



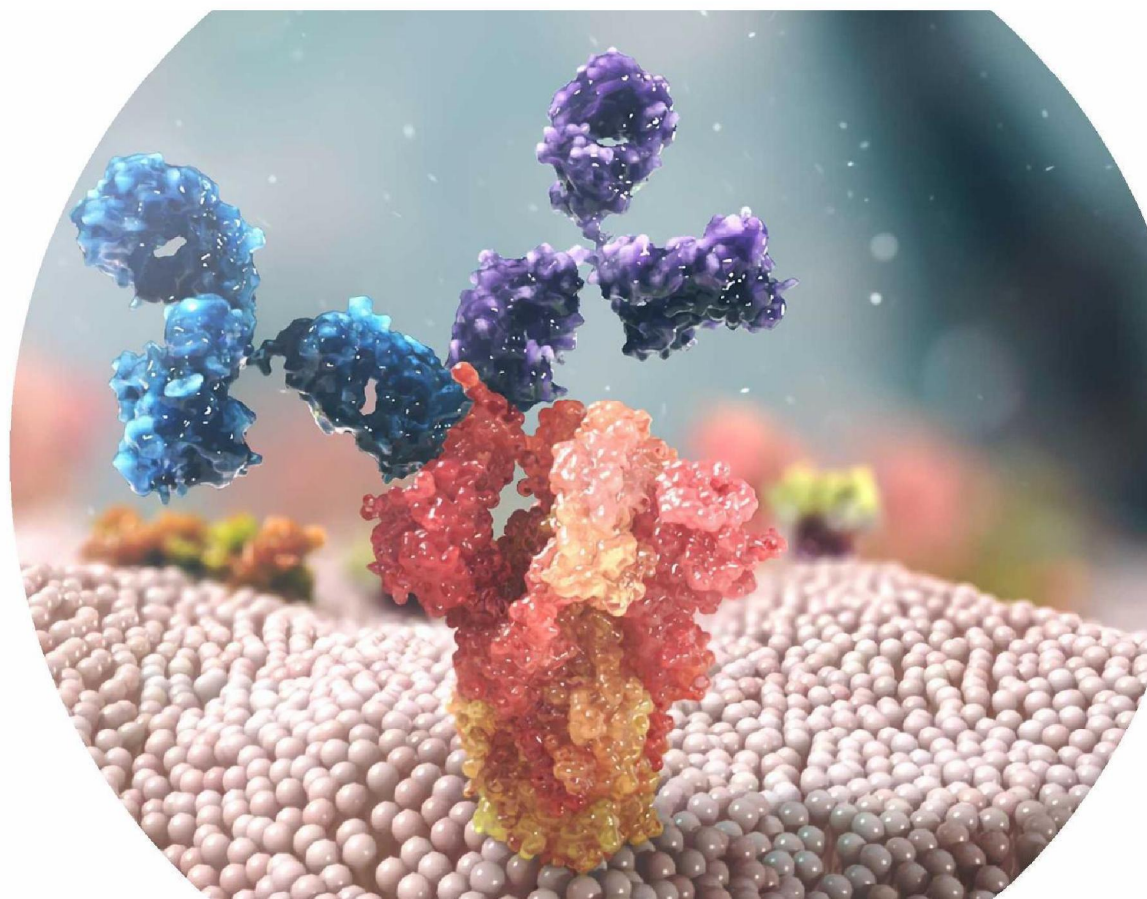
Meeting Dutch
Ministry Covid
Medicine
Taskforce &
AstraZeneca

AstraZeneca COVID-19
Long-Acting Neutralizing
Antibody Combination

8 December 2020

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Confidential



Agenda

- 1** Introductions & meeting purpose 5'
- 2** AZD7442 COVID-19 Long-Acting Neutralizing Antibody Combination 45'
 - Development update
 - Manufacturing update
 - Q&A
- 3** Interest in 2021 supply & next steps 10'



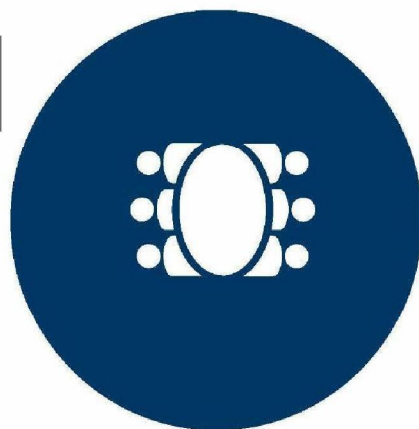
Dutch Ministry

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AstraZeneca

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AZD7442
Development update



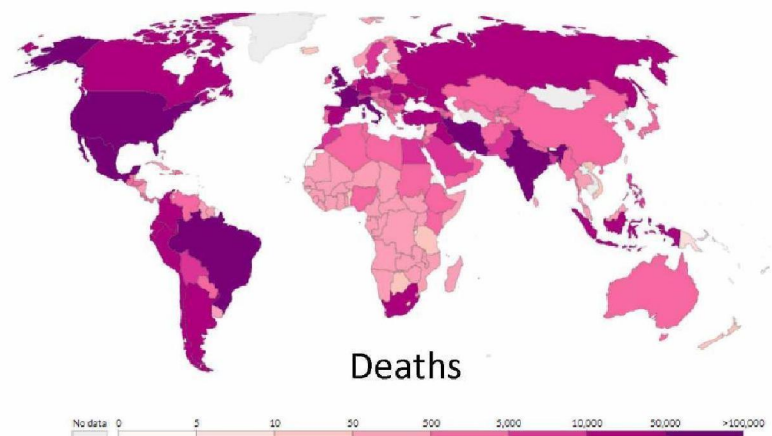
COVID-19 has significantly impacted global public health and economies, and is here to stay

Cumulative confirmed COVID-19 deaths, Dec 6, 2020

Limited testing and challenges in the attribution of the cause of death means that the number of confirmed deaths may not be an accurate count of the true number of deaths from COVID-19.

Our World
In Data

World



Source: Johns Hopkins University CSSE COVID-19 Data - Last updated 7 December, 06:06 (London time), Our World In Data

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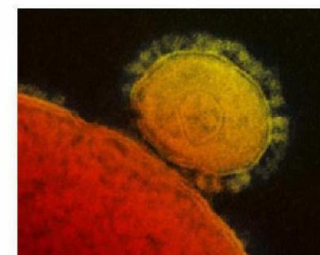
More than 65 million cases¹
 Over 1.3 million deaths^{1,2}
 \$76.7 billion global GDP loss³
 \$11 trillion in fiscal measures³

1. World Health Organization. <https://www.who.int/emergencies/diseases/novel-coronavirus-2019>. Accessed 07 December 2020.
2. Our world in data. <https://ourworldindata.org/covid-deaths>. Accessed 06 Dec 2020
3. Statista. <https://www.statista.com/topics/6139/covid-19-impact-on-the-global-economy>. Accessed 27 October 2020.

