VLA2001: COVID-19 Vaccine (inactivated, adjuvanted) Valneva

Extraordinary Meeting of the Strategic Advisory Group of Experts (SAGE) on Immunization

11 AUG 2022

valneva

Disclaimer

This presentation does not contain or constitute an offer of, or the solicitation of an offer to buy or subscribe for, Valneva SE shares to any person in any jurisdiction.

The information given in this presentation is confidential and is being provided on condition that it is kept in confidence in accordance with the confidentiality provisions of agreements in force between Valneva and the receiving persons or organizations.

All proposals set out in this presentation are non-binding and are made for discussion purposes only. Any legally binding transaction is subject to prior approval by Valneva's Management and Supervisory Boards.

This presentation includes only summary information and does not purport to be comprehensive. Any information in this presentation is purely indicative and subject to modification at any time. Valneva does not warrant the completeness, accuracy or correctness of the information or opinions contained in this presentation. None of Valneva, or any of their affiliates, directors, officers, advisors and employees shall bear any liability for any loss arising from any use of this presentation.

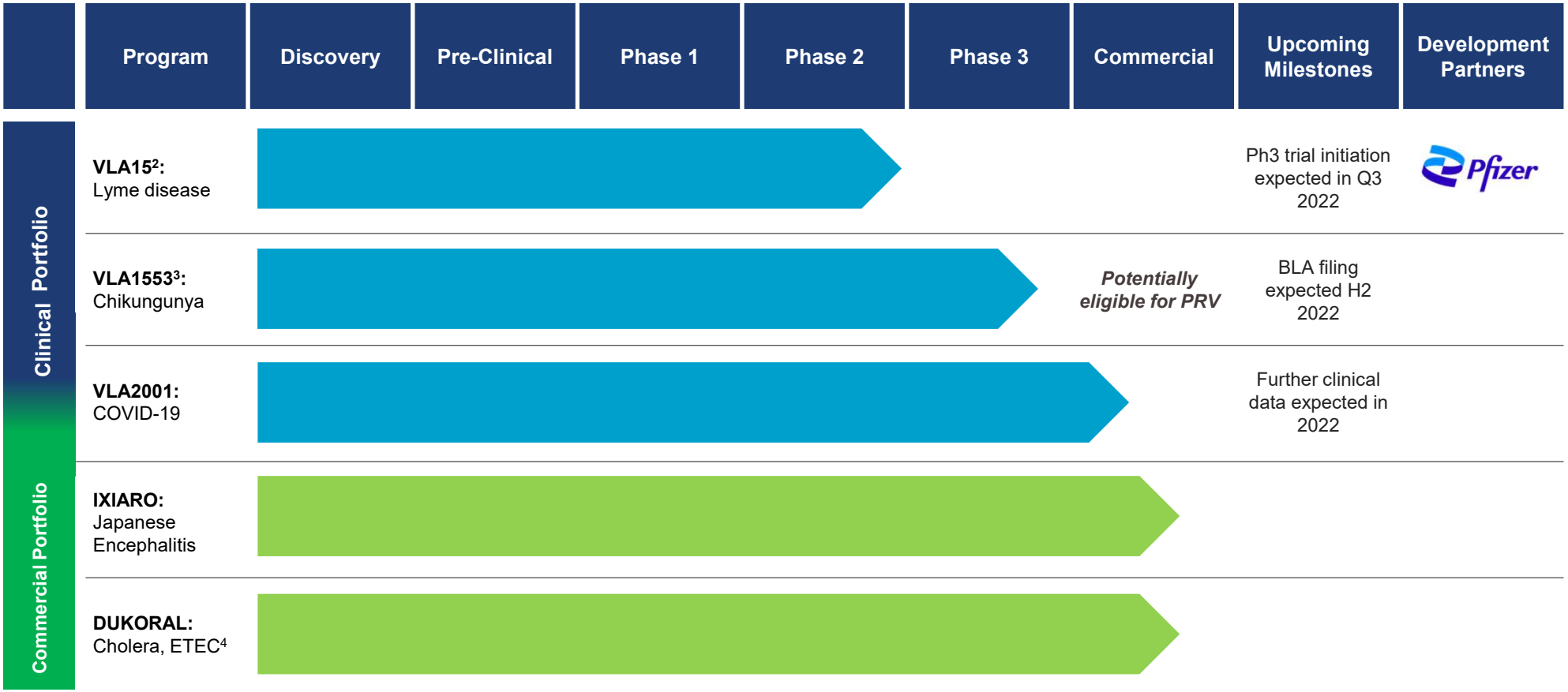
Valneva in Summary

Fully integrated specialty vaccine company focused on development and commercialization of **prophylactic vaccines for infectious diseases** with significant unmet medical need

- **Highly specialized and targeted approach to development of unique prophylactic vaccines**
- **Advanced pipeline of differentiated clinical-stage assets** designed to address large target populations
- **Highly experienced leadership team with vaccine development and regulatory expertise;** clear demonstrated ability of rapidly moving new vaccines through the clinic to commercialization
- **Highly developed, nimble and sophisticated manufacturing infrastructure**
- **Specialist sales infrastructure: two commercialized vaccines; distribution rights for third-party vaccines**

- **Total revenues of €348.1 million in 2021, compared to €110.3 million in 2020**
- **Strong cash position of €311.3 million at March 31, 2022**

