VLA2001 Cov-Compare Topline Results

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valneva

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Agenda

1. Introduction
2. Cov-Compare Trial and Topline Results
3. VLA2001 Route to Licensure and Development Plan
4. Closing Remarks

INTRODUCTION

Valneva's Response to the Global COVID-19 Crisis

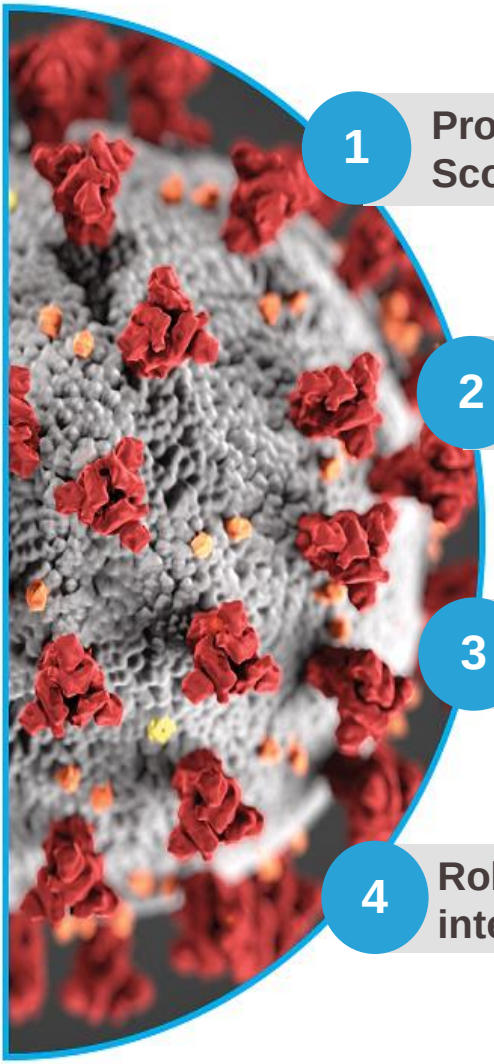
Well-Known Inactivated Approach Based on Proven Technology

VLA2001:

- Inactivated, adjuvanted SARS-Cov 2 whole virus vaccine

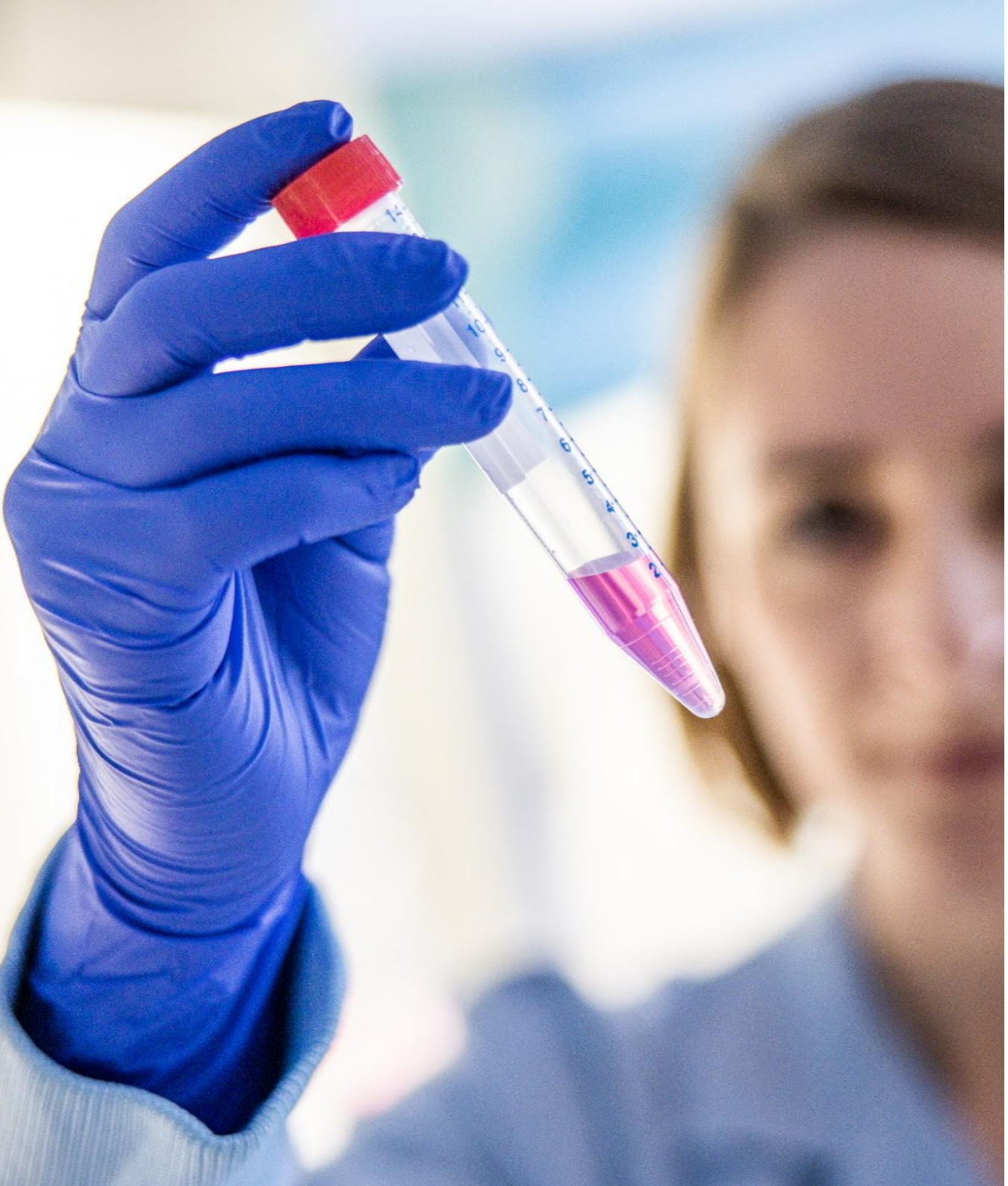
- Intended for active immunization of **at-risk populations** to prevent carriage and symptomatic infection with COVID-19 during the **ongoing pandemic** and potentially **later for routine vaccination,** including addressing **new variants**