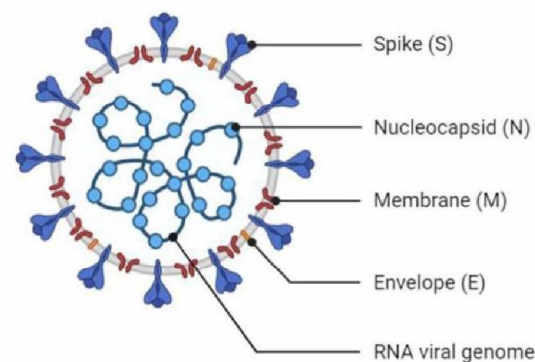
Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2)

SARS-CoV-2 infection causes COVID-19

- “Corona” refers to the “crown-like” appearance of the virus due to the S spike proteins
 - The S protein is a target for mAb and vaccine development
- Single stranded (+) RNA virus
 - Mutations occur at rate ~1-2 every 14+ days
- Seasonal strains: 229E, NL63, OC43 and HKU1
 - Endemic and cause ~30% of seasonal upper respiratory infections (5-10% in adults) generally benign
 - First identified in humans in the 1960’s
- SARS and MERS
 - 2002-03 Severe Acute Respiratory Syndrome (SARS) outbreak
 - Middle East Respiratory Syndrome outbreak since 2012

