological Products Co., Ltd. | Whole inactivated SARS-CoV-2 | Phase III (Not yet recruiting) | NR | China | [26,124] |
| Inactivated virus     | 8   | VLA2001 | 2 doses | Day 0 + 21 | IM | Valneva, National Institute for Health Research, United Kingdom | Whole inactivated SARS-CoV-2 with high S-protein density, in combination with two adjuvants, alum and CpG 1018 | Phase III (Not yet recruiting) | NR | Not yet approved in any country | [26,125] |
Table 1. Cont.

| Platform/Vaccine Type | No. | Vaccine Name | Number of Doses (Dosage) | Dosing Schedule | Route of Administration | Developer/Manufacturer | Construct and/or Targeted SARS-CoV-2 Protein | Current Stage of Clinical Trial (Recruitment Status) | Efficacy * | Current Approvals/Authorizations | Reference |
|-----------------------|-----|--------------|--------------------------|----------------|--------------------------|------------------------|-----------------------------------------------|-----------------------------------------------|-----------|--------------------------------|-----------|
| Inactivated virus     | 9   | ERUCOV-VAC (TURKO-VAC) | 2 doses (3 µg) | Day 0 + 28 | IM | Erciyes University + Health Institutes of Turkey | Whole inactivated SARS-CoV-2 | Phase III (Recruiting) | NR | Not yet approved in any country | [26,126] |
| Inactivated virus     | 10  | COVID-19 inactivated vaccine | 2 doses (5 µg) | Day 0 + 28 | IM | Shifa Pharmed Industrial Co | Whole inactivated SARS-CoV-2 | Phase II-III (Recruitment complete) | NR | Iran | [26,127] |
| Inactivated virus     | 11  | FAKHRAVAC (MFVAC) | 2 doses (10 µg) | Day 0 + 14 | IM | Organization of Defensive Innovation and Research | Whole inactivated SARS-CoV-2 | Phase II (Recruiting) | NR | Not yet approved in any country | [26,128] |
| Inactivated virus     | 12  | Inactivated (NDV-based) chimeric vaccine | 2 doses | Day 0 + 28 | IM | The Government Pharmaceutical Organization (GPO) + PATH + Dynavax | Whole inactivated NDV chimera stably expressing membrane-anchored SARS-CoV-2 S protein +/- Cpg 1018 adjuvant | Phase I-II (NR) | NR | Not yet approved in any country | [26,129] |
| Inactivated virus     | 13  | KD-414 | 2 doses | Day 0 + 28 | IM | KM Biologics Co., Ltd. | Whole inactivated SARS-CoV-2 | Phase I-II (Not Recruiting) | NR | Not yet approved in any country | [26,130] |
| Inactivated virus     | 14  | Koçak-19 | 2 doses (4 or 6 µg) | Day 0 + 21 | IM | Kocak Farma, Turkey | Whole inactivated SARS-CoV-2 with adjuvant | Phase I (Recruiting) | NR | Not yet approved in any country | [26,131] |
| Inactivated virus     | 15  | Adjuvanted inactivated vaccine | 2 doses (10 µg-3M or 20 µg-6M) | Day 0 + 20 | SC | The Scientific and Technological Research Council of Turkey (TÜBİTAK) | Whole inactivated SARS-CoV-2 with CpG ODN adjuvant | Phase I (Recruiting) | NR | Not yet approved in any country | [26,132] |
| Inactivated virus     | 16  | Live recombinant (rNDV) vector vaccine | 2 doses | Day 0 + 21 | IM or IN | Laboratorio Avi-Mex | Live recombinant NDV vector expressing SARS-CoV-2 S protein | Phase I (Recruiting) | NR | Not yet approved in any country | [26,133] |
## Table 1. Cont.

| Platform/Vaccine Type | No. | Vaccine Name | Number of Doses (Dosage) | Dosing Schedule | Route of Administration | Developer/Manufacturer | Construct and/or Targeted SARS-CoV-2 Protein | Current Stage of Clinical Trial (Recruitment Status) | Efficacy * | Current Approvals/Authorizations | Reference |
|-----------------------|-----|--------------|--------------------------|-----------------|-------------------------|------------------------|----------------------------------------------|--------------------------------|-------------------|----------------|----------------|
| Live-attenuated virus | 1   | COVI-VAC     | 1–2 doses                | Day 0 or Day 0 + 28 | IN                      | Codagenix, Inc + Serum Institute of India Meissa Vaccines, Inc. | Whole SARS-CoV-2 with all viral proteins | Phase I (Active, not recruiting) | NR              | Not yet approved in any country | [26,134] |
| Live-attenuated virus | 2   | MV-014-212   | 1 dose                   | Day 0            | IN                      | Meissa Vaccines, Inc. | RSV expressing SARS-CoV-2 S protein            | Phase I (Recruiting)                      | NR              | Not yet approved in any country | [26,55,135] |
| Viral vector (non-replicating) | 1   | ChAdOx1 AZD1222 | 2 doses                  | Day 0 + 28       | IM                      | AstraZeneca + University of Oxford | Chimpanzee adenovirus-vectored vaccine (ChAdOx1) expressing S protein | Phase IV (Recruiting) | Efficacy from clinical trials in UK: Brazil, and South Africa: 66.7%–70.4% overall efficacy ≥ 14 d after 2 doses, 62.1% after 2 standard doses 76.0% after single low dose within 20–90 d, 90.0% after one low dose and one standard dose. **Real-world effectiveness:** England: 68–75% after 1 dose. Scotland: 88% against hospitalization 28–34 d after 1 dose. U.S: 76% in adults, and 85% in elderly (≥ 65 y). **Efficacy/effectiveness against variants:** UK: 70.4% against Alpha (B.1.1.7) variant, 81.5% against non-B.1.1.7 lineages. South Africa: 10.4% against Beta (B.1.351) variant. England: 76.0% after 1 dose, 86.0% after 2 doses against Beta variant. 71.0% after 1 dose, 92.0% after 2 doses against Delta variant. Canada: 68% ≥ 14 d after dose 1 against symptomatic infection caused by Alpha variant. 48% ≥ 14 d after 1 dose against symptomatic infection caused by Beta or Gamma (P.1) variants. 67% ≥ 14 d after 1 dose against symptomatic infection caused by Delta variant. | WHO EUL Approved in 118 countries and issued an Endorsed by ART CARPHA EU recommendation EMA approved | [67,72–74,90,110,136–145] |
