COVID-19 Vaccine Janssen
COVID-19 vaccine (Ad26.COV2-S [recombinant])
Risk Management Plan

Summary of Activities in the Risk Management Plan (RMP)
for COVID-19 Vaccine Janssen (Ad26.COV2-S)

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The Risk Management Plan (RMP) is a comprehensive document submitted as part of the application dossier for market approval of a medicine. The RMP summary contains information on the medicine's safety profile and explains the measures that are taken in order to further investigate and follow the risks as well as to prevent or minimize them.

The RMP summary of COVID-19 Vaccine Janssen is a concise document and does not claim to be exhaustive. As the RMP is an international document, the summary might differ from the "Arzneimittelinformation/Information sur le medicament" approved and published in Switzerland, e.g. by mentioning risks occurring in populations or indications not included in the Swiss authorisation.

Please note that the reference document which is valid and relevant for the effective and safe use of COVID-19 Vaccine Janssen in Switzerland is the "Arzneimittleinformation / Information sur le medicament" (see www.swissmedic.ch) approved and authorized by Swissmedic.

Janssen-Cilag AG is fully responsible for the accuracy and correctness of the content of the published summary RMP of COVID-19 Vaccine Janssen.

Summary of Risk Management Plan for COVID-19 Vaccine Janssen

This is a summary of the risk management plan (RMP) for COVID-19 Vaccine Janssen. The RMP details important risks of COVID-19 Vaccine Janssen, how these risks can be minimized, and how more information will be obtained about COVID-19 Vaccine Janssen's risks and uncertainties (missing information).

COVID-19 Vaccine Janssen's summary of product characteristics (SmPC) and its package leaflet (PL) give essential information to healthcare professionals and patients on how COVID-19 Vaccine Janssen should be used.

This summary of the RMP for COVID-19 Vaccine Janssen should be read in the context of all this information including the assessment report of the evaluation and its plain-language summary, all which is part of the European Public Assessment Report (EPAR).

Important new concerns or changes to the current ones will be included in updates of COVID-19 Vaccine Janssen's RMP.

I. The Vaccine and What it is Used For

COVID-19 Vaccine Janssen is authorised for active immunization to prevent COVID-19 caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) in individuals 18 years of age and older (see SmPC for the full indication). It contains Ad26.COV2.S as the active substance and it is given by intramuscular injection.

Further information about the evaluation of COVID-19 Vaccine Janssen's benefits can be found in COVID-19 Vaccine Janssen's EPAR, including in its plain-language summary, available on the European Medicines Agency website, under the vaccine's webpage:

https://www.ema.europa.eu/en/medicines/human/EPAR/covid-19-vaccine-janssen.

II. Risks Associated With the Vaccine and Activities to Minimize or Further Characterize the Risks

Important risks of COVID-19 Vaccine Janssen, together with measures to minimize such risks and the proposed studies for learning more about COVID-19 Vaccine Janssen's risks, are outlined below.

Measures to minimize the risks identified for vaccines can be:

- Specific information, such as warnings, precautions, and advice on correct use, in the PL and SmPC addressed to individuals and healthcare professionals;
- Important advice on the vaccine's packaging;
- The authorised pack size — the amount of vaccine in a pack is chosen so to ensure that the vaccine is used correctly;
- The vaccine's legal status — the way a vaccine is supplied to the individual (eg, with or without prescription) can help to minimize its risks.

Together, these measures constitute routine risk minimization measures.

In addition to these measures, information about adverse reactions is collected continuously and regularly analyzed including Periodic Benefit-Risk Evaluation Report/Periodic Safety Update Report assessment so that immediate action can be taken as necessary. These measures constitute routine pharmacovigilance activities.

If important information that may affect the safe use of COVID-19 Vaccine Janssen is not yet available, it is listed under 'missing information' below.

II.A. List of Important Risks and Missing Information

Important risks of COVID-19 Vaccine Janssen are risks that need special risk management activities to further investigate or minimize the risk, so that the vaccine can be safely administered. Important risks can be regarded as identified or potential. Identified risks are concerns for which there is sufficient proof of a link with the use of COVID-19 Vaccine Janssen. Potential risks are concerns for which an association with the use of this vaccine is possible based on available data, but this association has not been established yet and needs further evaluation. Missing information refers to information on the safety of the vaccine that is currently missing and needs to be collected (eg, on the long-term use of the vaccine).