VLA2001 – The Only Inactivated Vaccine Against COVID-19 in Clinical Development in Europe



1. Program acceleration enabled through use of Valneva's FDA-registered facility in Scotland, where commercial manufacturing commenced January 2021[1]
2. Combines Valneva's proven expertise with inactivated vaccines and Dynavax's advanced CpG 1018 adjuvant[2]
3. Phase 1/2 clinical trial results reported in April 2021[3]
4. Rolling submission to MHRA commenced in Aug. 2021; Phase 3 "Cov-Compare" results intended to form the basis for potential regulatory approval in adults

Note: Photo credit: CDC/Alissa Eckert, MSMI; Dan Higgins, MAM.**1** Valneva commences manufacturing of its Inactivated, Adjuvanted COVID-19 vaccine, completes Phase 1/2 study recruitment. **2** Valneva and Dynavax announce commercial supply agreement for Inactivated, Adjuvanted COVID-19 vaccine; **3** Valneva Reports Positive Phase 1/2 Data for Its Inactivated, Adjuvanted COVID-19 Vaccine Candidate, VLA2001



COV-COMPARE TRIAL AND TOPLINE RESULTS

About Phase 3 Cov-Compare Trial (VLA2001-301)

- **Randomized, observer-blind, controlled, immunogenicity trial comparing VLA2001 to AstraZeneca's conditionally approved vaccine, AZD1222 (ChAdOx1-S)**

- **2,972 participants 30 years of age and older randomized (2:1) received two doses of either VLA2001 (n=1977) or AZD1222 (ChAdOx1-S) (n=995) at the recommended dose level, 28 days apart**

- **Primary objective: Compare VLA2001 to AZD1222 (ChAdOx1-S) administered as above, to determine:**
  1. Superiority in terms of Geometric Mean Titer ratio of SARS-CoV-2-specific neutralizing antibodies at two weeks after the second vaccination (Day 43) in adults aged 30 years and older; and
  2. Non-inferiority in terms of seroconversion rate and
  3. Frequency and severity of any Adverse Events

- **Also evaluating the safety and tolerability of VLA2001 in additional adults 18-29 years of age (n=1040), two weeks after the second vaccination**

Safety and Tolerability Results - VLA2001 was Well Tolerated

Primary Endpoint:
Frequency and severity of any Adverse Events (AE) up to Day 43 post-vaccination

Overall, 92.0% of participants reported any AE (92.6%, 88.7% and 98.1% in the VLA2001 Under 30 years, VLA2001 30 years and above, and AZD1222 (ChAdOx1-S) groups, respectively).