| Platform/Vaccine Type | No. | Vaccine Name | Number of Doses (Dosage) | Dosing Schedule | Route of Administration | Developer/Manufacturer | Construct and/or Targeted SARS-CoV-2 Protein | Current Stage of Clinical Trial (Recruitment Status) | Efficacy * | Current Approvals/Authorizations | Reference |
|-----------------------|-----|--------------|--------------------------|----------------|-------------------------|-----------------------|-----------------------------------------------|-----------------------------------------------|-----------|----------------------------------|-----------|
| Viral vector (non-replicating) | 2   | Convidicea (Ad5-nCoV) | 1 dose (5 × 10^10 viral particles per dose) | Day 0 | IM | CanSino Biological Inc. + Beijing Institute of Biotechnology | Recombinant replication-defective human type 5 adenovirus (Ad5) expressing S protein | Phase IV (Active, not recruiting) | Efficacy from clinical trials in Pakistan, Russia, Argentina, Mexico, and Chile: 68.8% and 65.7% against symptomatic disease ≥14 d and ≥28 d after vaccination, respectively. 95.5% and 91.0% against severe disease ≥14 d and ≥28 d after vaccination, respectively. Efficacy from clinical trials in Argentina, Brazil, Chile, Colombia, Mexico, Peru, South Africa, and the U.S: 66.3-76.3% and 65.5-83.5% against moderate to severe/critical disease ≥14 d and ≥28 d after vaccination, respectively. Real-world efficacy: U.S. and India: 76.7% against infection ≥14 d after vaccination. Efficacy/effectiveness against variants: South Africa (95% predominant B.1.351 variant): 52.0–73.1% and 64.0–81.7% against moderate to severe/critical disease ≥14 d and ≥28 d after vaccination, respectively. Brazil (69% predominant P2 lineages): 66.2–68.1% and 81.9–87.6% against moderate to severe/critical disease ≥14 d and ≥28 d after vaccination, respectively. | WHO EUL (Approval pending) | Approved in 8 countries 5 | [26,110,146–151] |
| Viral vector (non-replicating) | 3   | Ad26.COV2. | 1 dose (5 × 10^10 viral particles per dose) | Day 0 | IM | Janssen Pharmaceutical | Recombinant replication-incompetent adenovirus serotype 26 (Ad26) vector encoding full-length and stabilized S protein | Phase IV (NR) | | FDA EUA WHO EUL | Approved in 55 countries 6 Endorsed by ART EMA approved | [26,69,71,110,145,152,153] |
| Viral vector (non-replicating) | 4   | Gam-COVID-Vac (Sputnik V) | 2 doses (1 × 10^11 viral particles per dose) | Day 0 + 21 | IM | Gamaleya Research Institute + Health Ministry of the Russian Federation ReiThera + Leukocare + Univercells | Recombinant Ad26 and recombinant Ad5 encoding full-length S protein (rAd26-S and rAd5-S) | Phase III (Active, not recruiting) | Efficacy from clinical trials: 91.6% overall efficacy against symptomatic disease, 100% against moderate-severe disease, 73.1% after 1 dose, 91.1% after 2 doses. Efficacy/effectiveness against variants: 90% against Delta variant. | WHO EUL (Approval pending) | Approved in 69 countries 7 | [26,110,154–157] |
| Viral vector (non-replicating) | 5   | GRAd-COV2 | 1–2 doses (1 × 10^11 viral particles per dose) | Day 0 + 21 | IM | | Replication defective Simian Adenovirus (GRAd) encoding S protein | Phase II–III (Active, not recruiting) | | Not yet approved in any country | | [26,158–160] |
Table 1. Cont.

| Platform/Vaccine Type | No. | Vaccine Name | Number of Doses (Dosage) | Dosing Schedule | Route of Administration | Developer/Manufacturer | Construct and/or Targeted SARS-CoV-2 Protein | Current Stage of Clinical Trial (Recruitment Status) | Efficacy * | Current Approvals/Authorizations | Reference |
|-----------------------|-----|--------------|--------------------------|-----------------|-------------------------|-----------------------|-------------------------------------------|-----------------------------------------------|-----------|-------------------------------|-----------|
| Viral vector (non-replicating) | 6   | LV-SMENP-DC  | 1 dose ($5 \times 10^8$ cells of LV-DC vaccine and $1 \times 10^9$ antigen-specific CTLs) | Day 0 | SC (LV-DC vaccine) and IV (antigen-specific CTLs) | Shenzhen Geno-Immune Medical Institute | Modified dendritic cells (DC) with lentivirus vectors (LV) expressing minigenes SMENP and immune-modulatory genes. Cytotoxic T-cells (CTLs) are activated by LV-DC, presenting specific viral antigens | Phase I–II (Recruiting) | NR | Not yet approved in any country | [26,161] |
| Viral vector (non-replicating) | 7   | hAd5-S-Fusion + N-ETSD vaccine | 1 dose ($5 \times 10^{10}$ IU/ dose SC, $1 \times 10^{10}$ IU/ dose SL) | Day 0 | SC, oral, or SL | ImmunityBio, Inc. + NantKwest, Inc. | Human second-generation adenovirus 5 (hAd5) encoding S and N antigens | Phase I–II (Not recruiting) | NR | Not yet approved in any country | [26,162–164] |
| Viral vector (non-replicating) | 8   | AdCLD-CoV19  | 1 dose ($2.5 \times 10^{10}$, $5 \times 10^{10}$, or $1 \times 10^{11}$ virus particles per dose) | Day 0 | IM | Cellid Co., Ltd. | Replication-defective human adenovirus type 5/35 vector expressing S protein NDV expressing membrane-anchored pre-fusion-stabilized trimeric S protein +/− CpG 1018 adjuvant | Phase I–II (Recruiting) | NR | Not yet approved in any country | [26,165] |
| Viral vector (non-replicating) | 9   | COVIVAC      | 2 doses ($1 \times 10^7$ IU, $5 \times 10^7$ IU, or $1 \times 10^8$ IU per dose) | Day 0 + 28 | IM | Institute of Vaccines and Medical Biologicals, Vietnam | | Phase I–II (Recruiting) | NR | Not yet approved in any country | [26,166] |
| Viral vector (non-replicating) | 10  | MVA-SARS-2-ST | 2 doses ($1 \times 10^7$ IU, or $1 \times 10^8$ IU per dose) | Day 0 + 28 | IM | Universitätshilsklinikum Hamburg-Eppendorf + German Center for Infection Research | MVA vector expressing stabilized S protein | Phase I–II (Not recruiting) | NR | Not yet approved in any country | [26,167] |