Valneva has an Advanced Clinical Pipeline and Three Approved Products[1]



[1] As of June 24, 2022, VLA2001 has received emergency use authorization in Bahrain and in the United Arab Emirates, as well as Conditional Marketing Authorization in the UK and standard marketing authorization in Europe. [2] VLA15 received Fast Track designation from the FDA. [3] VLA1553 received Fast Track designation from the FDA, PRIME designation from the European Medicines Agency and is also potentially eligible for a U.S. Priority Review Voucher. [4] Indications differ by country - Please refer to Product / Prescribing Information (PI) / Medication Guide approved in your respective countries for complete information, incl. dosing, safety and age groups in which this vaccine is licensed, ETEC = Enterotoxigenic Escherichia coli (E. Coli) bacterium

How can Valneva's inactivated whole-virus COVID-19 vaccine help to address ongoing gaps in COVID-19 public health ?

PROBLEM

- Despite achieving worldwide good VCRs, **billions of people have not been vaccinated** – in part as they **remain hesitant** based on current vaccine options
- Vaccination strategy has led to **decreased hospitalization and death rates**, but…
- effectiveness against **emerging variants is not guaranteed**

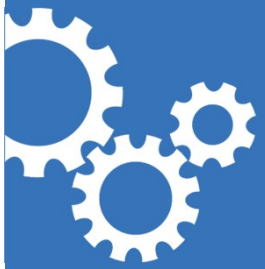
SOLUTION

+ **VLA2001** is the only **licensed inactivated whole-virus vaccine in Europe** (18-50 yoa)
+ **Broader immunity beyond S-protein** to combat against future variants
+ **Improved willingness to vaccinate** the hard-to-reach populations with inactivated platform
+ Evidence points to **enhanced effectiveness of heterologous boosting** vs homologous setting
+ Work initiated on development of a **bi-valent vaccine candidate**

VLA2001 has the potential to meet ongoing and future unmet medical needs

VLA2001 is currently the only inactivated, whole-virus against COVID-19 licensed in Europe

The vaccine candidate VLA2001 uses **well-established technology**…

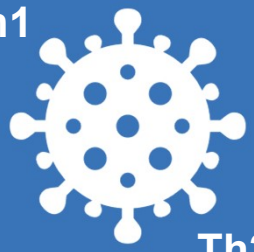


…which may help address vaccine

…is **well tolerated** with a good and **well-defined safety profile**…

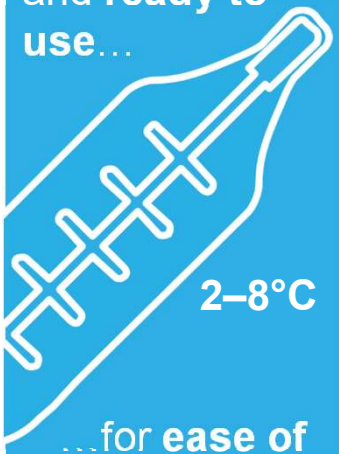
…which **may improve vaccine uptake**…

…provides robust and **broad protection**…



…with the potential to **protect against future variants…**

…is **thermostable** and **ready to use**…

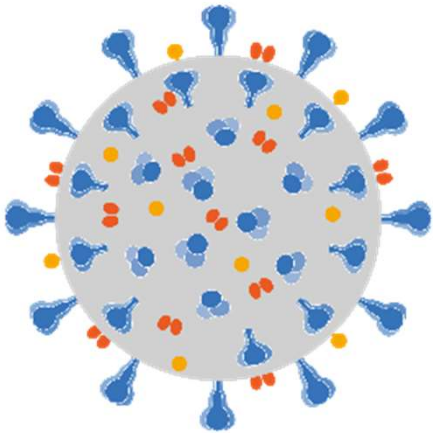


…for **ease of storage** and **handling**…

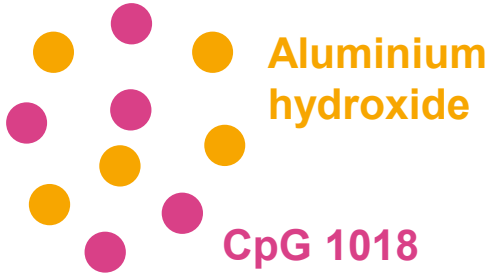
…and is **manufactured in Europe** using existing infrastructure…

…ensuring **reliable scale-up and supply**

The vaccine candidate VLA2001 uses an inactivated vaccine platform based on established vaccine technology



Inactivated whole-virus particles of COVID-19 with high S-protein density[1]



Dual adjuvant system enhances robustness of immune response[1–4]

Established vaccine technology may offer reassurance and increase vaccine uptake in non-vaccinated populations[5]

The vaccine candidate VLA2001 is produced on Valneva's established Vero cell platform, leveraging manufacturing technology for Valneva's licensed Japanese encephalitis vaccine[1]

S, spike.

1. Valneva press release. Available from: https://valneva.com/press-release/valneva-initiates-rolling-review-with-ema-and-provides-updates-on-its-covid-19-vaccine-program-vla2001/; 2. Bode C, et al. Expert Rev Vaccines 2011; 10(4):499–511; 3. Ulanova M, et al. Infect Immun 2001; 69(2):1151–9; 4. Nanishi E et al. Sci Transl Med 2022;14:eabj5305; 5. Goh S BMJ 2022; 376:o48.