List of Important Risks and Missing Information	
Important identified risks	Anaphylaxis Thrombosis with thrombocytopenia syndrome Guillain-Barré syndrome Thrombocytopenia, including immune thrombocytopenia

Important potential risks	Vaccine-associated enhanced disease (VAED), including vaccine-associated enhanced respiratory disease (VAERD) Venous thromboembolism
Missing information	Use in pregnancy and while breastfeeding Use in immunocompromised patients Use in patients with autoimmune or inflammatory disorders Use in frail patients with comorbidities (eg, chronic obstructive pulmonary disease [COPD], diabetes, chronic neurological disease, cardiovascular disorders) Interaction with other vaccines Long-term safety

II.B. Summary of Important Risks

Important Identified Risk: Anaphylaxis	
Evidence for linking the risk to the medicine	Allergic reactions, including possibly severe reactions (eg, hypersensitivity reactions and anaphylaxis), are known to occur with any injectable vaccine. COVID-19 Vaccine Janssen contains ingredients with known potential to cause allergic reactions, including polysorbate 80. The structure of polysorbate 80 presents similarities with polyethylene glycol, recently suspected to be involved in anaphylactic reactions with mRNA vaccines. The potential for polysorbate 80 to trigger hypersensitivity and the possibility of cross-reactivity between polyethylene glycol and polysorbate 80 have been discussed in the literature. Cases of polysorbate 80-induced hypersensitivity have been reported and have involved different drugs, including a human papillomavirus vaccine, and different routes of administration, including the intramuscular route. Severe allergic reactions and one case of anaphylaxis have been identified following vaccination with COVID-19 Vaccine Janssen. All of these events occurred in the context of study COV3012 in South Africa, with the exception of a single serious adverse event of Type IV (delayed) hypersensitivity from trial COV3001. Anaphylaxis is an adverse drug reaction described in the SmPC.
Risk factors and risk groups	Participants with a known history of hypersensitivity to any component of the vaccine may be at risk for hypersensitivity reactions.
Risk minimization measures	Routine risk minimization measures: • SmPC Section 4.3 • SmPC Section 4.8 • PL Section 2 • PL Section 4 • SmPC Section 4.4 and PL Section 3 provide recommendations to

	address the risk of anaphylaxis. Additional risk minimization measures: • None
Additional pharmacovigilance activities	Additional pharmacovigilance activities: • Trial VAC31518COV3001 • Trial VAC31518COV3009 • Study VAC31518COV4003 • Study VAC31518COV4001 See section II.C of this summary for an overview of the post-authorisation development plan.
Important Identified Risk: Thrombosis with thrombocytopenia syndrome	
Evidence for linking the risk to the medicine	Thrombosis in combination with thrombocytopenia (TTS), in some cases accompanied by bleeding, has been observed very rarely following vaccination with COVID-19 Vaccine Janssen. Similar adverse events have also been described following administration of Vaxzevria. A causal relationship with COVID-19 Vaccine Janssen is considered plausible. The background incidence rate of thrombosis in combination with thrombocytopenia ('combination' defined as thrombocytopenia occurring 10 days before or after thrombosis) was computed as part of the ACCESS project. Cases of thrombosis were categorized into 4 types, including venous thrombosis, arterial thrombosis, venous or arterial thrombosis, and cerebral venous sinus thrombosis. The incidence rates for all 4 types, in combination with thrombocytopenia, were extremely low, with rates estimated at 1/100,000 person-years (95% confidence interval [CI]: 0.70-1.43); 1.46/100,000 person-years (95% CI: 1.09-1.96); 2.43/100,000 person-years (95% CI: 1.93-3.06), and 0.03/100,000 person-years (95% CI: 0.0-0.21) for venous, arterial, venous or arterial, and cerebral venous sinus thrombosis, respectively. These events are likely to be observed in the hospital setting, therefore rates were extracted from a hospitalization record linkage database, which also includes emergency room visits. Thrombosis in combination with thrombocytopenia is an adverse drug reaction described in the SmPC.
Risk factors and risk groups	Although no clear risk factors have been identified, the cases of TTS reported in the postmarketing setting more commonly occurred in women aged <60 years.
Risk minimization measures	Routine risk minimization measures: • SmPC Section 4.4 • SmPC Section 4.8 • PL Section 2