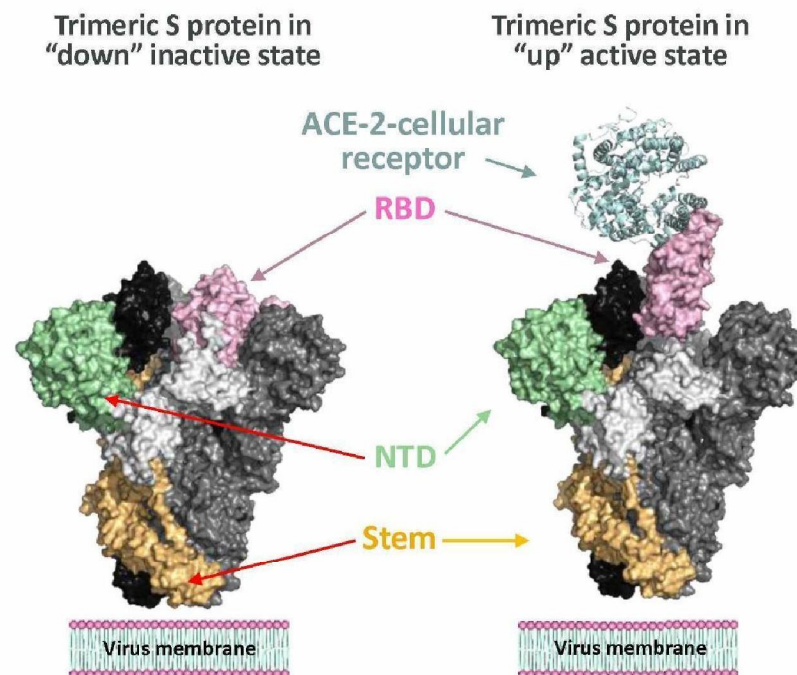


Transmission electron micrograph Frederick National Laboratory

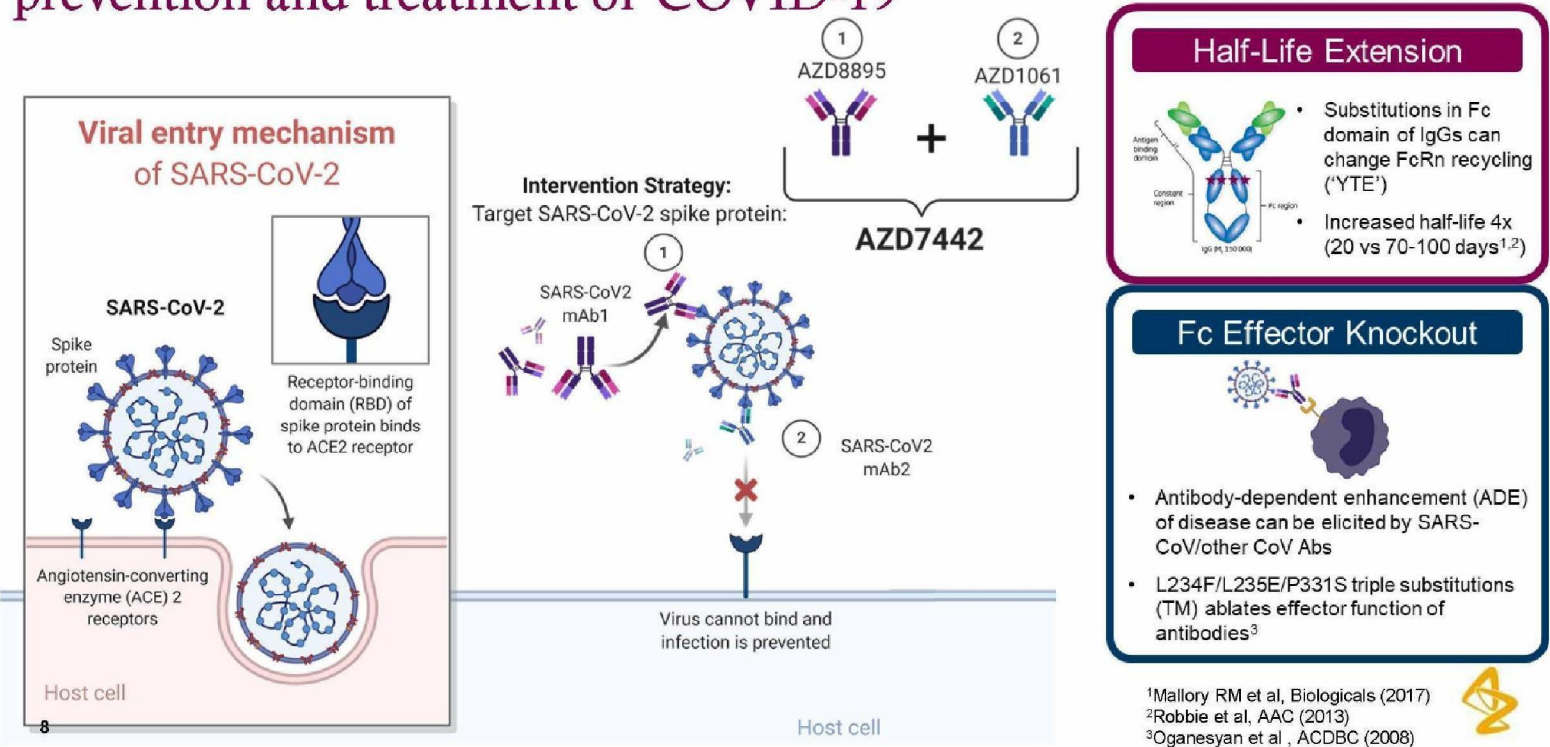


Spike protein is the primary target for COVID-19 mAb and vaccine development

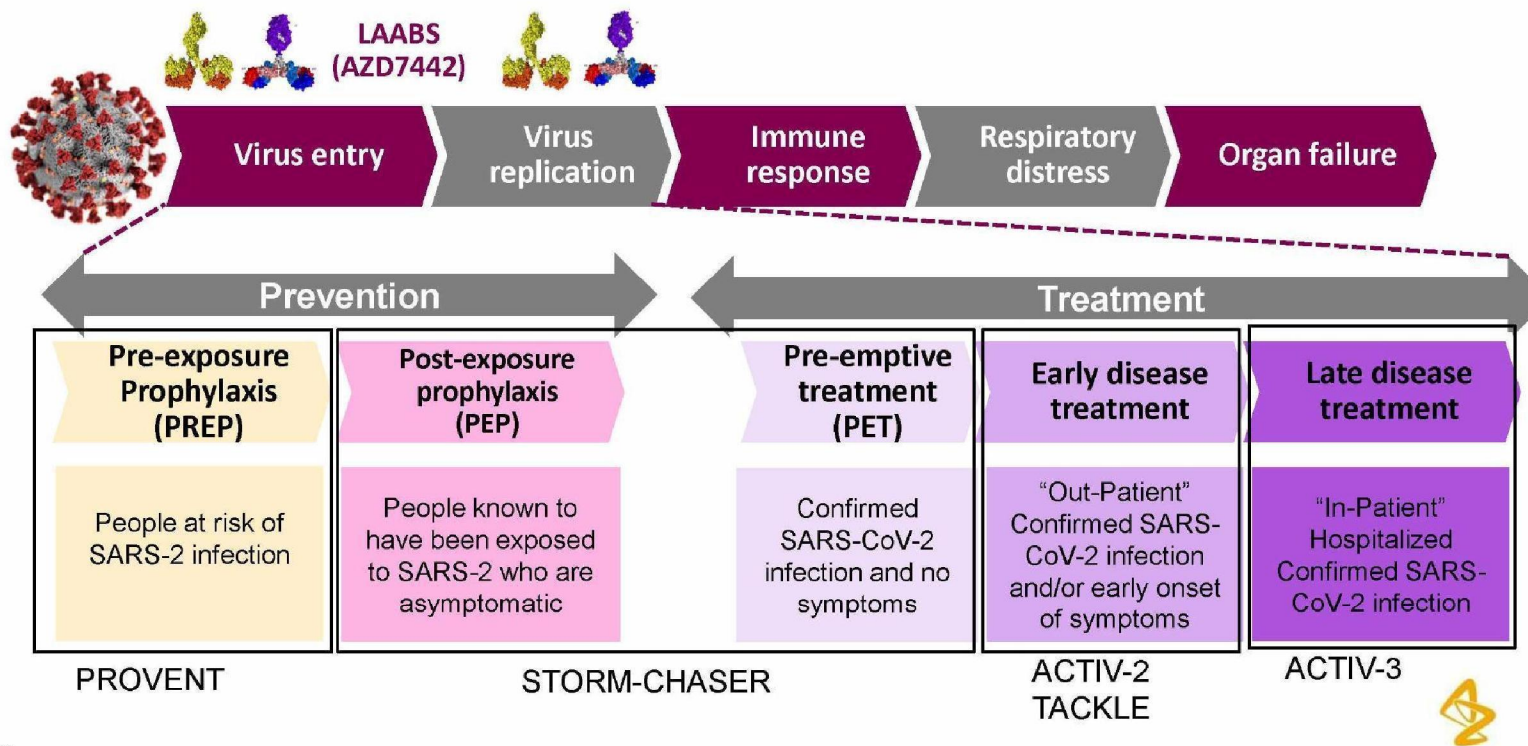
- Spike (S) protein is responsible for binding and fusion to host cell membrane
- Spike receptor binding domain (RBD) binds to the host cellular receptor ACE-2
- Multi-step conformation change required for ACE-2 receptor binding
- Most SARS and MERS neutralizing Abs target major domains of the spike protein



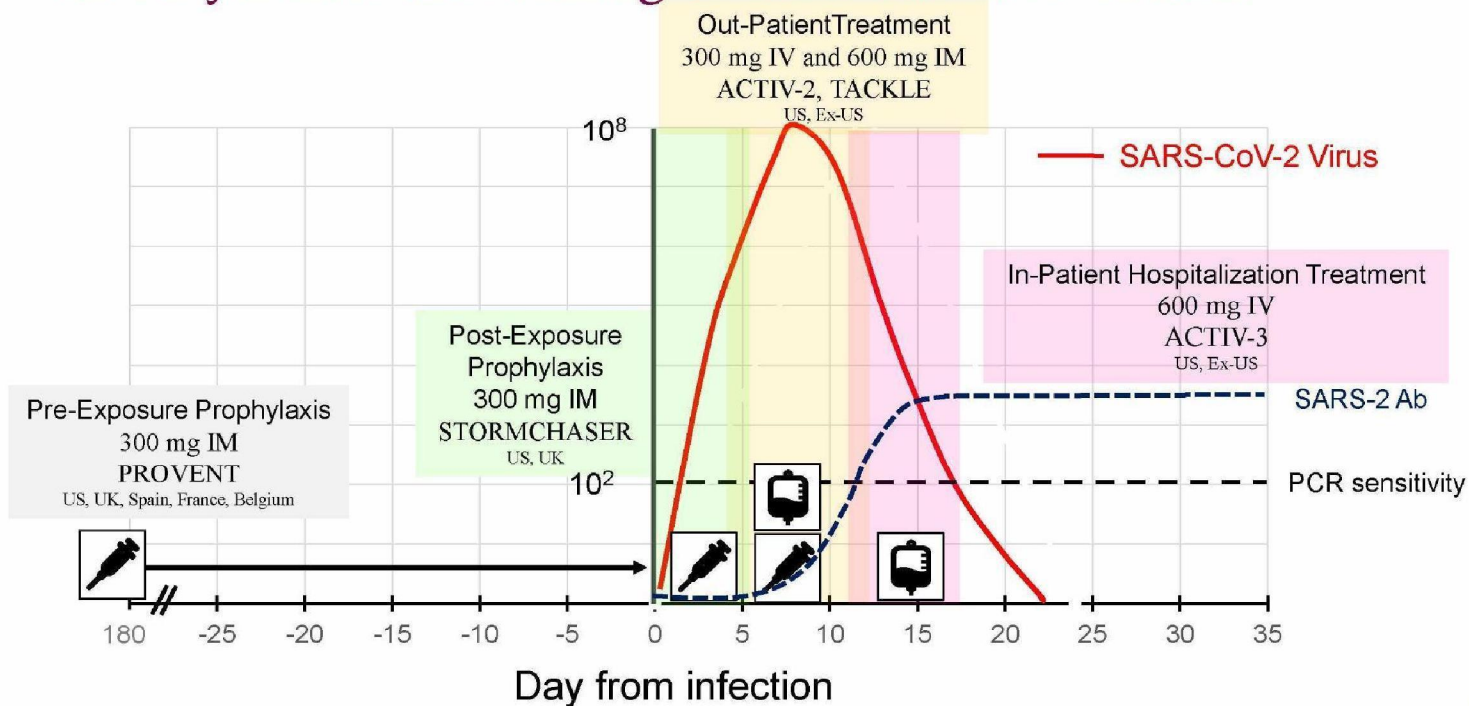
AZD7442: a long-acting monoclonal antibody combination for prevention and treatment of COVID-19