Inactivated vaccines have a well-established safety record and mild reactogenicity profile

Inactivated vaccine technology has been used for **>100 years** and has led to **numerous successful human vaccines**[1,2]

+ Used to prevent infectious diseases such as polio, hepatitis A, influenza, rabies and Japanese encephalitis[2]
+ Meta-analyses of vaccine safety (6 studies) showed risk of serious AE after ≥1 dose was lower with COVID-19 inactivated vaccines vs. mRNA vaccines[3]

Valneva's licensed Japanese encephalitis vaccine, which uses the **same inactivated virus technology as the vaccine candidate VLA2001**,[4] has been in use for **13 years**[5]

Good safety profile in clinical trials and post-marketing use[6]

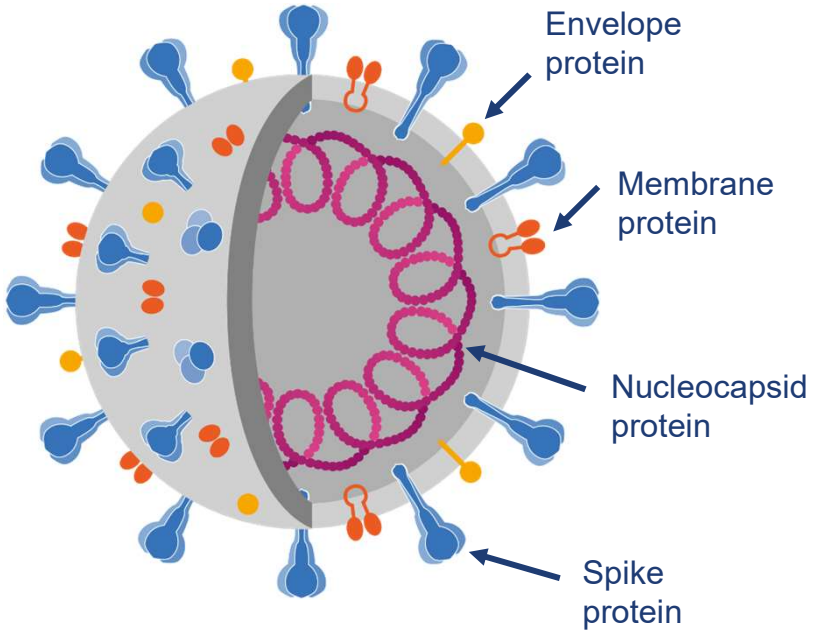
+ Low rate of serious AEs in clinical trials
  - › 2% of all subjects
+ Adverse drug reactions reported for only 1.6/100,000 doses distributed
+ No serious allergic reactions in 12-mo post-marketing period

AE, adverse event.

1. Pollard J & Bijker E.M. Nature Rev Immunol 2021;21:83–100; 2. Plotkin S. PNAS 2014;111(34):12283–87; 3. Fan Y, et al. Vaccines 2021; 9(9):989. 4. Data on file (Valneva Austria GmbH. SARS-CoV-2 vaccine 2.5 Clinical Overview. 16 Dec 2021); 5.Firbas A & Jilma B. Hum Vaccin Immunother 2015; 11(2):411–420. 6. Schuller E, et al. Vaccine 2011; 29(47):8669–76.

Whole inactivated virus has the potential to provide broader immunity against COVID-19 variants

The vaccine candidate VLA2001 contains **whole inactivated virus** with a **preserved envelope and structural proteins**[1,2]



Whole inactivated COVID-19 virus[4]

+ Multiple proteins may elicit a **broad immune response**[2]
+ This may help to **combat future variants**, even if the **S protein has mutated**[3]
+ Vaccine candidate VLA2001 is **potentially adaptable** to new and emerging **variants**[2]

S, spike.
1. Valneva press release. Available from: https://valneva.com/press-release/valnevas-inactivated-covid-19-vaccine-candidate-shown-to-neutralize-omicron-variant/ ; 2. Valneva press release. Available from: https://valneva.com/press-release/valneva-initiates-rolling-review-with-ema-and-provides-updates-on-its-covid-19-vaccine-program-vla2001/; 3. Poland G, et al. Vaccine 2021; 39(31):4239–41; 4. Adapted from: Florindo HF, et al. Nature Nanotech 2020; 15:630–45.

Dual adjuvant system may enhance robustness of immune response

Two adjuvants act synergistically, stimulating **two types of immune response: cellular and humoral**[1–3]

CpG 1018

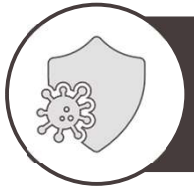
Component of a well-established US FDA- and EMA-approved hepatitis B vaccine[4]

Stimulates **cellular (Th1)** immune responses via TLR-9 activation[2]

Aluminum hydroxide

Widely used in vaccines for >70 years[3]

Stimulates **humoral (Th2)** immune responses[3]