| Viral vector (non-replicating) | 11  | MVA-SARS-2-S | 2 doses ($1 \times 10^7$ IU, or $1 \times 10^8$ IU per dose) | Day 0 + 28 | IM | University of Munich (Ludwig-Maximilians) | MVA vector expressing S protein | Phase I (Recruiting) | NR | Not yet approved in any country | [26,168] |
| Viral vector (non-replicating) | 12  | VXA-CoV2-1   | 1–2 doses ($1 \times 10^{10}$ IU, or $1 \times 10^{11}$ IU per dose) | Day 0 or Day 0 + 28 | Oral | Vaxart | Non-replicating adenovirus vector expressing viral antigens and dsRNA adjuvant | Phase I (Active, not recruiting) | NR | Not yet approved in any country | [26,169,170] |
| Viral vector (non-replicating) | 13  | AdCOVID, 1   | 1–2 doses | Day 0 + NR | IN | Alimmune, Inc. | Adenovirus expressing the RBD of S protein | Phase I (Recruiting) | NR | Not yet approved in any country | [26,171] |
| Platform/Vaccine Type | No. | Vaccine Name | Number of Doses (Dosage) | Dosing Schedule | Developer/Manufacturer | Construct and/or Targeted SARS-CoV-2 Protein | Current Stage of Clinical Trial (Recruitment Status) | Efficacy * | Current Approvals/Authorizations | Reference |
|-----------------------|-----|--------------|--------------------------|----------------|------------------------|----------------------------------------------|-------------------------------------------------|-----------|-------------------------------|-----------|
| Viral vector (non-replicating) | 14  | COH04S1 (MVA-SARS-2-S) | 2 doses (1 × 10⁷, 1 × 10⁸, or 2.5 × 10⁹ PFU per dose) | Day 0 + 28 | City of Hope Medical Center + National Cancer Institute Gritstone Oncology | Synthetic MVA carrying small pieces of SARS-CoV-2 DNA (the chemical form of genes) Chimpanzee Adenovirus serotype 68 (ChAd) and self-amplifying mRNA (SAM) vectors expressing either S protein alone, or S protein with additional T-cell epitopes (TCE) | Phase I (Recruiting) | NR | Not yet approved in any country | [26,172] |
| Viral vector (non-replicating) | 15  | ChAdV68-S, ChAdV68-S-TCE (Homologous and heterologous prime-boost schedule) | 2–3 doses (5 × 10¹⁰ or 1 × 10¹¹ viral particles of ChAdV68-S, 10 µg or 30 µg SEM) | Day 0 + 28, or Day 0 + 56, or Day 0 + 112, or Day 0 + 56 + 112 | Gritstone Oncology | Chimpanzee Adenovirus serotype 68 (ChAd) and self-amplifying mRNA (SAM) vectors expressing either S protein alone, or S protein with additional T-cell epitopes (TCE) | Phase I (Recruiting) | NR | Not yet approved in any country | [26,173] |
| Viral vector (non-replicating) | 16  | SC-Ad6-1 | 1–2 doses | Day 0 or Day 0 + 21 | Tetherex Pharmaceuticals Corporation | Adenovirus vector vaccine | Phase I (Not yet recruiting) | NR | Not yet approved in any country | [26,174] |
| Viral vector (non-replicating) | 17  | BBV154 | 1–2 doses (1 × 10¹⁰ viral particles per dose) | Day 0 or Day 0 + 28 | Bharat Biotech International Limited | S protein | Phase I (Active, not recruiting) | NR | Not yet approved in any country | [26,175] |
| Viral vector (replicating) | 18  | DelNS1-2019-nCoV-RBD-OPT1 | 2 doses (1 × 10⁷ EID50 and 1 × 10⁷ EID50) | Day 0 + 28 | University of Hong Kong, Xiamen University + Beijing Wantai Biological Pharmacy | Genetically engineered live attenuated influenza virus vector expressing the RBD of S protein | Phase II (Recruiting) | NR | Not yet approved in any country | [26,176, 177] |
| Viral vector (replicating) | 19  | rVSV-SARS-CoV-2-S Vaccine | 2 doses (1 × 10⁵, 1 × 10⁶, 1 × 10⁷, or 1 × 10⁸ PFU/mL) | Day 0 + 28 | Institute for Biological Research | cDNA vector encoding the sequence of the N, P, M, and L genes of the VSV genome, and SARS-CoV-2 S protein | Phase I–II (Recruiting) | NR | Not yet approved in any country | [26,178] |
| Viral vector (replicating) | 20  | Covid-19/aAPC vaccine | 1 dose (0.1, 0.33, or 1.0 mg) | Day 0 | Aivita Biomedical, Inc. + National Institute of Health Research and Development + Ministry of Health Republic of Indonesia | Autologous dendritic cells loaded with antigens from SARS-CoV-2 +/- GM-CSF | Phase I–II (Not yet recruiting) | NR | Not yet approved in any country | [26,179] |
| Viral vector (replicating) | 21  | Covid-19/aAPC vaccine | 3 doses | Day 0 + 14 + 28 | Shenzhen Gene-Immune Medical Institute | Lentivirus vector system expressing viral minigenes to the artificial antigen-presenting cells (aAPCs) | Phase I (Recruiting) | NR | Not yet approved in any country | [26,180] |
| Platform/Vaccine Type | No. | Vaccine Name | Number of Doses (Dosage) | Dosing Schedule | Route of Administration | Developer/Manufacturer | Construct and/or Targeted SARS-CoV-2 Protein | Current Stage of Clinical Trial (Recruitment Status) | Efficacy * | Current Approvals/Authorizations | Reference |
|-----------------------|-----|--------------|--------------------------|-----------------|-------------------------|-----------------------|---------------------------------|-----------------------------------------------|-----------|----------------------------------|-----------|
| DNA based vaccine     | 1   | nCov vaccine (ZyCoV-D) | 3 doses (1 or 2 mg) | Day 0 + 28 + 56 | ID | Zydus Cadila | S protein | Phase III (Not recruiting) | Efficacy from clinical trials in India: 66.6% | NR       | Not yet approved in any country | [26,81,181,182] |
| DNA based vaccine     | 2   | INO-4800+ electroporation | 2 doses (1 mg) | Day 0 + 28 | ID | Inovio Pharmaceuticals + International Vaccine Institute + Advaccine Biopharmaceutical Co., Ltd. | S1 and S2 subunits of SARS-CoV-2 S protein | Phase II–III (Active, not recruiting) | NR       | Not yet approved in any country | [26,183,184] |
| DNA based vaccine     | 3   | AG0301-COVID19 | 2 doses (2 mg) | Day 0 + 14 | IM | AnGes + Takara Bio + Osaka University | S protein | Phase II–III (Active, not recruiting) | NR       | Not yet approved in any country | [26,185] |