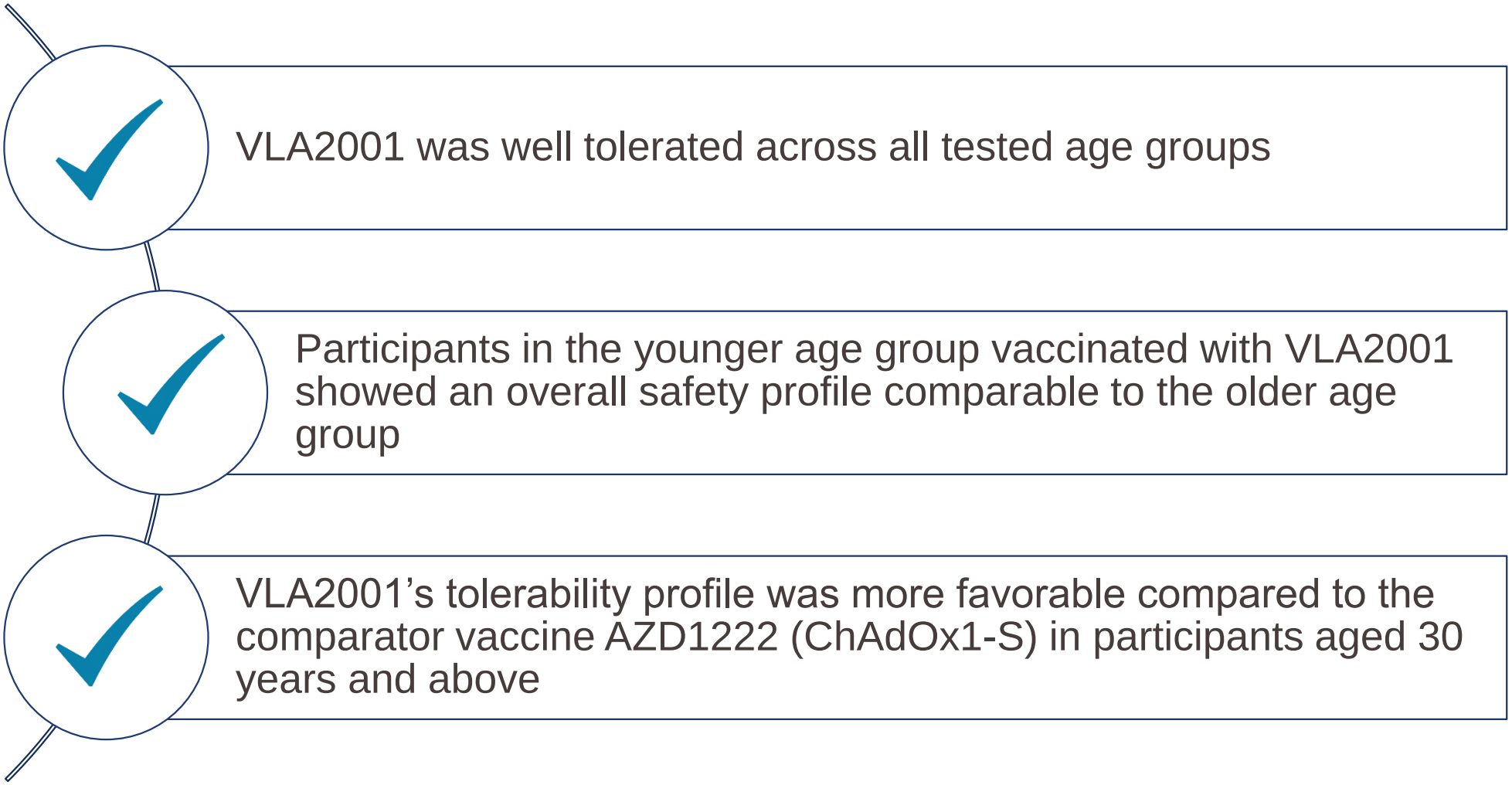
- After any vaccination, statistically significantly fewer participants experienced at least one **solicited Injection Site Reaction:** 73.2% in the VLA2001 (30 years +) group compared to 91.1% in the AZD1222 (ChAdOx1-S) group (p≤ 0.0001).

- After any vaccination, statistically significantly fewer participants experienced at least one **solicited Systemic Reaction:** 70.2% in the VLA2001 (30 years +) group compared to 91.1% in the AZD1222 (ChAdOx1-S) group (p≤ 0.0001).