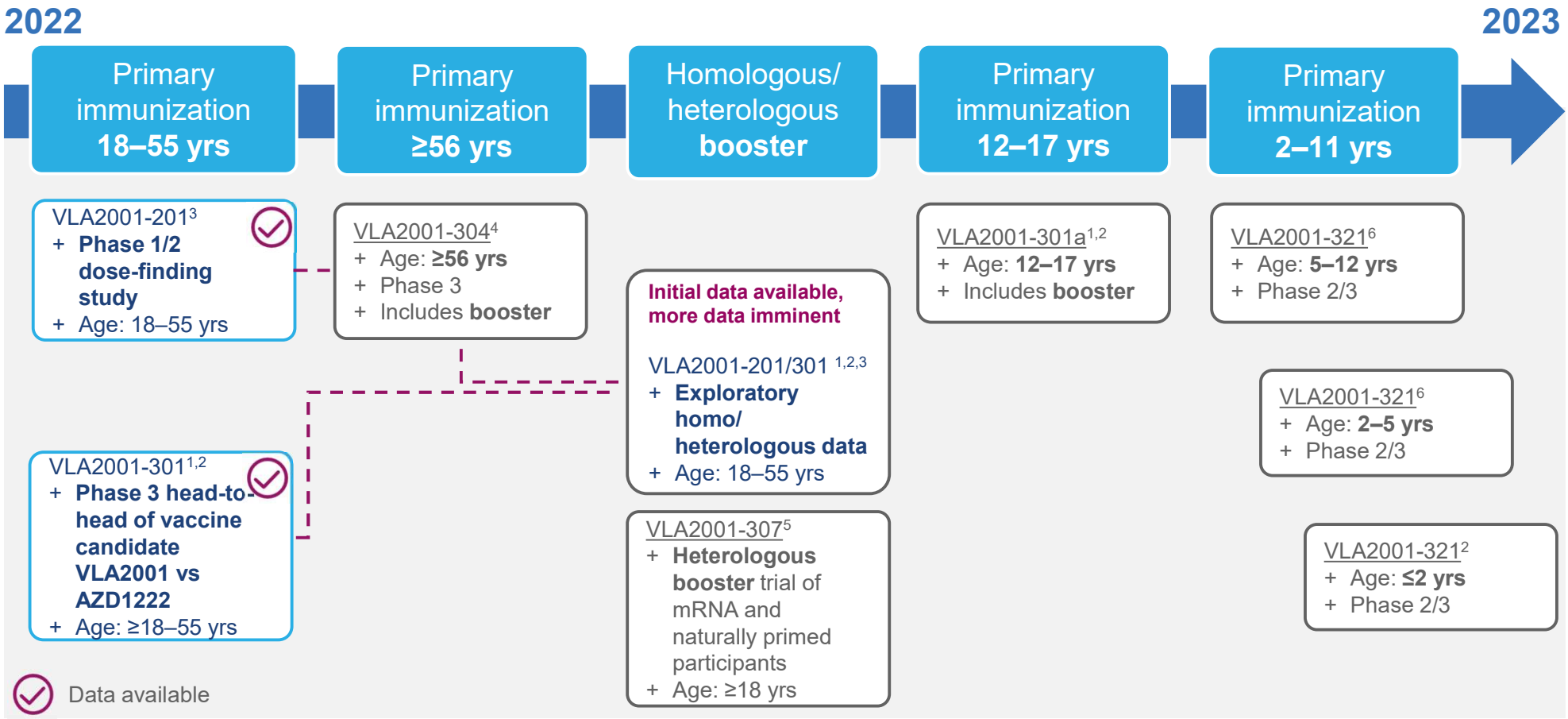
Alum:CpG adjuvants shown to promote **stronger immune response**[1,5]

Both adjuvants have a **track record of use** and a **strong safety record**[3–5]

Alum, aluminum hydroxide; EMA, European Medicines Agency; FDA, Food and Drug Administration; Th, T helper cell; TLR, Toll-like receptor.

1. Nanishi E, et al. Sci Transl Med 2022; 14:eabj5305; 2. Bode C, et al. Expert Rev Vaccines 2011; 10(4):499–511; 3. Ulanova M, et al. Infect Immun 2001; 69(2):1151–9; 4. Dynavax. Available from: https://investors.dynavax.com/node/17231/pdf (accessed Mar 2022); 5. Petrovsky N. Drug Saf 2015; 38:1059–74.

Overview of clinical trial data for vaccine candidate VLA2001



1. ClinicalTrials.gov: NCT04864561. Available from: https://clinicaltrials.gov/ct2/show/NCT04864561 (accessed Mar 2022); 2. Data on file; 3. ClinicalTrials.gov: NCT04671017. Available from: https://clinicaltrials.gov/ct2/show/NCT04671017 (accessed Mar 2022); 4. ClinicalTrials.gov: NCT04956224. Available from: https://clinicaltrials.gov/ct2/show/NCT04956224 (accessed Mar 2022); 5. Valneva press release. Available from: https://valneva.com/press-release/valneva-announces-positive-homologous-booster-data-for-inactivated-adjuvanted-covid-19-vaccine-candidate-vla2001/; 6. ClinicalTrials.gov: NCT05298644. Available from: https://clinicaltrials.gov/ct2/show/NCT05298644 (accessed Apr 2022).