| DNA based vaccine     | 4   | GX-19 | 2 doses | Day 0 + 28 | IM | Genexine Consortium | S protein | Phase I–II (Recruiting) | NR       | Not yet approved in any country | [26,186] |
| DNA based vaccine     | 5   | Covigenix VAX-001 | 2 doses | Day 0 + 14 | IM | Entos Pharmaceuticals Inc. | Full-length S protein | Phase I–II (Recruiting) | NR       | Not yet approved in any country | [26,187] |
| DNA based vaccine     | 6   | GLS-5310 | 2 doses (0.6 or 1.2 mg) | Day 0 + 56 or Day 0 + 84 | ID | GeneOne Life Science, Inc. | S protein and a second antigenic target of SARS-CoV-2 | Phase I–II (Recruiting) | NR       | Not yet approved in any country | [26,188,189] |
| DNA based vaccine     | 7   | COVID-eVax | 2 doses (0.5, 1, or 2 mg) | Day 0 + 28 | IM | Takis + Rottapharm Biotech | RBD of S protein | Phase I–II (Recruiting) | NR       | Not yet approved in any country | [26,190] |
| DNA based vaccine     | 8   | CORVax | 2 doses | Day 0 + 14 | ID | Providence Health and Services | S protein + – the combination of electroporated IL-12p70 plasmid | Phase I (Active, not recruiting) | NR       | Not yet approved in any country | [26,191] |
| DNA based vaccine     | 9   | bacTRL | 1–2 doses | Day 0 or Day 0 + 28 | Oral | Symvivo Corporation | S protein | Phase I (Active, not recruiting) | NR       | Not yet approved in any country | [26,192] |
| DNA based vaccine     | 10  | COVIGEN (COV-ALIA) | 2 doses (0.8, 2, or 4 mg) | Day 0 + 28 | IM or ID | University of Sydney, Bionet Co., Ltd. | S protein | Phase I (Not yet recruiting) | NR       | Not yet approved in any country | [26,193] |
| Platform/Vaccine Type | No. | Vaccine Name | Number of Doses (Dosage) | Dosing Schedule | Route of Administration | Developer/Manufacturer | Construct and/or Targeted SARS-CoV-2 Protein | Current Stage of Clinical Trial (Recruitment Status) | Efficacy | Current Approvals/Authorizations | Reference |
|-----------------------|-----|--------------|--------------------------|-----------------|-------------------------|-----------------------|---------------------------------------------|-----------------------------------------------|----------|---------------------------------|-----------|
| RNA vaccine           | 1   | mRNA-1273    | 2 doses (100 µg)         | Day 0 + 28      | IM                      | Moderna + National Institute of Allergy and Infectious Diseases (NIAID) | Full-length S protein with proline substitutions | Phase IV (Recruiting) | Efficacy from clinical trials in the U.S.: 92.1% against symptomatic disease ≥14 d after 1 dose, 94.1% ≥ 14 d after 2 doses, and 100% against severe disease. Real-world efficacy: U.S.: 80% ≥ 14 d after 1 dose and 90% ≥ 14 d after 2 doses. 83% ≥ 14 d after 1 dose and 82% after 2 doses. 88.7% against infection ≥ 36 d after 1 dose. Canada: 72% against infection after 1 dose and 94% after 2 doses. Efficacy/ effectiveness against variants: Qatar: 88.1% ≥ 14 d after 1 dose, 100% after 2 doses against Alpha variant. 61.3% ≥ 14 d after 1 dose, 96.4% after 2 doses against Betavariant. Canada: 83% ≥ 14 d after 1 dose and 92% ≥ 7 d after 2 doses against symptomatic infection caused by Alpha variant. 77% ≥ 14 d after 1 dose against symptomatic infection caused by Beta or Gammmavariants. 72% ≥ 14 d after 1 dose against symptomatic infection caused by Delta variant. | FDA EUA WHO EUL approved | [26,73,88,92,94,110,137,145,194–198] |
| Platform/Vaccine Type | No. | Vaccine Name | Number of Doses (Dosage) | Dosing Schedule | Route of Administration | Developer/Manufacturer | Construct and/or Targeted SARS-CoV-2 Protein | Current Stage of Clinical Trial (Recruitment Status) | Efficacy * | Current Approvals/Authorizations | Reference |
|-----------------------|-----|-------------|--------------------------|----------------|------------------------|-----------------------|----------------------------------|-----------------------------------------------|------------|--------------------------------|-----------|
| RNA vaccine           | 2   | BNT162b2    | 2 doses (30 µg)          | Day 0 + 21     | IM                     | Pfizer/BioN + Fosun Pharma | Full-length S protein with proline substitutions | Phase IV (Recruiting)                          | Efficacy from clinical trials: 52.4% after 1 dose and 94.6% ≥ 7 d after 2 doses in adults. Real-world efficacy: England: 60-70% against infection after 1 dose, 85-90% after 2 doses in elderly (≥80 y). 72% against infection ≥21 d after 1 dose, and 86% ≥ 7 d after 2 doses. 91% against infection 15–28 d after 1 dose. UK: 70% ≥ 21 d after 1 dose, 85% ≥ 7 d after 2 doses. Denmark: 17% ≥ 14 d after 1 dose, 64–90% ≥ 7 d after 2 doses. Scotland: 91% against hospitalization 28–34 d after 1 dose. U.S.: 80% ≥ 14 d after 1 dose, 93% ≥ 14 d after 2 doses. 88.7% against infection ≥ 36 d after 1 dose. Sweden: 42% against infection ≥ 14 d after 1 dose, 86% ≥ 7 d after 2 doses. Canada: 59% ≥ 14 d after 1 dose and 91% after 2 doses. Qatar: 39.4% against disease after 1 dose and 97.4% ≥ 14 d after 2 doses. Efficacy/ effectiveness against variants: England: 83.0% against hospitalization after 1 dose, 95.0% after 2 doses against Alpha variant. 94.0% against hospitalization after 1 dose, 96.0% after 2 doses against Deltavoriant. Canada: 89% ≥ 7 d after 2 doses against symptomatic infection caused by Alpha variant. 60% ≥ 14 d after 1 dose and 84% ≥ 7 d against symptomatic infection caused by Beta or Gammavariants. 56% ≥ 14 d after 1 dose and 87% ≥ 7 d against symptomatic infection caused by Delta variant. Qatar: 29.5% after 1 dose and 89.5% ≥ 14 d after 2 doses against infection caused by Alpha variant. 16.9% after 1 dose and 75.0% after 2 doses against infection caused by Beta variant. | FDA EUA WHO EUL Approved in 93 countries  CARPHA EU recommendation EMA approved | [26,73,89,92,93,110,141,142,145,196,197,199–209] |
Table 1. Cont.