	• PL Section 4 • SmPC Section 4.4, and PL Sections 2 and 4 provide recommendations to address the risk of thrombosis with thrombocytopenia syndrome. Additional risk minimization measures: • Initial Direct Healthcare Professional Communication (DHPC) to inform healthcare professionals to facilitate early detection/diagnosis and correct clinical management of TTS, and updated DHPC to reinforce the initial messages, in particular with regard to the required specialist clinical management of TTS and to emphasize the need to investigate for other TTS symptoms following presentation with post-vaccination thrombosis or thrombocytopenia.
Additional pharmacovigilance activities	Additional pharmacovigilance activities: • Trial VAC31518COV3001 • Trial VAC31518COV3009 • Study VAC31518COV4003 • Study VAC31518COV4001 • Trial VAC31518COV2001 • TV-TEC-207316 – Molecular mimicry of PF4 • TV-TEC-207437 – RNA sequencing of Ad26.COV2.S transduced cells in vitro • TOX15155 – Study in NZW rabbits to determine spike protein expression after Ad26.COV2.S immunization • Anti-PF4 antibody levels in immune sera of Ad26.COV2.S immunized animals • TOX15252 – Systemic exposure to Ad26.COV2.S • TOX15258 – RNA transcriptome analysis after dosing with Ad26.COV2.S in Cynomolgus monkey • Thromboembolic case control study using clinical samples from Ad26.COV2.S studies • Thromboembolic case control study using clinical samples from Ad26-based Company vaccine studies other than Ad26.COV2.S • Test pre- and post-vaccination serum using clinical samples from Ad26.COV2.S studies • Test pre- and post-vaccination serum using clinical samples from Ad26-based Company vaccine studies other than Ad26.COV2.S • Test baseline and post-COVID-19 clinical samples • RNA transcriptome analyses post-vaccination using clinical

	samples from Ad26.COV2.S and other Ad26-based Company vaccine studies See section II.C of this summary for an overview of the post-authorisation development plan.
Important Identified Risk: Guillain-Barré syndrome	
Evidence for linking the risk to the medicine	Guillain-Barré syndrome (GBS) has been observed very rarely following vaccination with COVID-19 Vaccine Janssen both in clinical trials and in the postmarketing setting. Similar adverse events have also been described following administration of other COVID-19 vaccines. Despite no clear biological mechanism being identified, the Company considers the increase in observed versus expected ratios since authorisation to be sufficient evidence for a plausible association between COVID-19 Vaccine Janssen and GBS. Guillain-Barré syndrome is an adverse drug reaction described in the SmPC.
Risk factors and risk groups	Based mainly on data from North America and Europe, it has been shown in literature that the GBS incidence increased by 20% for every 10-year increase in age; GBS is usually more frequent in males, with the highest incidence between 50 to 70 years of age. Approximately a third of all GBS patients report symptoms of respiratory or gastrointestinal tract infection before the onset of GBS. Although many different infections have been identified in patients with GBS, case-control studies have revealed associations with only a few pathogens. *Campylobacter jejuni* is the most widely reported infection: it has been found in 25% to 50% of the adult GBS population and is more frequent in Asian countries. Other infections associated with GBS are those due to cytomegalovirus, Epstein–Barr virus, measles, influenza A virus and *Mycoplasma pneumoniae*, as well as enterovirus D68 and Zika virus. More recently, GBS has been reported in association with SARS-CoV-2 infection. GBS has been linked in the past with some vaccines, namely, rabies, polio, and influenza, as well as hepatitis A and B; measles, mumps, rubella and varicella; and shingles. Most recently, cases of GBS have been reported following vaccination with COVID-19 vaccines, including mRNA and adenovectored vaccines.
Risk minimization measures	Routine risk minimization measures: • SmPC Section 4.4 • SmPC Section 4.8 • PL Section 2 • PL Section 4 • SmPC Section 4.4, and PL Sections 2 and 4 provide recommendations to address the risk of Guillain-Barré syndrome. Additional risk minimization measures:

	• None.
Additional pharmacovigilance activities	Additional pharmacovigilance activities: • Study VAC31518COV4003 • Study VAC31518COV4001 See section II.C of this summary for an overview of the post-authorisation development plan.
Important Identified Risk: Thrombocytopenia, including immune thrombocytopenia	
Evidence for linking the risk to the medicine	Asymptomatic, transient platelet count decreases have been previously reported as an AEFI with several vaccines such as hepatitis A and B, influenza, pneumococcal vaccines, measles, mumps and rubella, varicella, smallpox, rabies, HIV, diphtheria-tetanus-pertussis, *Haemophilus influenzae* type b, and poliomyelitis. Thrombocytopenia following immunization has also been described following administration of other COVID-19 vaccines, including mRNA and adenovector-based vaccines. Low platelet values have been observed in individuals receiving non-COVID-19 Ad26-based vaccines during clinical trials at rates higher than placebo. Most of these events were asymptomatic and resolved spontaneously. Thrombocytopenia without immune thrombocytopenia (ITP) or TTS has been observed following vaccination with COVID-19 Vaccine Janssen in clinical trials and in the postmarketing setting. Cases of immune thrombocytopenia (ITP) with very low platelet levels (<20,000 per µL) have been reported very rarely after vaccination with COVID-19 Vaccine Janssen, usually within the first 4 weeks after receiving COVID-19 Vaccine Janssen. This included cases with bleeding and cases with fatal outcome. Some of these cases occurred in individuals with a history of ITP. Based on the observed imbalance in postmarketing events, ITP is an adverse drug reaction described in the SmPC.
Risk factors and risk groups	Risk factors for thrombocytopenia are dependent on the underlying cause. ITP is more common in young and middle-aged female adults, and more common in male children and older male adults. Adults are more likely to develop chronic ITP compared to children. In patients with ITP, the occurrence of bleeding is strongly inversely correlated with platelet levels, with individuals with $<20x10^9$/L being at a higher risk for bleeding. Limited data from postmarketing experience with COVID-19 Vaccine Janssen, including literature, suggest that individuals with chronic or recurrent ITP may be at increased risk of developing ITP following vaccination with COVID-19 Vaccine Janssen.

Risk minimization measures	Routine risk minimization measures: • SmPC Section 4.4 • SmPC Section 4.8 • PL Section 2 • PL Section 4 • SmPC Section 4.4 and PL Sections 2 and 4 provide recommendations to address the risk of thrombocytopenia, including immune thrombocytopenia. Additional risk minimization measures: • None
Additional pharmacovigilance activities	Additional pharmacovigilance activities: • Trial VAC31518COV3001 • Trial VAC31518COV3009 • Study VAC31518COV4003 (this study will only address immune thrombocytopenia) • Study VAC31518COV4001 (this study will only address immune thrombocytopenia) • Trial VAC31518COV2001 • TV-TEC-207316 – Molecular mimicry of PF4 (this study will only address immune thrombocytopenia) • TV-TEC-207437 – RNA sequencing of Ad26.COV2.S transduced cells in vitro (this study will only address immune thrombocytopenia) • TOX15155 – Study in NZW rabbits to determine spike protein expression after Ad26.COV2.S immunization (this study will only address immune thrombocytopenia) • Anti-PF4 antibody levels in immune sera of Ad26.COV2.S immunized animals (this study will only address immune thrombocytopenia) • TOX15252 – Systemic exposure to Ad26.COV2.S • TOX15258 – RNA transcriptome analysis after dosing with Ad26.COV2.S in Cynomolgus monkey See section II.C of this summary for an overview of the post-authorisation development plan.

Important Potential Risk: Vaccine-associated enhanced disease (VAED), including vaccine-associated enhanced respiratory disease (VAERD)	
Evidence for linking the risk to the medicine	VAERD was first seen in the 1960s in infants with respiratory syncytial virus (RSV) infection after receiving a vaccine against RSV that led to markedly worse respiratory disease as compared to non-vaccinated infants. Subsequently, reports of VAED were reported in individuals without prior exposure to Dengue who received tetravalent Dengue vaccines. Nonclinical experience with severe acute respiratory syndrome coronavirus (SARS-CoV)- and Middle East respiratory syndrome coronavirus-based vaccines also indicated a risk for VAERD, however, this risk could not be confirmed in humans due to the lack of efficacy studies. For candidate SARS-CoV-2 vaccines, no evidence of VAED or VAERD after intramuscular immunization has been reported to date in nonclinical studies or clinical trials. Nevertheless, in the absence of long-term safety and efficacy data, the evidence is not yet sufficient to fully dismiss VAED, including VAERD as a safety concern, and it remains an important potential risk.
Risk factors and risk groups	It is postulated that the potential risk may be increased in individuals producing lower neutralizing antibody titers or in those demonstrating waning immunity.
Risk minimization measures	Routine risk minimization measures • None Additional risk minimization measures • None
Additional pharmacovigilance activities	Additional pharmacovigilance activities: • Trial VAC31518COV3001 • Trial VAC31518COV3009 • Study VAC31518COV4004 See section II.C of this summary for an overview of the post-authorisation development plan.