Phase 3 trial showed VLA2001 is highly immunogenic

VLA2001 is **highly immunogenic across all tested age groups**

VLA2001 met both co-primary endpoints* vs. AZD1222, demonstrating:

Superior geometric mean titre for neutralisation antibodies at Day 43

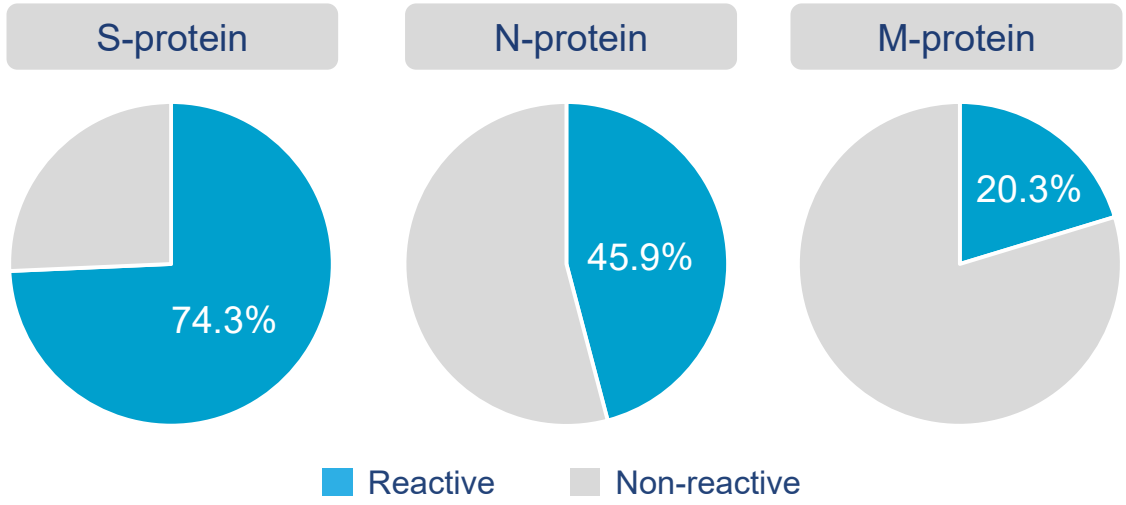
+ **GMT ratio = 1.39 (P<0.0001)**

	VLA2001	AZD1222
GMT	803.5	576.6
95% CI	748.5, 862.6	543.6, 611.7

Non-inferior seroconversion rate at D43

+ **>95% in both treatment groups**

VLA2001 induced **broad antigen-specific IFN-gamma-producing T-cells** reactive against S, N and M-proteins

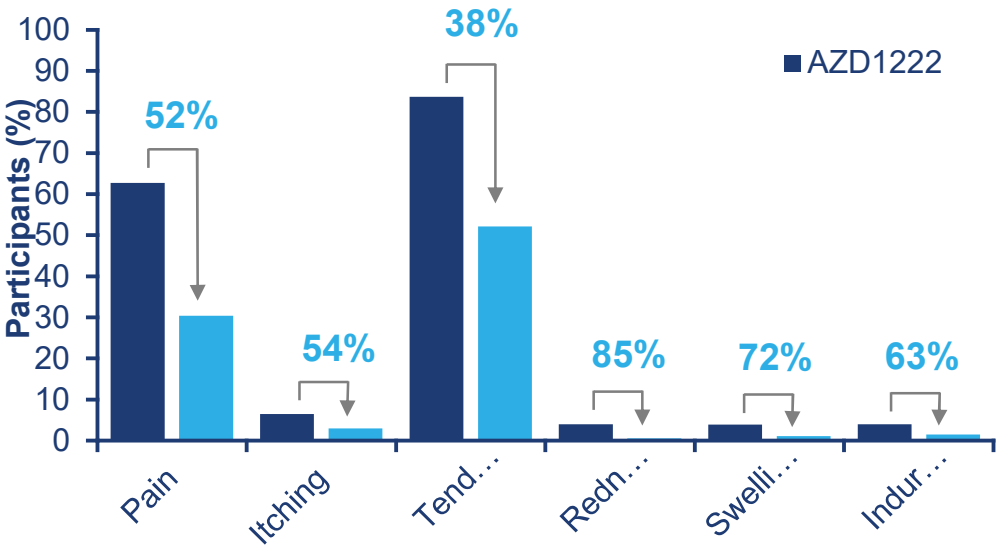


*Primary endpoints were assessed for adults aged ≥30 years.
GMT, geometric mean titre; IFN, interferon; M, membrane; N, nucleocapsid; S, spike.
Valneva press release. Available from: https://valneva.com/press-release/valneva-reports-positive-phase-3-results-for-inactivated-adjuvanted-covid-19-vaccine-candidate-vla2001/.

Phase 3 trial showed that VLA2001 has more favourable reactogenicity profile vs. AZD1222