| Platform Type | No. | Vaccine Name | Number of Doses (Dosage) | Dosing Schedule | Route of Administration | Developer/Manufacturer | Construct and/or Targeted SARS-CoV-2 Protein | Current Stage of Clinical Trial (Recruitment Status) | Efficacy * | Current Approvals/Authorizations | Reference |
|---------------|-----|--------------|--------------------------|-----------------|------------------------|-----------------------|---------------------------------------------|---------------------------------------------------|------------|----------------------------------|----------|
| RNA vaccine   | 3   | CVnCoV       | 2 doses (12 µg)          | Day 0 + 28      | IM                     | CureVac AG            | LNP-encapsulated mRNA vaccine encoding the full-length, pre-fusion stabilized S protein | Phase III (Active, not recruiting)                  | Efficacy from clinical trials conducted in 10 countries in Latin America and Europe: 47% against symptomatic disease across all age groups and 15 variants, 53% against any disease severity, 77% against moderate and severe disease. | WHO EUL (Pending approval) Not yet approved in any country | [26,110, 210–212] |
| RNA vaccine   | 4   | ARCoV or ARCoVax | 1 dose (15 µg) | Day 0 | IM | Academy of Military Science (AMS), Walvax Biotechnology and Suzhou Abogen Biosciences | LNP-encapsulated mRNA vaccine encoding the RBD of S protein | Phase III (Not yet recruiting) | NR | Not yet approved in any country | [26,213, 214] |
| RNA vaccine   | 5   | mRNA-1273.211 | 1 dose (50 µg)          | Day 0 | IM | ModernaTX, Inc. | A multivalent booster candidate combining mRNA-1273 + mRNA-1273.351 Full-length prefusion stabilized S protein of SARS-CoV-2 B.1.351 variant | Phase II-III (Active, not recruiting) | Phase II (Active, not recruiting) | NR | Not yet approved in any country | [26,215] |
| RNA vaccine   | 6   | mRNA-1273.351 | 1–2 doses (20 or 50 µg) | Day 0, or Day 0 + 28, or Day 56 after 2nd dose of mRNA-1273 | IM | Moderna + NIAID | Full-length prefusion stabilized S protein | Phase II (Two trials: one is recruiting, and the other is active, not recruiting) | NR | Not yet approved in any country | [26,216–218] |
| RNA vaccine   | 7   | ARCT-021     | 1–2 doses ± booster dose (5 or 7.5 µg) | Day 0, or Day 0 + 28, or Day 0 + 28 ± 208 (booster) | IM | Arcturus Therapeutics | S protein | Phase I–II (Recruiting) | NR | Not yet approved in any country | [26,219–221] |
| RNA vaccine   | 8   | MRT5500      | 2 doses (15, 45 or 135 µg) | Day 0 + 21 | IM | Sanofi Pasteur and Translate Bio Daiichi Sankyo Co., Ltd. | S protein | Phase I–II (Recruiting) | NR | Not yet approved in any country | [26,222–224] |
| RNA vaccine   | 9   | DS-5670a     | 2 doses (10, 30, 60 or 100 µg) | Day 0 + 21 | IM | NR | Temperature-sensitive ssRNA vaccine expressing the RBD of S protein | Phase I–II (Recruiting) | Phase I–II (Recruiting) | NR | Not yet approved in any country | [26,225, 226] |
| RNA vaccine   | 10  | EXG-5003     | 1 dose                  | Day 0 | ID | Elixirgen Therapeutics, Inc | Temperature-sensitive ssRNA vaccine expressing the RBD of S protein | | | Not yet approved in any country | [26,227] |
| Platform/Type | No. | Vaccine Name | Number of Doses (Dosage) | Dosing Schedule | Route of Administration | Developer/Manufacturer | Construct and/or Targeted SARS-CoV-2 Protein | Current Stage of Clinical Trial (Recruitment Status) | Efficacy * | Current Approvals/Authorizations | Reference |
|---------------|-----|---------------|--------------------------|-----------------|------------------------|-----------------------|---------------------------------------------|-----------------------------------------------|-----------|----------------------------------|-----------|
| RNA vaccine   | 11  | LNP-nCoVsaRNA (COVAC1) | 2 doses (0.1–10.0 µg) | ND              | IM                     | Imperial College London | S protein                        | Phase I (No longer recruiting) | NR        | Not yet approved in any country | [26,228, 229] |
| RNA vaccine   | 12  | ChulaCov19 mRNA vaccine | 2 doses (10, 25, 50, or 100 µg) | Day 0 + 21      | IM                     | Chulalongkorn University | S protein                        | Phase I (Not yet recruiting) | NR        | Not yet approved in any country | [26,230, 231] |
| RNA vaccine   | 13  | PTX-COVID19-B | 2 doses (16, 40, or 100 µg) | Day 0 + 28      | IM                     | Providence Therapeutics | Full-length membrane-anchored S protein | Phase I (Active, not recruiting) | NR        | Not yet approved in any country | [26,232, 233] |
| RNA vaccine   | 14  | CoV2 SAM (LNP) | 2 doses (1.0 µg) | Day 0 + 30      | IM                     | GSK                    | S protein                        | Phase I (Active, not recruiting) | NR        | Not yet approved in any country | [26,234] |
| RNA vaccine   | 15  | HDT-301 | 2 doses (1, 5, or 25 µg) | Day 0 + 28      | IM                     | SENAI CIMATEC           | Full-length S protein            | Phase I (Active, not recruiting) | NR        | Not yet approved in any country | [26,235] |
| RNA vaccine   | 16  | mRNA-1283 | 1–2 doses (10, 30, or 100 µg) | Day 0 or Day 0 + 28 | IM                     | ModernaTX, Inc.          | RBD and NTD of S protein         | Phase I (Recruiting)            | NR        | Not yet approved in any country | [26,236, 237] |
| RNA vaccine   | 17  | SW-0123 | 2 doses             | NR              | IM                     | Shanghai East Hospital + Stemirna Therapeutics | NR                             | Phase I (Recruiting)            | NR        | Not yet approved in any country | [26,238, 239] |
| RNA vaccine   | 18  | LNP-nCOVsaRNA-02 (COVAC-Uganda) | 2 doses (5.0 µg) | Day 0 + 28      | IM                     | MRC/UVRI and LSHTM Uganda Research Unit | S protein                        | Phase I (Not yet recruiting) | NR        | Not yet approved in any country | [26,240] |