Important Potential Risk: Venous thromboembolism	
Evidence for linking the risk to the medicine	Natural infection with SARS-CoV-2 has shown to be associated with hypercoagulability, pulmonary intravascular coagulation, microangiopathy, and venous thromboembolism (VTE) or arterial thrombosis. The occurrence of embolic and thrombotic events in context of coronavirus disease-2019 (COVID-19) is associated with a poor outcome. The hypercoagulable state observed in patients with severe COVID-19 is thought to be related to the high-grade systemic inflammatory response, although other mechanisms such as the higher incidence of severe COVID-19 in individuals with risk factors for embolic and thrombotic events have been proposed. It is unknown whether these proposed mechanisms linking COVID-19 and thromboembolic events could also be applicable for vaccines against COVID-19.
Risk factors and risk groups	In the general population, important intrinsic factors for the onset of deep vein thrombosis (DVT) and pulmonary embolism (PE) include a prior medical or family history of DVT or PE, venous insufficiency, heart disease, obesity, long periods of standing position, and multiparity. Important triggering factors for a DVT/PE event include pregnancy, trauma or a violent effort, deterioration of the general condition, immobilization, long distance travel, and infection. On the other hand, transverse sinus thrombosis is a disease more commonly observed in children and young adults. Important risk factors for transverse sinus thrombosis include thrombophilia, trauma, puerperium, and chronic inflammatory diseases. In addition, patients with transverse sinus stenosis have a strong risk for thrombosis, usually misdiagnosed as idiopathic intracranial hypertension. In trial COV3001, the following underlying risk factors have been identified in participants with VTE: male gender, old age (>65 years), long-haul travel, thrombophilia, obesity, hypertension, and COPD. SARS-CoV-2 infection is also considered an important risk factor, with 11 participants (4 in COVID-19 Vaccine Janssen group, 4 in Placebo group, 3 in the crossvaccinated group) having a positive polymerase chain reaction test.
Risk minimization measures	Routine risk minimization measures: • None Additional risk minimization measures: • None

Additional pharmacovigilance activities	Additional pharmacovigilance activities: • Trial VAC31518COV3001 • Trial VAC31518COV3009 • Study VAC31518COV4003 • Study VAC31518COV4001 • Trial VAC31518COV2001 See section II.C of this summary for an overview of the post-authorisation development plan.
Missing Information: Use in pregnancy and while breastfeeding	
Risk minimization measures	Routine risk minimization measures • SmPC Section 4.6 (only for use in pregnancy) • PL Section 2 Additional risk minimization measures • None
Additional pharmacovigilance activities	Additional pharmacovigilance activities: • Trial VAC31518COV3001 (This trial will only address use while breastfeeding) • Trial VAC31518COV3009 (This trial will only address use while breastfeeding) • Trial VAC31518COV2004 • Study VAC31518COV4005 (This study will only address use in pregnancy) • Study VAC31518COV4003 (The adequacy of the study to address pregnancy outcomes is to be assessed. The safety of Ad26.COV2.S in breastfeeding women will not be studied.) See section II.C of this summary for an overview of the post-authorisation development plan.
Missing Information: Use in immunocompromised patients	
Risk minimization measures	Routine risk minimization measures • SmPC Section 4.4 • PL Section 2 Additional risk minimization measures • None

Additional pharmacovigilance activities	Additional pharmacovigilance activities: • Interventional trial to evaluate the safety and immunogenicity of Ad26.COV2.S in immunocompromised patients • Study VAC31518COV4003 • Study VAC31518COV4004 • Study VAC31518COV4001 • Study VAC31518COV4002 See section II.C of this summary for an overview of the post-authorisation development plan.
Missing Information: Use in patients with autoimmune or inflammatory disorders	
Risk minimization measures	Routine risk minimization measures • None Additional risk minimization measures • None
Additional pharmacovigilance activities	Additional pharmacovigilance activities: • Study VAC31518COV4003 • Study VAC31518COV4001 See section II.C of this summary for an overview of the post-authorisation development plan.
Missing Information: Use in frail patients with comorbidities (eg, chronic obstructive pulmonary disease [COPD], diabetes, chronic neurological disease, cardiovascular disorders)	
Risk minimization measures	Routine risk minimization measures • None Additional risk minimization measures • None
Additional pharmacovigilance activities	Additional pharmacovigilance activities: • Trial VAC31518COV3001 • Study VAC31518COV4003 • Study VAC31518COV4001 • Study VAC31518COV4002 See section II.C of this summary for an overview of the post-authorisation development plan.