Prevention and treatment studies

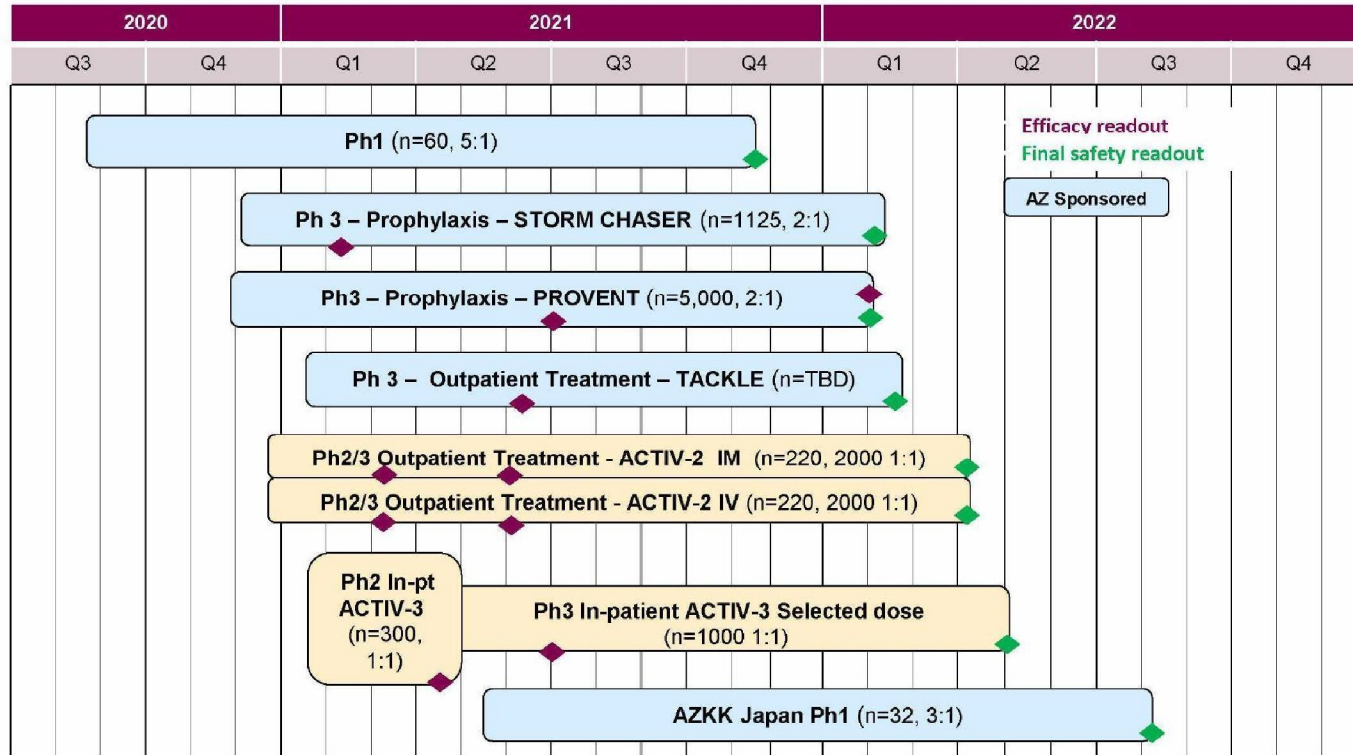


Viral Dynamics and Timing of Different Interventions

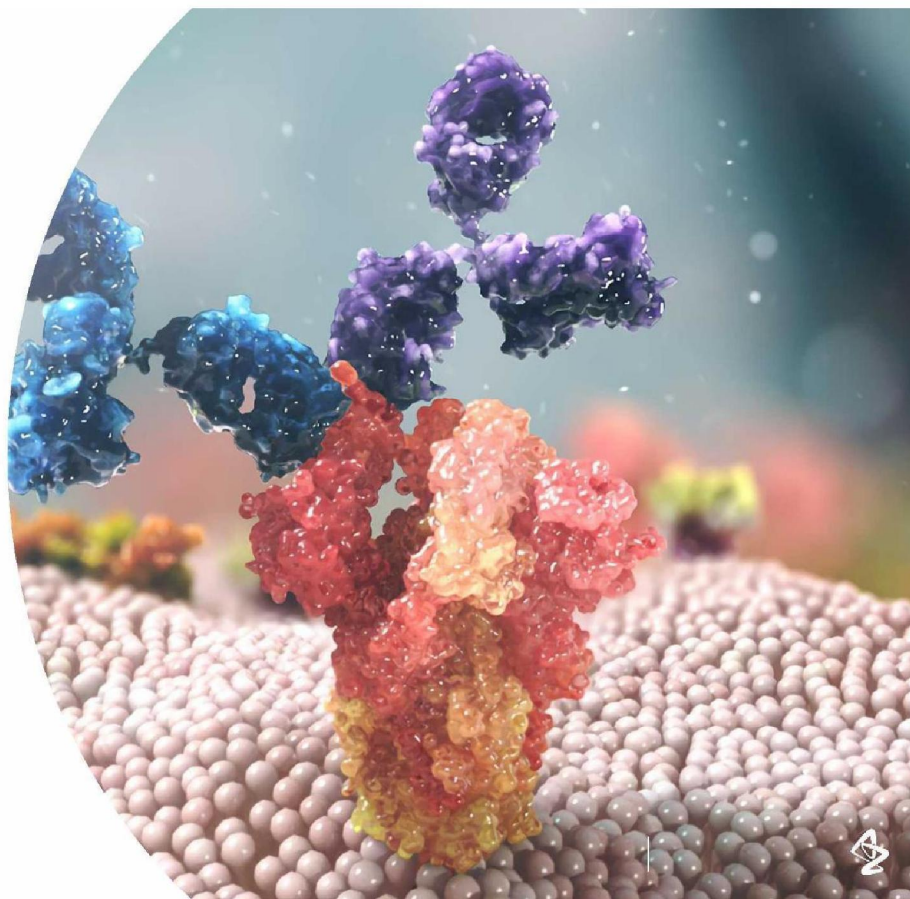


AZD7442 Summary of Projected Global Clinical Studies

7 Dec 2020 update



Pre-clinical Research



AZD8895 and AZD1061 simultaneously bind to unique, non-overlapping epitopes on the spike protein RBD

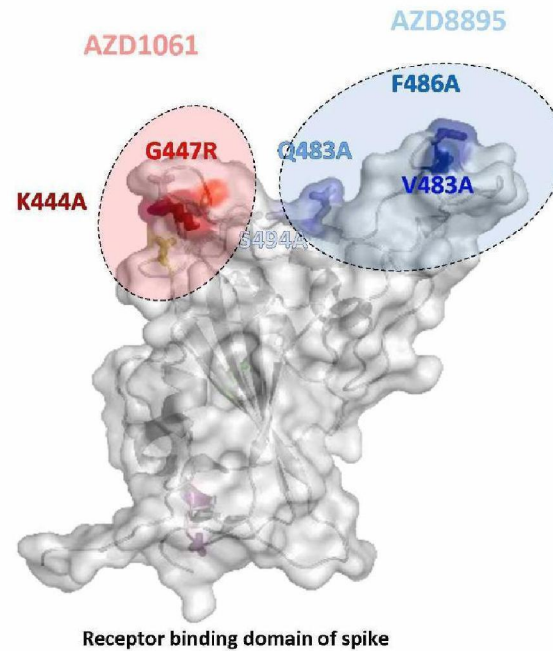
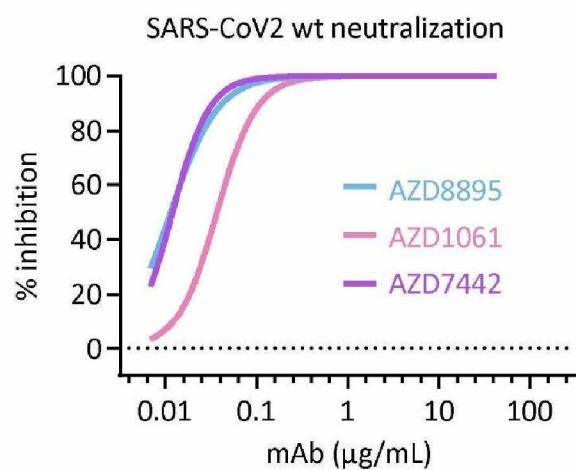


Figure reproduced with permission from Zost SJ et al. Potently neutralizing and protective human antibodies against SARS-CoV-2. Nature 2020; 584: 443–449.