### Table 1. Cont.

| Platform/Vaccine Type | No. | Vaccine Name | Number of Doses (Dosage) | Dosing Schedule | Route of Administration | Developer/Manufacturer | Construct and/or Targeted SARS-CoV-2 Protein | Current Stage of Clinical Trial (Recruitment Status) | Efficacy * | Current Approvals/Authorizations | Reference |
|-----------------------|-----|--------------|--------------------------|-----------------|-------------------------|------------------------|---------------------------------------------|-----------------------------------------------|------------|---------------------------------|-----------|
| Protein subunit       | 1   | NVX-CoV2373  | 2 doses (5 µg)           | Day 0 + 21      | IM                      | Novavax                | S protein with Matrix-M adjuvant            | Phase III (Recruiting)                         |            | WHO EUL (Approval pending) Not yet approved in any country | [26,102, 103,110, 241–243] |
| Protein subunit       | 2   | ZF2001 (Recombinant SARS-CoV-2 vaccine) | 3 doses (25 µg) | Day 0 + 30 + 93 | IM | Anhui Zhifei Longcom Biopharmaceutical Institute of Microbiology, Chinese Academy of Sciences | RBD-Dimer with alum adjuvant | Phase III (Recruiting) |            | China (EUA), Uzbekistan | [26,244, 245] |
| Protein subunit       | 3   | VAT00008     | 2 doses                  | Day 0 + 21      | IM | Sanofi Pasteur + GSK | Monovalent and bivalent S protein with adjuvant FINLAY-FR-2: chemically conjugated RBD to tetanus toxoid plus adjuvant FINLAY-FR-1A: dimeric RBD + alum adjuvant | Phase III (Not yet recruiting) | NR | Not yet approved in any country | [26,246, 247] |
| Protein subunit       | 4   | FINLAY-FR-2  | 2 doses (25 µg) + booster dose (FINLAY-FR-1A, 50 µg) | Day 0 + 28 Day 56 (booster dose) | IM | Instituto Finlay de Vacunas | FINLAY-FR-2: chemically conjugated RBD to tetanus toxoid plus adjuvant FINLAY-FR-1A: dimeric RBD + alum adjuvant | Phase III (P ending) | 62% | Not yet approved in any country | [26,248–250] |
| Platform/Vaccine Type | No. | Vaccine Name | Number of Doses (Dosage) | Dosing Schedule | Route of Administration | Developer/Manufacturer | Construct and/or Targeted SARS-CoV-2 Protein | Current Stage of Clinical Trial (Recruitment Status) | Efficacy * | Current Approvals/Authorizations | Reference |
|-----------------------|-----|--------------|--------------------------|-----------------|-------------------------|------------------------|---------------------------------|------------------------------------------|-----------|------------------------------|-----------|
| Protein subunit       | 5   | Recombinant SARS-CoV-2 vaccine (SF9 Cell) | 3 doses | Day 0 + 28 + 42 | IM | West China Hospital + Sichuan University | RBD with alum adjuvant | Phase III (Enrolling by invitation) | NR | Not yet approved in any country | [26,251] |
| Protein subunit       | 6   | EpiVacCoro | 2 doses | Day 0 + 21 | IM | Federal Budgetary Research Institution State Research Center of Virology and Biotechnology (CIGB) | Peptide antigens of SARS-CoV-2 proteins with alum adjuvant | Phase III (Active, not recruiting) | Efficacy from clinical trials: 100% | Russia, Turkmenistan | [26,252,253] |
| Protein subunit       | 7   | CIGB-66     | 3 doses (50 µg RBD + 0.3 mg aluminum hydroxide) | Day 0 + 14 + 28 or Day 0 + 28 + 56 | IM | Center for Genetic Engineering and Biotechnology (CIGB) | RBD with aluminum hydroxide adjuvant | Phase III (Pending) | Efficacy from clinical trials: 91.6% | Not yet approved in any country | [26,254,255] |
| Protein subunit       | 8   | NanoCovax   | 2 doses (25 µg) | Day 0 + 28 | IM | Nanogen Pharmaceutical Biotechnology | Recombinant S protein with alum adjuvant | Phase III (Recruiting) | NR | Not yet approved in any country | [26,256] |
| Protein subunit       | 9   | SCB-2019    | 2 doses (30 µg) | Day 0 + 21 | IM | Clover Biopharmaceuticals Inc. + GSK + Dynavax Vaxxinity, Inc. + Diagnósticos da América S/A (DASA) | Trimeric S protein with CpG 1018 and Alum adjuvants | Phase II–III (Not yet recruiting) | NR | Not yet approved in any country | [26,257–259] |
| Protein subunit       | 10  | UB-612      | 2 doses (100 µg) | Day 0 + 28 | IM | Instituto Finlay de Vacunas Vaxine Pty Ltd. + Dynavax | RBD of S protein | Phase II–III (Not yet recruiting) | NR | Not yet approved in any country | [26,260] |
| Protein subunit       | 11  | FINLAY-FR-1 | 2 doses (10 or 20 µg) | Day 0 + 28 | IM | Instituto Finlay de Vacunas Vaxine Pty Ltd. + CinnaGen Co. | RBD with adjuvant | Phase II (Pending) | NR | Not yet approved in any country | [26,261] |
| Protein subunit       | 12  | COVAX-19    | 2 doses (25 µg) | Day 0 + 21 | IM | Medigen Vaccine Biologics + Dynavax + NIAID | Recombinant S protein with Advax-CpG adjuvant | Phase II (Recruiting) | NR | Not yet approved in any country | [26,262] |
| Protein subunit       | 13  | MVC-COV1901 | 2 doses (5, 15, or 25 µg) | Day 0 + 28 | IM | Medigen Vaccine Biologics + Dynavax | Recombinant S protein with CpG 1018 and alum adjuvants | Phase II (Active, not recruiting for adults, recruiting for elderly) | NR | Not yet approved in any country | [26,263–265] |
| Protein subunit       | 14  | Razi Cov Pars | 3 doses | Day 0 + 21 (IM) + 51 (IN) | IM and IN | Razi Vaccine and Serum Research Institute | Recombinant S protein | Phase II (Complete) | NR | Not yet approved in any country | [26,266] |
## Table 1. Cont.

| Platform/Vaccine Type | No. | Vaccine Name          | Number of Doses (Dosage) | Dosing Schedule | Route of Administration | Developer/Manufacturer                                                                 | Construct and/or Targeted SARS-CoV-2 Protein | Current Stage of Clinical Trial (Recruitment Status) | Efficacy * | Current Approvals/Authorizations | Reference |
|-----------------------|-----|-----------------------|--------------------------|-----------------|-------------------------|----------------------------------------------------------------------------------------|---------------------------------------------|-----------------------------------------------------|------------|----------------------------------|-----------|
| Protein subunit       | 15  | V-01                  | 2 doses (10 or 25 µg)    | Day 0 + 21      | IM                      | Guangdong Provincial Center for Disease Control and Prevention/Gaozhou Center for Disease Control and Prevention | Recombinant S protein                      | Phase II (Not yet recruiting)                         | NR         | Not yet approved in any country | [26,267] |
| Protein subunit       | 16  | CIGB-669              | 3 doses (50 µg RBD + 40 µg AgnHB) | Day 0 + 14 + 28 or Day 0 + 28 + 56 | IN                      | Center for Genetic Engineering and Biotechnology (CIGB)                                | Recombinant RBD with AgnHB                 | Phase I–II (Pending)                                 | NR         | Not yet approved in any country | [26,268] |