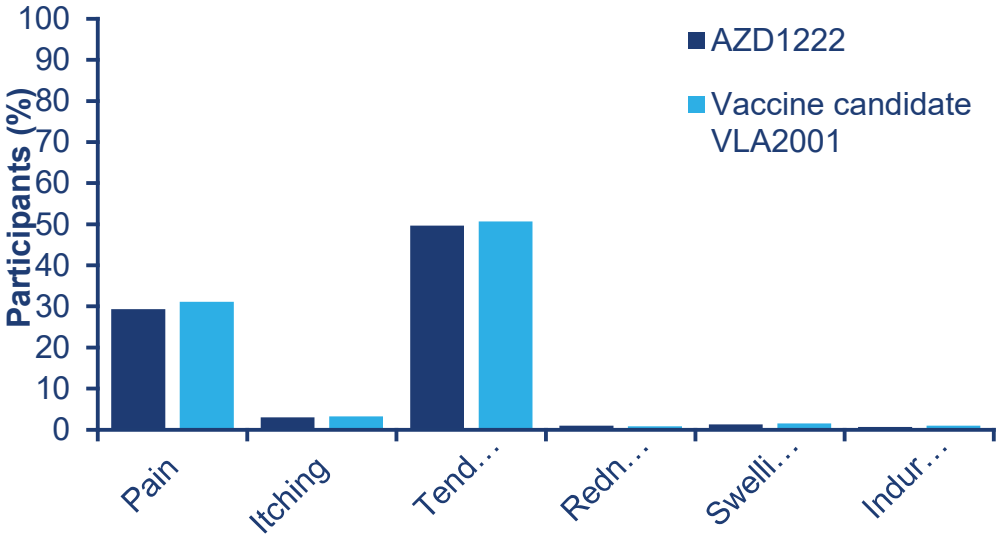
Reactogenicity profile significantly more favourable vs. AZD1222 in participants aged 30–55 years

Solicited injection site reactions 7 days after first vaccination



38–85% reduction in solicited injection site reactions vs. AZD1222 after first vaccination

Solicited injection site reactions 7 days after second vaccination



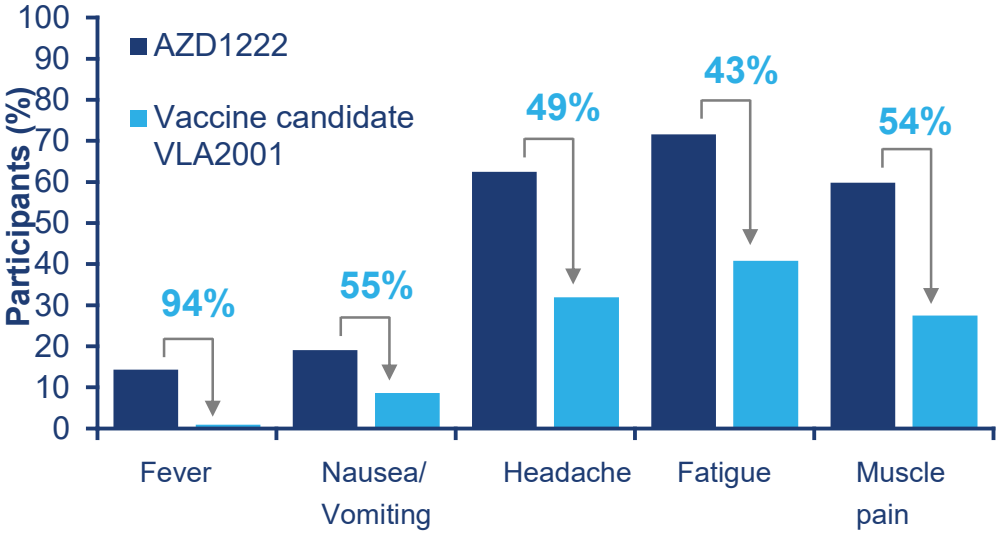
Comparable reactogenicity profile vs. AZD1222 after second vaccination

Data on file (Valneva Austria GmbH. SARS-CoV-2 vaccine 2.5 Clinical Overview. 16 Dec 2021).

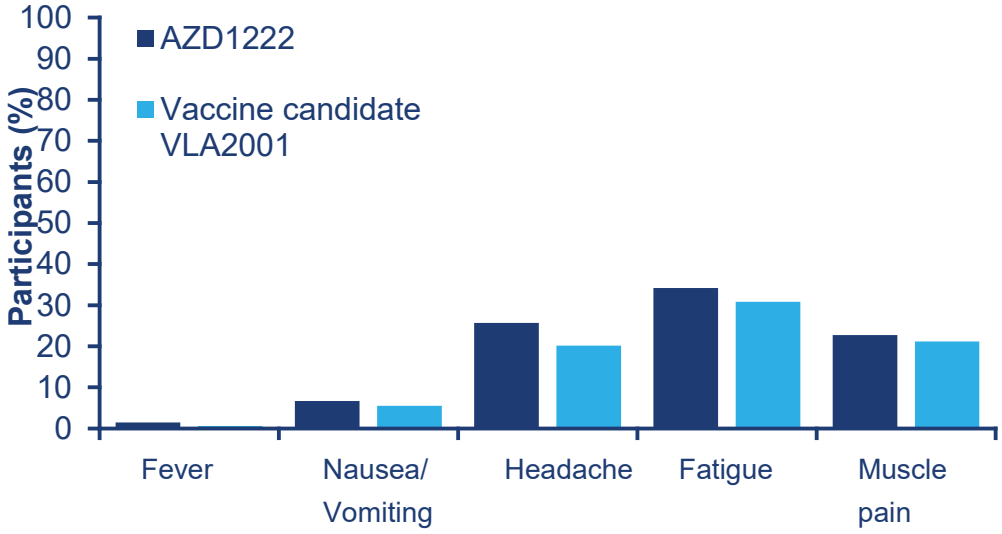
Phase 3 trial showed that VLA2001 has more favourable tolerability profile vs. AZD1222

Tolerability profile significantly more favourable vs. AZD1222 in participants aged 30–55 years