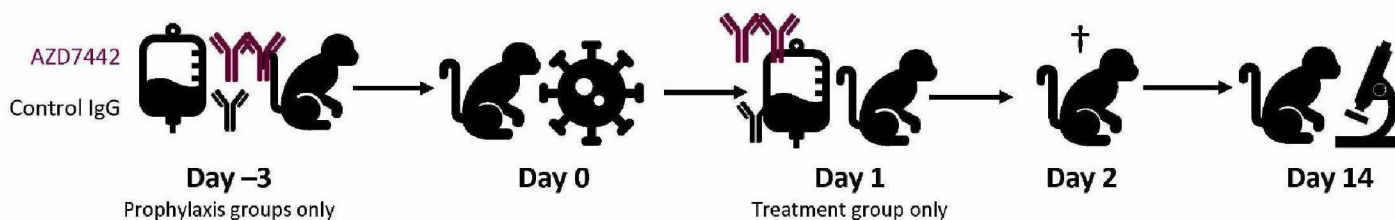
AZD8895 and AZD1061 are highly potent neutralizing antibodies



mAb	Pseudovirus (IC ₅₀ ng/mL)	Live virus neutralization assay		
		Vanderbilt (IC ₅₀ ng/mL)	USAMRIID (IC ₅₀ ng/mL)	UMD (IC ₉₉ ng/ml)
AZD8895	0.2	32	12.4	2.9
AZD1061	1.2	115	36.6	3.4
AZD7442 (1:1)	0.1	26	11.9	2.3

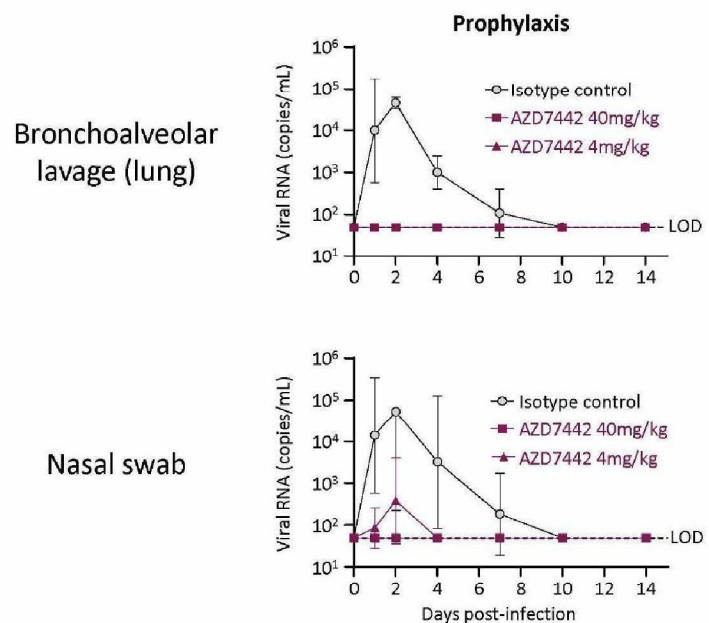
Prophylaxis or treatment with AZD7442 protects rhesus monkeys from SARS-CoV-2 infection

- Rhesus monkeys
- Prophylaxis groups: mAb administered on Day -3
 - AZD7442 at 40 mg/kg (N=3) or 4 mg/kg (N=4)
 - Isotype mAb at 40 mg/kg (N=3)
- 1×10^5 TCID₅₀ SARS-CoV-2 was used to infect animals via the intranasal *and* intratracheal route on Day 0
- Treatment group: 40 mg/kg AZD7442 administered on Day 1 (N=4)
- One animal in AZD7442 and control groups were euthanized and necropsied on Day 2
- PK and viral loads measured through day 14



Data on file.

AZD7442 protects non-human primates from SARS-CoV-2 infection in prophylaxis and treatment

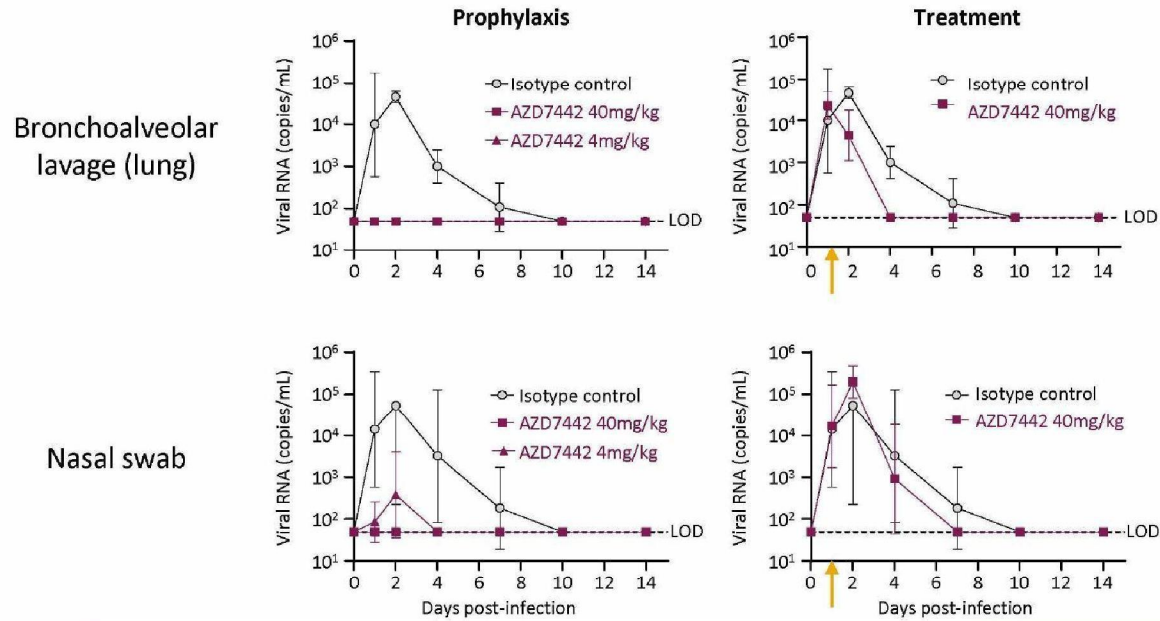


Prophylaxis: AZD7442 administered 3 days prior to infection

Treatment: AZD7442 administered 1 day after infection (↑)