| Protein subunit       | 17  | KBP-COVID-19          | 2 doses (15 µg in phase I, 45 µg in phase II) | Day 0 + 21      | IM                      | Kentucky Bioprocessing Inc.                                                            | RBD of S protein                           | Phase I–II (Recruiting)                              | NR         | Not yet approved in any country | [26,269,270] |
| Protein subunit       | 18  | BECOV2                | 2 doses                  | Day 0 + 28      | IM                      | Biological E. Limited                                                                 | Recombinant RBD                            | Phase I–II (Closed)                                 | NR         | Not yet approved in any country | [26,271] |
| Protein subunit       | 19  | S-268019              | 2 doses                  | Day 0 + 21      | IM                      | Shionogi                                                                               | Recombinant S protein                      | Phase I–II (Recruiting)                              | NR         | Not yet approved in any country | [26,272] |
| Protein subunit       | 20  | AKS-452               | 1–2 doses (22.5, 45, or 90 µg) | NR              | SC or IM                | University Medical Center Groningen + Akton Biosciences Inc.                         | RBD-Fc fusion protein                     | Phase I–II (Enrolling by invitation)                 | NR         | Not yet approved in any country | [26,273] |
| Protein subunit       | 21  | COVAC-1 and COVAC-2   | 2 doses (25, 50, or 100 µg) | Day 0 + 28      | IM                      | University of Saskatchewan                                                             | S1 protein with SWE adjuvant               | Phase I–II (Recruiting)                              | NR         | Not yet approved in any country | [26,274] |
| Protein subunit       | 22  | COV510                | 2 doses (10, or 25 µg)   | Day 0 + 28      | IM                      | SK Bioscience Co., Ltd. And CEPI                                                    | Recombinant RBD with AS03 aluminum hydroxide adjuvant | Phase I–II (Recruiting)                              | NR         | Not yet approved in any country | [26,275] |
| Protein subunit       | 23  | QazCoVac-P            | 1–2 doses                | Day 0 + 21      | IM                      | Research Institute for Biological Safety Problems                                      | Recombinant S protein with an adjuvant    | Phase I–II (Active, not recruiting)                  | NR         | Not yet approved in any country | [26,276] |
| Protein subunit       | 24  | EuCorVac-19           | 2 doses                  | Day 0 + 21      | IM                      | POP Biotechnologies and EuBiologics Co., Ltd                                           | Recombinant S protein                      | Phase I–II (Recruiting)                              | NR         | Not yet approved in any country | [26,277] |
| Protein subunit       | 25  | Recombinant SARS-CoV-2 Vaccine (CHO cell) | 3 doses                  | Day 0 + 30 + 60 | IM                      | National Vaccine and Serum Institute, China                                            | Recombinant SARS-CoV-2                    | Phase I–II (Recruiting)                              | NR         | Not yet approved in any country | [26,278] |
| Platform/Type | No. | Vaccine Name | Number of Doses (Dosage) | Dosing Schedule | Route of Administration | Developer/Manufacturer | Construct and/or Targeted SARS-CoV-2 Protein | Current Stage of Clinical Trial (Recruitment Status) | Efficacy (*) | Current Approvals/Authorizations | Reference |
|--------------|-----|--------------|--------------------------|-----------------|-------------------------|------------------------|----------------------------------------------|-----------------------------------------------|------------|----------------------------------|-----------|
| Protein subunit | 26 | SARS-CoV-2 Sclamp vaccine | 2 doses (5, 15, or 45 µg) | Day 0 + 28 | IM | University of Queensland + Synexos Health + CEPI | Recombinant S protein with MF59 adjuvant | Phase I (Recruiting) | NR | Not yet approved in any country | [26,279–281] |
| Protein subunit | 27 | IMP CoVac-1 | 1 dose (500 µL) | Day 0 | SC | University Hospital Tuebingen Adimmune Corporation | SARS-CoV-2 HLA-DR peptides Recombinant RBD with alum adjuvant | Phase I (Recruiting) | NR | Not yet approved in any country | [26,282] |
| Protein subunit | 28 | AdimrSC-2f | 2 doses (30 or 50 µg) | Day 0 + 28 | IM | SK Bioscience Co., Ltd. | Recombinant RBD protein with alum adjuvant | Phase I (Recruiting) | NR | Not yet approved in any country | [26,283] |
| Protein subunit | 29 | NBP2001 | 2 doses (20 or 40 µg) | Day 0 + 21 | IM | Jiangsu Rec-Biotechnology | Recombinant two-component S and RBD protein | Phase I (Not yet recruiting) | NR | Not yet approved in any country | [26,285] |
| Protein subunit | 30 | ReCOV | 2 doses (20 or 40 µg) | Day 0 + 21 | IM | Walter Reed Army Institute of Research (WRAIR) | S proteins with a liposomal formulation QS21 (ALFQ) adjuvant | Phase I (Recruiting) | NR | Not yet approved in any country | [26,286–288] |
| Protein subunit | 31 | Spike-Ferritin-Nanoparticle (SpFN) | 2–3 doses (25 or 50 µg) | Day 0 + 28 + 180 | IM | Walter Reed Army Institute of Research (WRAIR) | Target 11 viral protein (S, M, N, and several non-structural proteins) | Phase I (Recruiting) | NR | Not yet approved in any country | [26,289] |
| Protein subunit | 32 | CoVepiT | 1–2 doses | Day 0 or Day 0 + 21 | SC | OSE Immunotherapeutics | Recombinant RBD protein | Phase I (Not yet recruiting) | NR | Not yet approved in any country | [26,290] |
| Protein subunit | 33 | CoV2-0GEN1 | 1–2 doses (50, 100, or 200 µg) | Day 0 + 14 | Oral | VaxForm | Recombinant RBD protein | Phase I (Not yet recruiting) | NR | Not yet approved in any country | [26,290] |
| Virus-like particle | 1 | CoVLP | 2 doses (3.75 µg) 2 doses (5 or 25 µg) | Day 0 + 21 | IM | Medicago Inc. | Trimeric S protein with AS03 adjuvant RBD conjugated to the hepatitis B surface antigen | Phase II–III (Recruiting) | NR | Not yet approved in any country | [26,291,292] |
| Virus-like particle | 2 | RBD SARS-CoV-2 HBsAg VLP Vaccine | 2 doses (5 or 10 µg) | Day 0 + 28 | IM | Serum Institute of India + Accelagen Pty + SpyBiotech | Enveloped S glycoprotein with aluminum phosphate adjuvant | Phase I–II (Active, not recruiting) | NR | Not yet approved in any country | [26,293] |
| Virus-like particle | 3 | VBI-2902a | 2 doses (5 or 10 µg) | Day 0 + 28 | IM | VBI Vaccines Inc. | The Scientific and Technological Research Council of Turkey | Phase I–II (Active, not recruiting) | NR | Not yet approved in any country | [26,294] |
| Virus-like particle | 4 | SARS-CoV-2 VLP Vaccine | 2 doses | NR | SC | The Scientific and Technological Research Council of Turkey | SARS-CoV-2 VLP adjuvanted with alum and CpG ODN-K3 | Phase I (Recruiting) | NR | Not yet approved in any country | [26,295] |