Solicited systemic reactions 7 days after first vaccination



Solicited systemic reactions 7 days after second vaccination



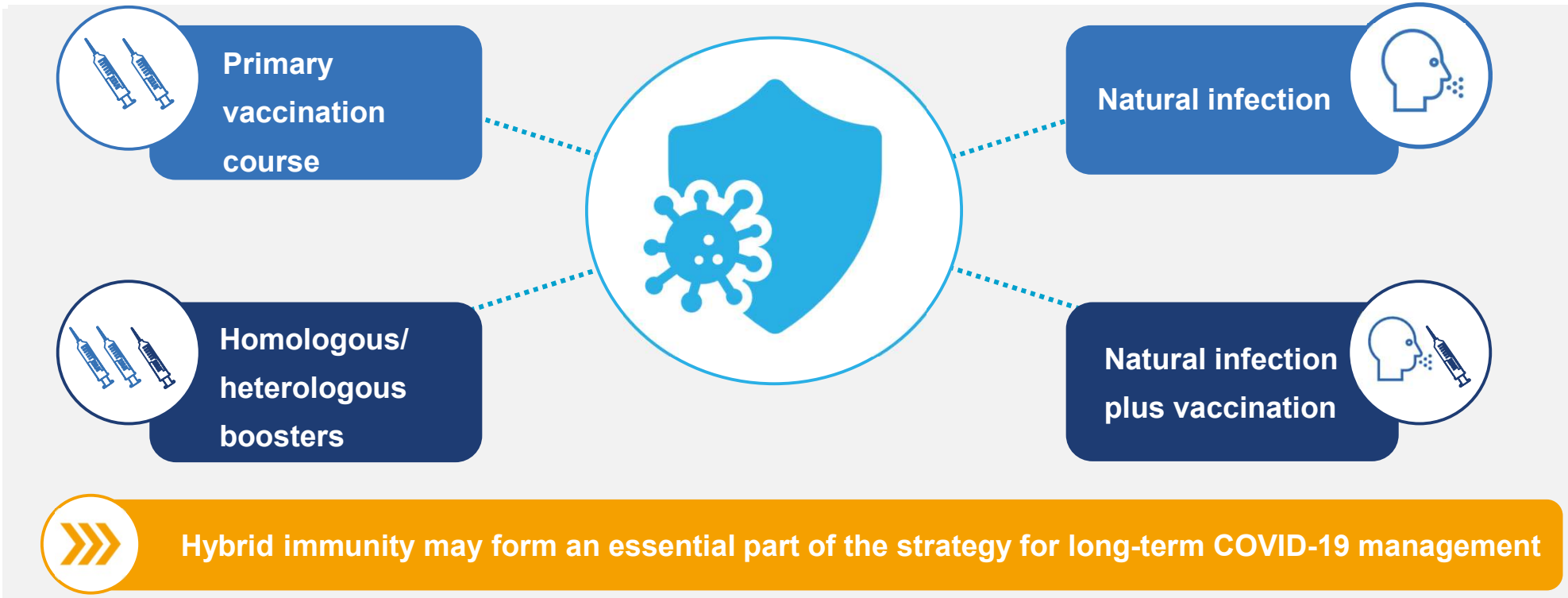
43–94% reduction in solicited systemic reactions vs. AZD1222

Comparable tolerability profile vs. AZD1222 after second vaccination

Data on file (Valneva Austria GmbH. SARS-CoV-2 vaccine 2.5 Clinical Overview. 16 Dec 2021).

Duration of COVID-19 immunity varies depending on exposure type; recently demonstrated in large cohort surveillance conducted in Israel

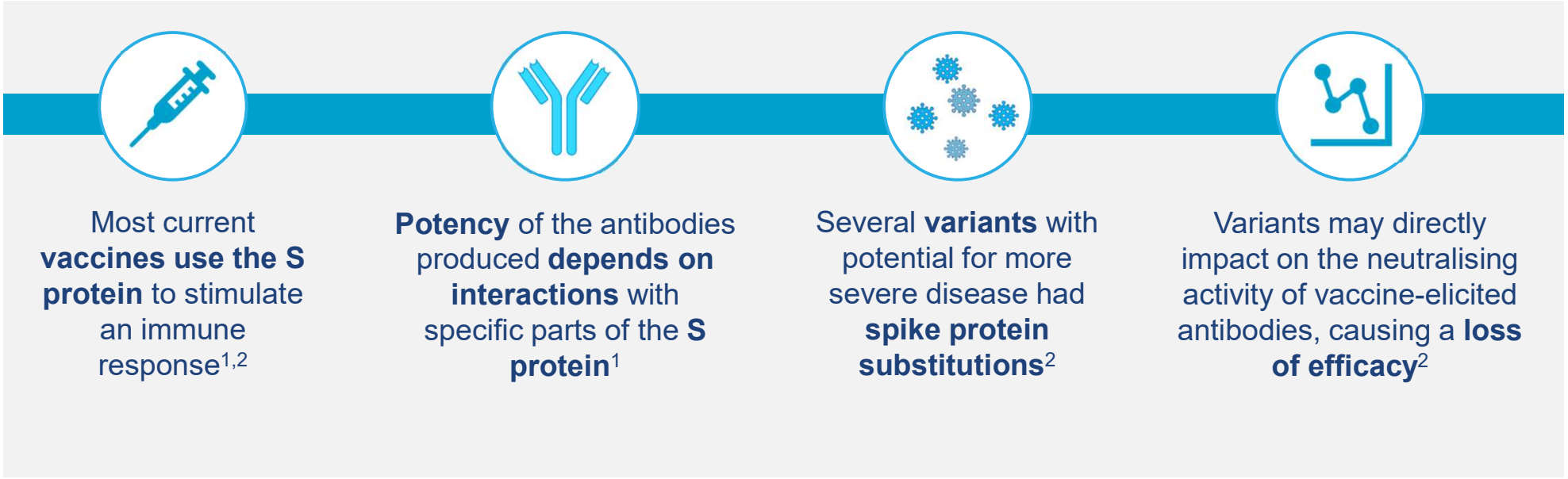
Heterologous boosters can provide a more robust immune response than homologous booster[1,2]
Natural infection boosted by vaccination can last for over 1 year since initial infection[3]