Missing Information: Interaction with other vaccines	
Risk minimization measures	Routine risk minimization measures • SmPC Section 4.5 • PL Section 2 Additional risk minimization measures • None
Additional pharmacovigilance activities	Additional pharmacovigilance activities: • Coadministration study of Ad26.COV2.S with seasonal influenza vaccine See section II.C of this summary for an overview of the post-authorisation development plan.
Missing Information: Long-term safety	
Risk minimization measures	Routine risk minimization measures • None Additional risk minimization measures • None
Additional pharmacovigilance activities	Additional pharmacovigilance activities: • Trial VAC31518COV3001 • Trial VAC31518COV3009 • Study VAC31518COV4003 • Study VAC31518COV4001 See section II.C of this summary for an overview of the post-authorisation development plan.

II.C. Post-authorisation Development Plan

II.C.1. Studies Which are Conditions of the Marketing Authorisation

VAC31518COV3001: A randomized, double-blind, placebo-controlled Phase 3 study to assess the efficacy and safety of Ad26.COV2.S for the prevention of SARS-CoV-2-mediated COVID-19 in adults aged 18 years and older.

Purpose of the study: To evaluate the efficacy safety, reactogenicity, and immunogenicity of Ad26.COV2.S for the prevention of SARS-CoV-2-mediated COVID-19.

II.C.2. Other Studies in Post-authorisation Development Plan

VAC31518COV3009: A randomized, double-blind, placebo-controlled Phase 3 study to assess the efficacy and safety of Ad26.COV2.S for the prevention of SARS-CoV-2-mediated COVID-19 in adults aged 18 years and older.

Purpose of the study: To evaluate the efficacy, safety, reactogenicity, and immunogenicity of 2 doses of Ad26.COV2.S for the prevention of SARS-CoV-2-mediated COVID-19.

VAC31518COV2004: An open-label, Phase 2 study to evaluate the safety, reactogenicity, and immunogenicity of Ad26.COV2.S in healthy pregnant participants.

Purpose of the study: To assess the safety, reactogenicity, and immunogenicity of Ad26.COV2.S in adult participants during the 2nd and/or 3rd trimester of pregnancy, to assess the safety and reactogenicity of Ad26.COV2.S (potentially) post-partum, and to assess pregnancy outcomes. To assess the presence of immunoglobulins against SARS-CoV-2 in colostrum and breast milk.

Interventional trial to evaluate the safety and immunogenicity of Ad26.COV2.S in immunocompromised patients.

Purpose of the study: To assess the safety and immunogenicity of Ad26.COV2.S in immunocompromised patients.

VAC31518COV4005: COVID-19 Vaccines International Pregnancy Exposure Registry (C-VIPER).

Purpose of the study: To assess the occurrence of obstetric, neonatal, and infant outcomes among women administered with Ad26.COV2.S during pregnancy.

VAC31518COV4003: An observational post-authorization safety study to assess the safety of Ad26.COV2.S using European healthcare data through VAC4EU.

Purpose of the study: To assess the occurrence of pre-specified adverse events of special interest (AESIs) within specific risk periods following administration of Ad26.COV2.S.

VAC31518COV4004: Post-authorization, observational, prospective study to assess the effectiveness of Ad26.COV2.S in Europe.

Purpose of the study: To estimate the effectiveness of Ad26.COV2.S in preventing laboratory-confirmed SARS-CoV-2 hospitalizations up to 2 years post-vaccination.

VAC31518COV4001: An observational post-authorization safety study to assess the safety of Ad26.COV2.S using health insurance databases in the United States.

Purpose of the study: To assess the occurrence of pre-specified AESIs within specific risk periods following administration of Ad26.COV2.S.