| Platform/Type | No. | Vaccine Name | Number of Doses | Dosing Schedule | Route of Administration | Developer/Manufacturer | Construct and/or Targeted SARS-CoV-2 Protein | Current Stage of Clinical Trial (Recruitment Status) | Efficacy * | Current Approvals/Authorizations | Reference |
|--------------|-----|--------------|-----------------|-----------------|-------------------------|-----------------------|---------------------------------|-----------------------------------------------|----------|-----------------------------|----------|
| Virus-like particle | 5 | ABVCoV2 | 2 doses | Day 0 + 28 | IM | Radboud University | capsid virus-like particle (cVLP) +/− adjuvant MF59 | Phase I (Recruiting) | NR | Not yet approved in any country | [26,296] |

**Table 1. Cont.**

| Platform/Type | No. | Vaccine Name | Number of Doses | Dosing Schedule | Route of Administration | Developer/Manufacturer | Construct and/or Targeted SARS-CoV-2 Protein | Current Stage of Clinical Trial (Recruitment Status) | Efficacy * | Current Approvals/Authorizations | Reference |
|--------------|-----|--------------|-----------------|-----------------|-------------------------|-----------------------|---------------------------------|-----------------------------------------------|----------|-----------------------------|----------|
| Virus-like particle | 5 | ABVCoV2 | 2 doses | Day 0 + 28 | IM | Radboud University | capsid virus-like particle (cVLP) +/− adjuvant MF59 | Phase I (Recruiting) | NR | Not yet approved in any country | [26,296] |

**Abbreviations:** IM: Intramuscular, IN: Intranasal, IV: Intravenous, SC: Subcutaneous, ID: Intradermal, SL: Sublingual, NR: Not reported, d: days, FDA: Food and Drug Administration, WHO: World Health Organization, EAU: Emergency Use Authorization, EUL: Emergency Use Listing, ART: Africa Regulatory Taskforce, CRS: Caribbean Regulatory System, EMA: European Medicines Agency, EU: Equivalent units, IU: Infectious unit, PFU: Plaque-forming unit, S: Spike, RBD: Receptor-binding domain, N: nucleocapsid, M: membrane, NTD: N-terminal domain, Al(OH): aluminum hydroxide, Algel-IMDG: chemosorbed imidazoquinoline onto aluminum hydroxide gel, CpG 1018: cytosine phosphate-guanine 1018, CpG ODN: CpG oligodeoxynucleotide, NVD: Newcastle Disease Virus, RSV: Respiratory syncytial virus, MVA: Modified vaccinia virus Ankara, VSV: Vesicular stomatitis virus, GM-CSF: Granulocyte-macrophage colony-stimulating factor, ssRNA: Self-amplifying ribonucleic acid, LNP: Lipid nanoparticles, AgnHBL antigen of Hepatitis B, VOCs: variants of concern, VOIs: variants of interest. *Efficacy against COVID-19 varies by age and time after vaccinations. 1 Albania, Armenia, Azerbaijan, Bangladesh, Benin, Brazil, Cambodia, Chile, China, Colombia, Dominican Republic, Egypt, El Salvador, Georgia, Hong Kong, Indonesia, Kazakhstan, Lao People’s Democratic Republic, Malaysia, Mexico, Nepal, Oman, Pakistan, Panama, Paraguay, Philippines, South Africa, Tajikistan, Thailand, Timor-Leste, Togo, Tunisia, Turkey, Ukraine, Uruguay, and Zimbabwe. 2 Angola, Argentina, Bahrain, Bangladesh, Belarus, Belize, Bolivia, Brazil, Brunei Darussalam, Cambodia, Cameroon, China, Comoros, Egypt, Equatorial Guinea, Gabon, Gambia, Georgia, Guyana, Hungary, Indonesia, Iran, Iraq, Jordan, Kyrgyzstan, Lao People’s Democratic Republic, Lebanon, Maldives, Mauritania, Mauritius, Mongolia, Montenegro, Morocco, Mozambique, Namibia, Nepal, Niger, North Macedonia, Pakistan, Paraguay, Peru, Philippines, Republic of the Congo, Senegal, Serbia, Seychelles, Sierra Leone, Solomon Islands, Somalia, Sri Lanka, Thailand, Trinidad and Tobago, United Arab Emirates, Venezuela (Bolivarian Republic of Venezuela), Vietnam, and Zimbabwe. 3 Guyana, India, Iran, Mauritius, Mexico, Nepal, Paraguay, Philippines, and Zimbabwe. 4 Albania, Angola, Argentina, Armenia, Australia, Austria, Azerbaijan, Belgium, Belize, Benin, Bermuda, Bosnia and Herzegovina, Botswana, Brazil, Brunei Darussalam, Bulgaria, Burkina Faso, Cambodia, Canada, Central African Republic, Chile, Colombia, Costa Rica, Croatia, Cyprus, Czechia, Côte d’Ivoire, Democratic Republic of the Congo, Dominican Republic, Croatia, Egypt, El Salvador, Estonia, Eswatini, Fiji, Finland, France, Gambia, Georgia, Germany, Ghana, Greece, Grenada, Guatemala, Guinea-Bissau, Guyana, Haiti, Hungary, Iceland, India, Indonesia, Iran, Iraq, Ireland, Italy, Jamaica, Japan, Jordan, Kenya, Kosovo, Kuwait, Latvia, Lithuania, Luxembourg, Malawi, Malaysia, Mali, Malta, Mauritius, Mexico, Mongolia, Morocco, Nauru, Netherlands, Niger, Nigeria, North Macedonia, Oman, Pakistan, Panama, Papua New Guinea, Paraguay, Peru, Philippines, Poland, Portugal, Republic of Korea, Republic of Moldova, Romania, Rwanda, Sao Tome and Principe, Saudi Arabia, Senegal, Serbia, Sierra Leone, Slovakia, Slovenia, South Sudan, Spain, Sudan, Sweden, Taiwan, Tajikistan, Thailand, Timor-Leste, Togo, Uganda, United Arab Emirates, United Kingdom of Great Britain and Northern Ireland, Uzbekistan, Vanuatu, Viet Nam, Yemen, and Zambia. 5 Argentina, China, Ecuador, Hungary, Malaysia, Mexico, and Pakistan. 6 Austria, Bahrain, Bangladesh, Belgium, Brazil, Bulgaria, Canada, Chile, Colombia, Croatia, Cyprus, Czechia, Denmark, Estonia, Faroe Islands, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Kuwait, Latvia, Libya, Liechtenstein, Lithuania, Luxembourg, Malaysia, Maldives, Malta, Mexico, Netherlands, New Zealand, Nigeria, Norway, Philippines, Poland, Portugal, Republic of Korea, Romania, Russian Federation, Senegal, South Africa, Spain, Sri Lanka, Sweden, Switzerland, Tunisia, Turkey, Ukraine, United Arab Emirates, United Kingdom of Great Britain and Northern Ireland, United States of America, Uruguay, Vatican, Vietnam, and World Bank. 9 Afghanistan, Antigua and Barbuda, Angola, Argentina, Armenia, Austria, Azerbaijan, Bangladesh, Belarus, Belize, Bolivia, Brazil, Brunei Darussalam, Cambodia, Cameroon, China, Comoros, Egypt, Equatorial Guinea, Gabon, Gambia, Georgia, Hong Kong, Indonesia, Iran, Iraq, Jordan, Kyrgyzstan, Lao People’s Democratic Republic, Lebanon, Maldives, Mauritania, Mauritius, Mongolia, Montenegro, Morocco, Mozambique, Namibia, Nepal, Niger, North Macedonia, Pakistan, Paraguay, Peru, Philippines, Republic of the Congo, Senegal, Serbia, Seychelles, Sierra Leone, Solomon Islands, Somalia, Sri Lanka, Thailand, Trinidad and Tobago, United Arab Emirates, Venezuela (Bolivarian Republic of Venezuela), Vietnam, and Zimbabwe.
3. Conclusions

With the ongoing SARS-CoV-2 pandemic, safe and effective vaccines could be the major aid in retrenching this outbreak and probably the best bet to return us to ‘normal life’. The impulse of an accelerated vaccine development process, though needed, is faced with a broad spectrum of challenges that necessitates collective strives from both the public and the private sectors to fully understand the potential utility of these vaccines not only for overcoming the current pandemic but also for preventing future waves.

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