1. Clemens S, et al. Lancet 2022; 399(10324):521–529; 2. Goldberg et al., Protection and Waning of Natural and Hybrid Immunity to SARS-CoV-2, N ENGL J MED, 2022; 3. Hall V, et al. N Engl J Med 2022; 386:1207–1220

New variants provide potential pathways for COVID-19 to escape immunity produced by vaccines

Improving effectiveness against future variants is vital,[1,2] which means that vaccines that provide broad immunity and do not rely on the S protein alone are needed



Most current **vaccines use the S protein** to stimulate an immune response[1,2]

Potency of the antibodies produced **depends on interactions** with specific parts of the **S protein**[1]

Several **variants** with potential for more severe disease had **spike protein substitutions**[2]

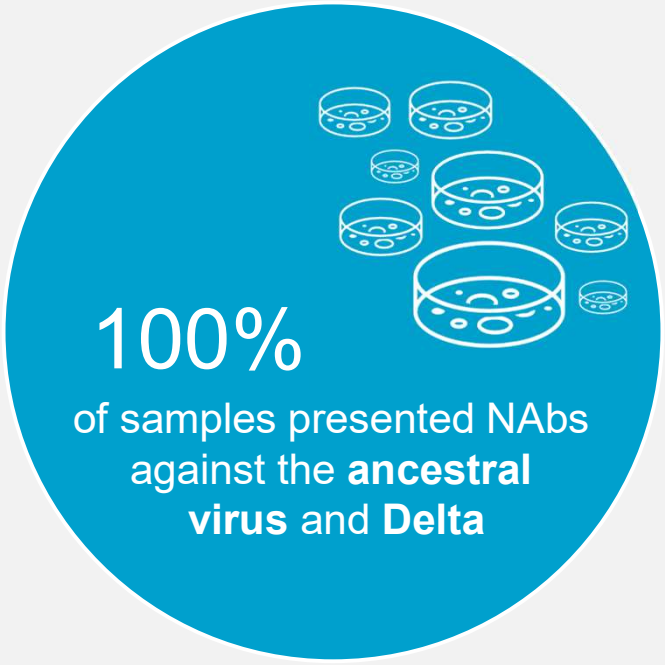
Variants may directly impact on the neutralising activity of vaccine-elicited antibodies, causing a **loss of efficacy**[2]

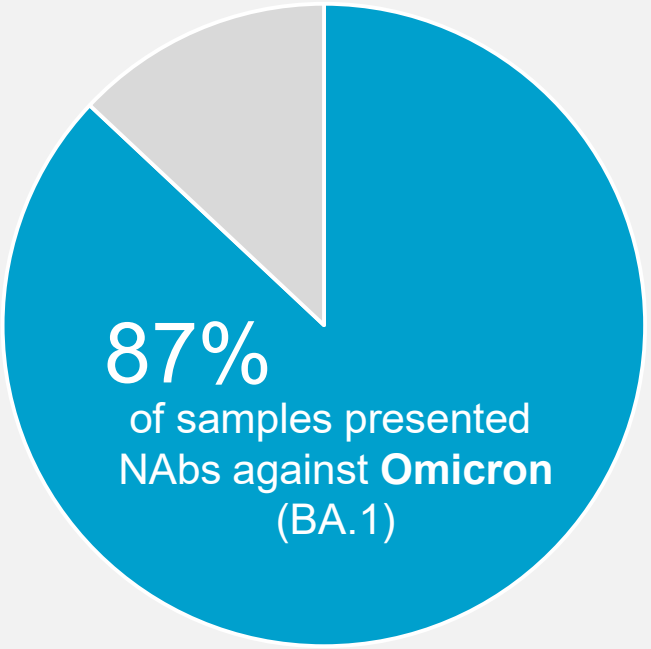
S protein, spike protein.

1. Heinz FX, Stiasny K. NPJ Vaccines 2021; 6(1):104; 2. Sharun K et al. Hum Vaccine Immunother 2021; 17(10):3491–4.

VLA2001 has potential to provide protection against emerging variants

In the Phase 1/2 trial of participants who had received three doses of the vaccine candidate VLA2001, sera samples presented NAbs against the ancestral COVID-19 virus and emerging variants





NAbs, neutralizing antibodies; VoC, variants of concern.
Valneva press release. Available from: https://valneva.com/press-release/valnevas-inactivated-covid-19-vaccine-candidate-shown-to-neutralize-omicron-variant/.

Thank you.

valneva