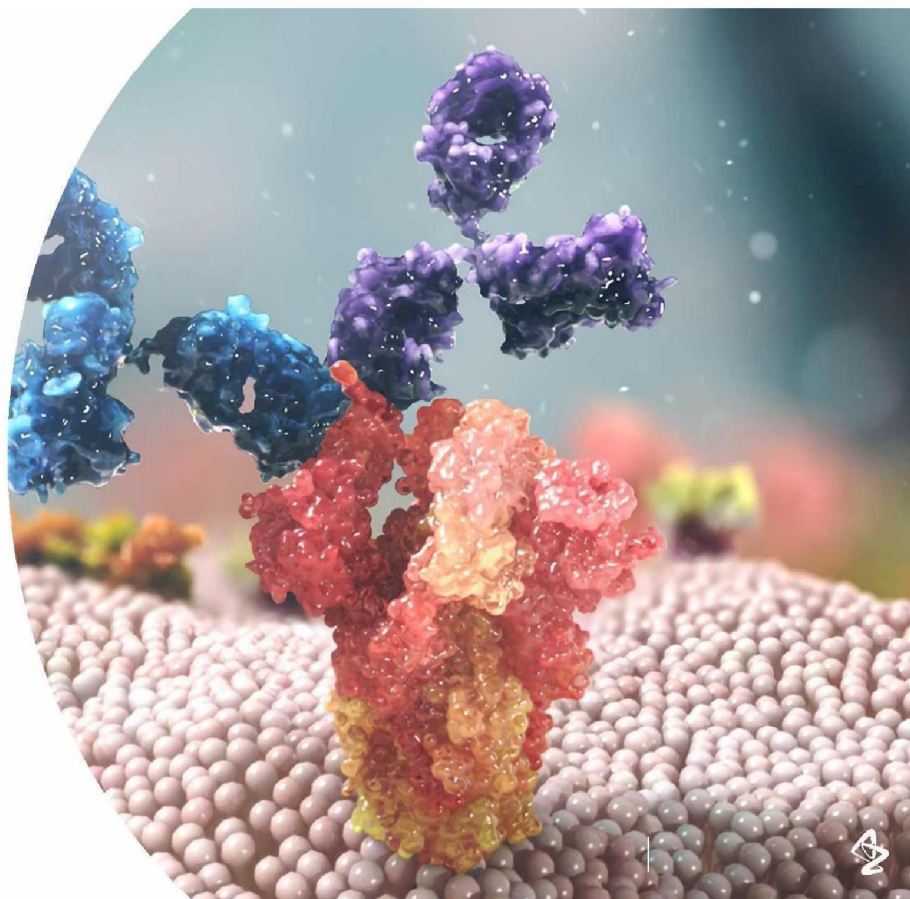
Data on file. Draft Report MCBS7442-0006

AZD7442 protects non-human primates from SARS-CoV-2 infection in prophylaxis and treatment

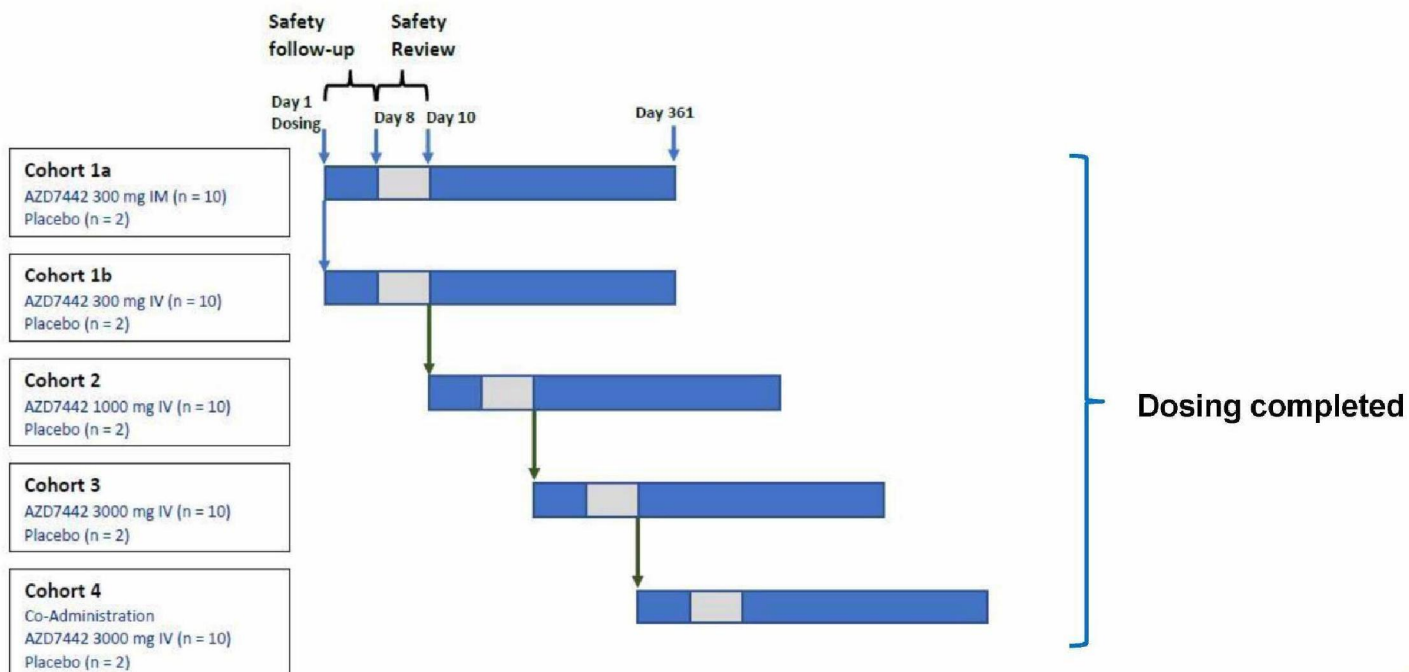


Prophylaxis: AZD7442 administered 3 days prior to infection **Treatment:** AZD7442 administered 1 day after infection (↑)