VAC31518COV4002: An observational post-authorization study to assess the effectiveness of Ad26.COV2.S for prevention of COVID-19 using real-world data.

Purpose of the study: To estimate the effectiveness of Ad26.COV2.S in preventing medically-attended COVID-19 up to 2 years post-vaccination.

Coadministration study of Ad26.COV2.S with seasonal influenza vaccine

Purpose of the study: To assess the safety and immunogenicity of Ad26.COV2.S and seasonal influenza vaccine when administered separately or concomitantly.

VAC31518COV2001: A randomized, double-blind, placebo-controlled Phase 2a study to evaluate a range of dose levels and vaccination intervals of Ad26.COV2.S in healthy adults aged 18 to 55 years inclusive and adults aged 65 years and older and to evaluate 2 dose levels of Ad26.COV2.S in healthy adolescents aged 12 to 17 years inclusive.

Purpose of the study: To evaluate the efficacy, safety, reactogenicity, and immunogenicity of Ad26.COV2.S at different dose levels and as a 2-dose or a 1-dose schedule.

TV-TEC-207316: Molecular mimicry of PF4.

Purpose of the study: To compare linear amino acid sequences of the SARS-CoV-2 Spike protein, TetR, and adenovirus proteins present on the outside of the virion with the known human proteome sequences and PF4.

TV-TEC-207437: RNA sequencing of Ad26.COV2.S transduced cells in vitro.

Purpose of the study: To analyze cells transduced with Ad26.COV2.S by RNA sequencing for possible alternative splicing events.

TOX15155: Study in NZW rabbits to determine spike protein expression after Ad26.COV2.S immunization.

Purpose of the study: To compare distribution of Spike protein following IM injection of Ad26.COV2.S to non-stabilized Spike protein that is known to shed the S1 portion.

Study to test presence of anti-PF4 antibody levels in immune sera of Ad26.COV2.S immunized animals

Purpose of the study: To assess anti-PF4 antibody induction by different Ad26-based vaccine candidates encoding SARS-CoV-2 Spike antigens or non-SARS-CoV-2 antigens compared with control treatment.

TOX15252: Study in NZW rabbits to assess the potential impact of intravenous/systemic exposure to Ad26.COV2.S

Purpose of the study: To assess effects of Ad26.COV2.S on platelets/coagulation and immunogenicity parameters following intravenous dosing.

TOX15258: Comparative RNA transcriptome analysis of blood from Cynomolgus monkey immunized with Ad26.COV2.S or control vaccines.

Purpose of the study: RNA transcriptome analysis after single and 2-dose immunization with Ad26.COV2.S compared to control vaccines.

Thromboembolic case control study: anti-PF4/heparin ELISA and confirmation by platelet activation assay using clinical samples from Ad26.COV2.S studies

Purpose of the study: To test for association of anti-PF4 antibodies and the ability of these antibodies to activate platelets in participants with thrombotic events after vaccination with Ad26.COV2.S.

Thromboembolic case control study: anti-PF4/heparin ELISA and confirmation by platelet activation assay using clinical samples from Ad26-based Company vaccine studies other than Ad26.COV2.S

Purpose of the study: To test for association of anti-PF4 antibodies and the ability of these antibodies to activate platelets in participants with thrombotic events after vaccination with Ad26-based Company vaccines other than Ad26.COV2.S.

Test pre- and post-vaccination serum across all populations using clinical samples from Ad26.COV2.S studies

Purpose of the study: To assess increases in anti-PF4 antibody levels in recipients of Ad26.COV2.S who did not develop thrombotic events.

Test pre- and post-vaccination serum across all populations using clinical samples from Ad26-based Company vaccine studies other than Ad26.COV2.S

Purpose of the study: To assess increases in anti-PF4 antibody levels in recipients of Ad26-based Company vaccines other than Ad26.COV2.S who did not develop thrombotic events.

Test baseline and post-COVID-19 clinical samples (using samples from COV3001 placebo COVID-19 cases)

Purpose of the study: To assess increases in anti-PF4 antibody levels in samples of SARS-CoV-2 positive participants.

RNA transcriptome analyses post-vaccination using clinical samples from Ad26.COV2.S and other Ad26-based Company vaccine studies

Purpose of the study: To examine gene expression in whole blood, that may inform on the inflammation signals triggered by Ad26.COV2.S and other Ad26-based Company vaccines.