AZD7442:
Phase 1 Clinical
Study



AZD7442 Phase 1 Study Design



06 Dec 2020

AZD7442 Global Phase 1 Study: Safety

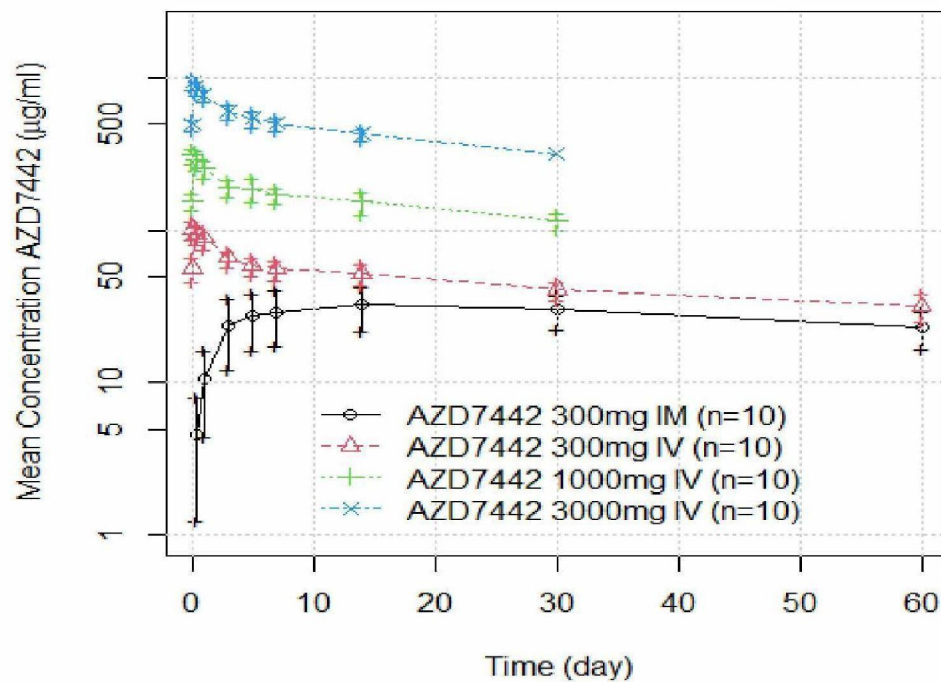
- Second Interim Analysis (27 Nov 2020): Safety
 - Approx. 3 months follow-up for 300 mg IM and IV cohorts
 - 7 Days follow-up for 3,000 mg co-administered
- Observations:
 - No SAEs
 - All observed AEs of mild or moderate severity
 - No hypersensitivity reactions
 - No injection site reactions
 - No infusion reactions
 - No imbalance between placebo and active treatment arms



06 Dec 2020

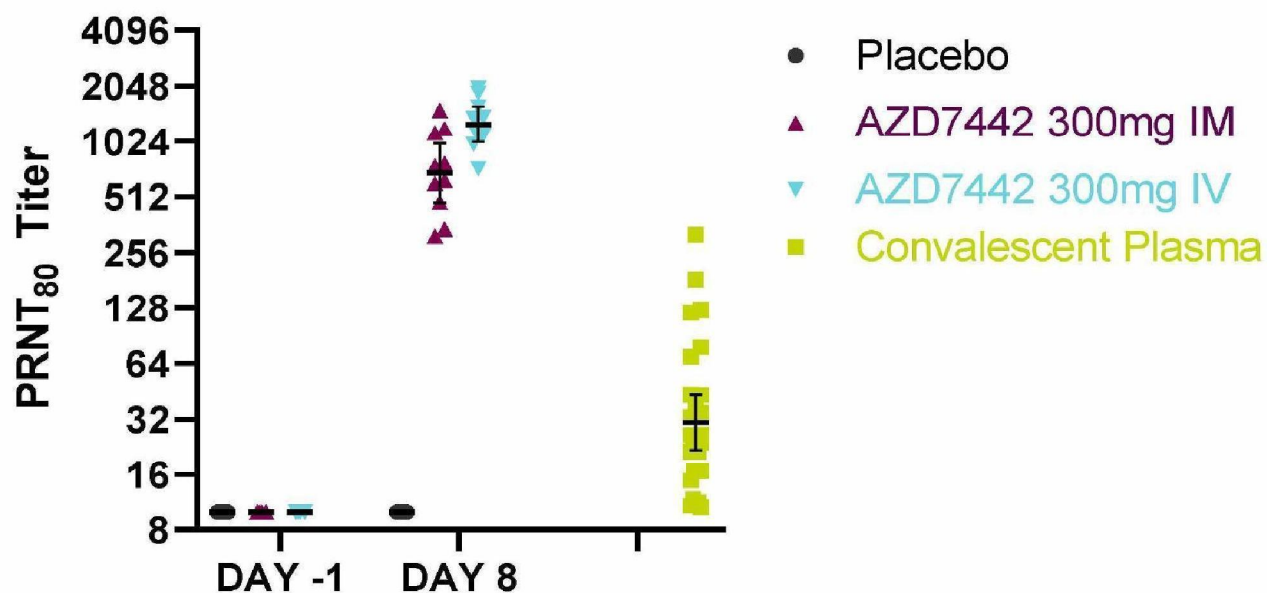
AZD7442 Global Phase 1 Study: PK

Second Interim Analysis (27 Nov 2020): PK

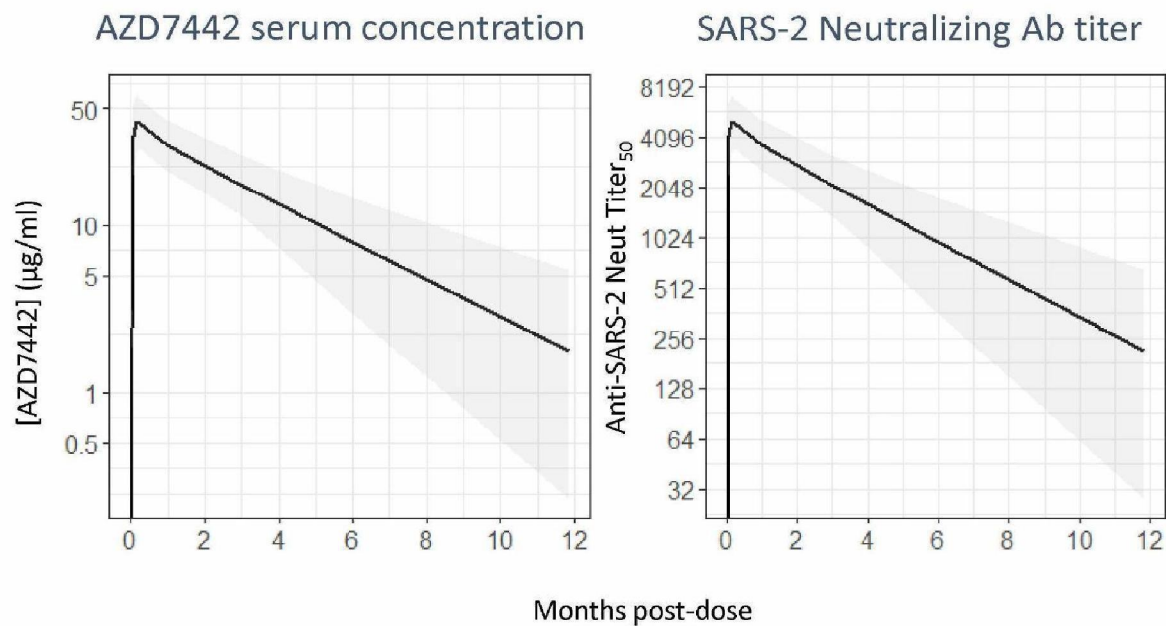


High levels of neutralizing antibodies observed in serum after 300mg IM and 300mg IV AZD7442 dosing

nAb Titers from AZD7442 Phase 1 study in a validated live SARS-CoV-2 PRNT₈₀ assay



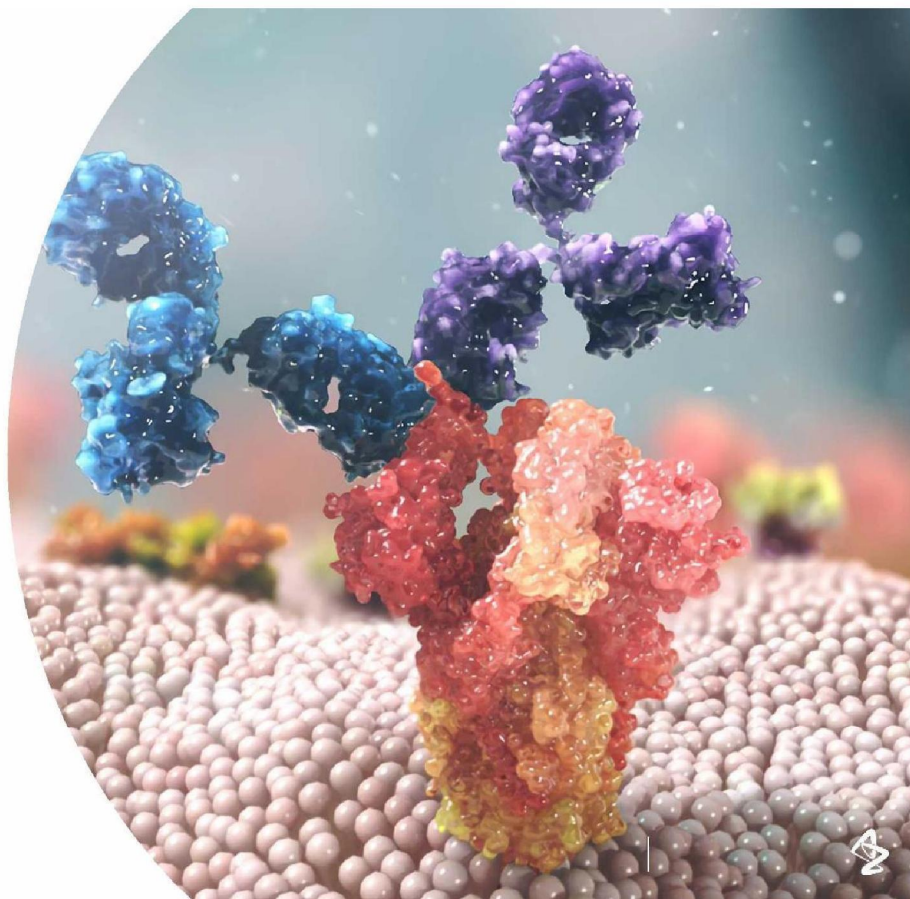
Predicted serum AZD7442 concentration and anti-SARS-2 CoV-2 neutralizing Ab titers over time following a single dose administration of 300 mg IM AZD7442



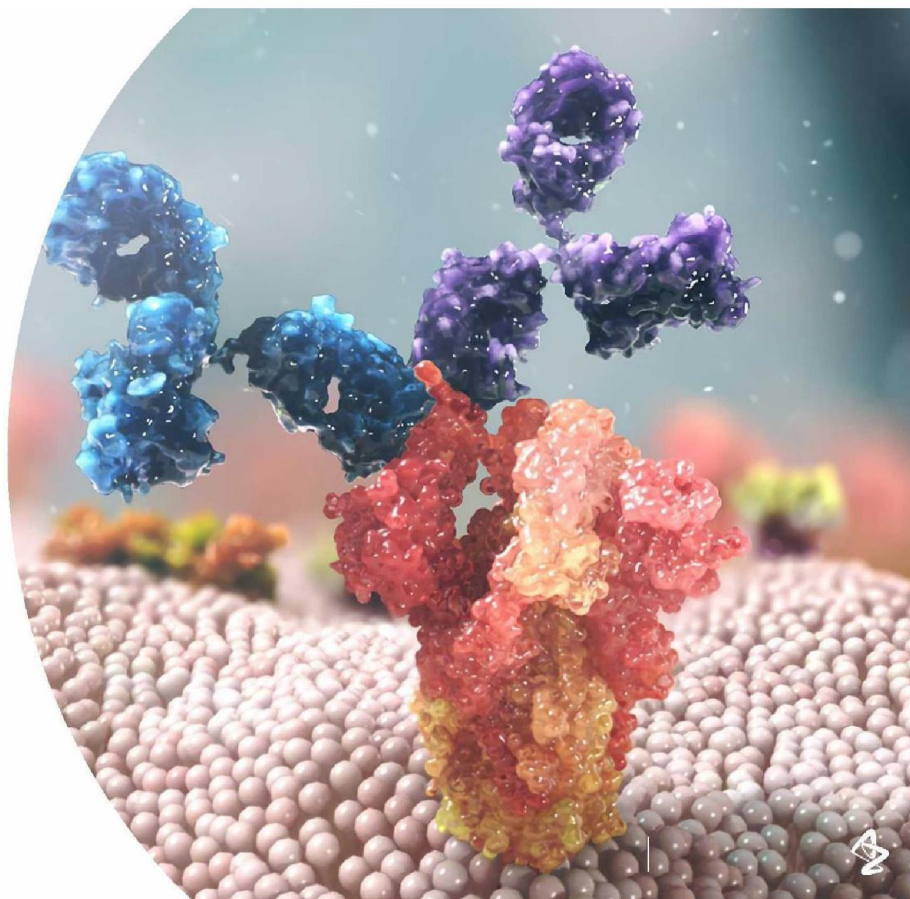
AZD7442
Manufacturing update



Questions &
discussion?



Thank you



PROVENT Patient Population

Adults ≥ 18 years of age who are candidates for benefit from passive immunization with antibodies:

1. Having increased risk for inadequate response to active immunization (predicted poor responders to vaccines), OR
 2. Having increased risk for SARS CoV 2 infection, defined as those whose locations or circumstances put them at appreciable risk of exposure to SARS-CoV-2 and COVID-19
- **Cohort 1: Adults ≥ 60 years of age. Of these, 40 to 60% will be residents of long-term care facilities.** All such participants will be considered as being at increased risk for inadequate response to active immunization on the basis of age (presumed immunosenescence). Cohort 1 will be capped, not to exceed 65% of total participants randomized. **Stratified by residence in LTCF or not.**
 - **Cohort 2: Adults < 60 years of age. Of these, 40 to 60% will be enrolled on the basis of being at increased risk of SARS-CoV-2 infection** due to location or circumstances that put them at appreciable of infection. Cohort 2 will be capped, not to exceed 50% of total participants randomized. **Stratified by risk of exposure to infection with SARS-CoV-2**



STORMCHASER Patient Population

- Adults ≥ 18 years of age with ***potential exposure to a specific identified individual with laboratory-confirmed SARS-COV-2 infection***, symptomatic or asymptomatic, who are therefore at appreciable risk of imminently developing COVID-19
- **Cohort 1: Adults ≥ 60 years of age, living in long term care facilities**
 - In this context, includes skilled nursing facilities, assisted living facilities, and independent living facilities for senior adults
 - Cohort 1 will be capped, not to exceed 80% of total participants
- **Cohort 2: Other adults ≥ 18 years of age with potential exposure** to a specific identified individual SARS-COV-2 infection
 - May include, but are not limited to those living in institutional residences (military lodging, dormitories, etc.), household contacts, health care workers, long term care facility workers, and workers in occupational or industrial settings in which close contact is common
 - Cohort 2 will be capped, not to exceed 50% of total participants