- Statistically significantly fewer participants experienced **any unsolicited AE** (27.9% in the VLA2001 (30 years +) compared to 32.7% in the AZD1222 (ChAdOx1-S) group) (p = 0.0075)
  - Rates of participants with **unsolicited serious AEs** (0.3% vs. 0.2%) or medically attended unsolicited AEs (7.2% vs. 6.5%) were comparable between the VLA2001 (30 years +) group and the AZD1222 (ChAdOx1-S) group.
  - No related unsolicited serious AEs have been reported.

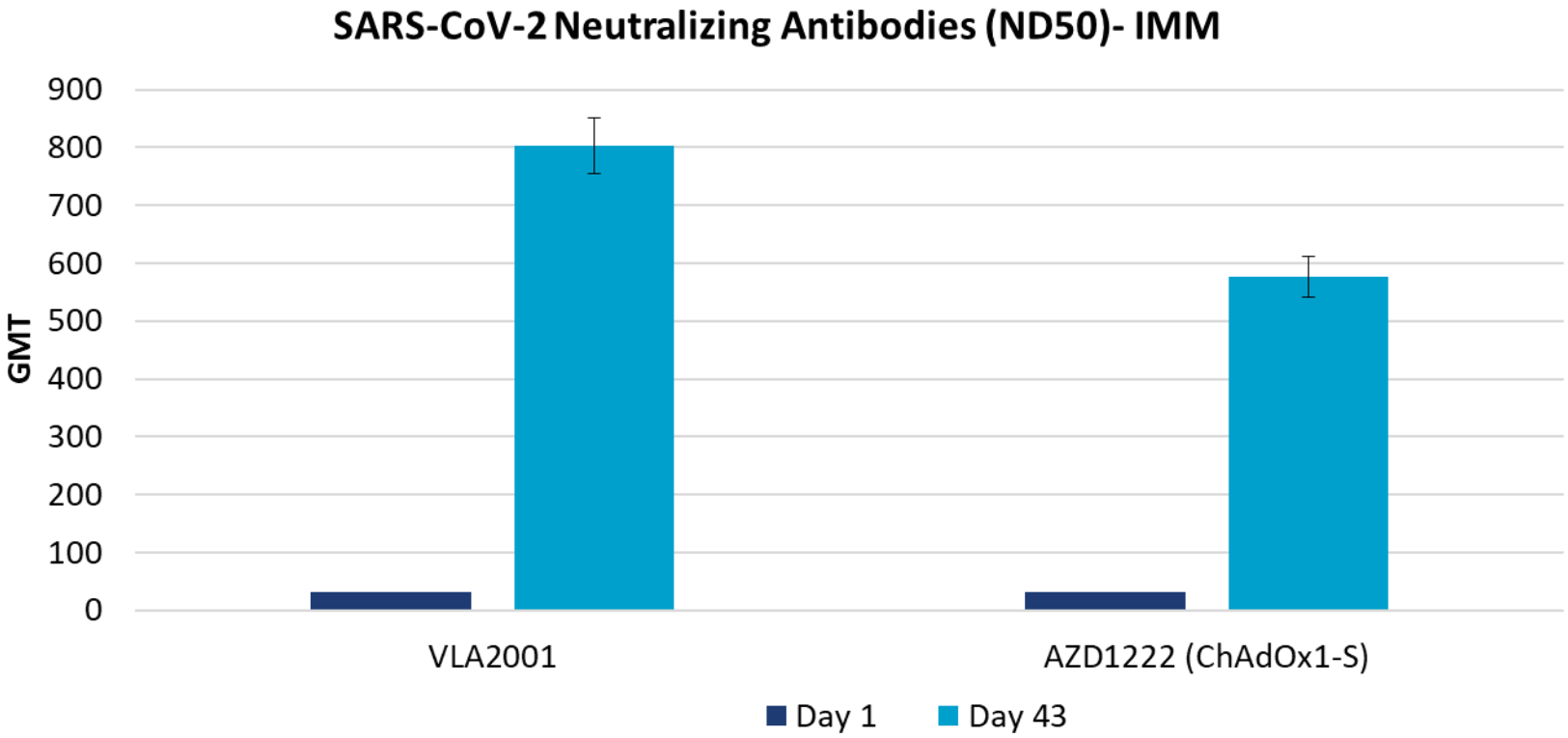
- Majority of solicited and unsolicited AEs were mild and moderate.

VLA2001-301 – Preliminary Safety Conclusions



- VLA2001 was well tolerated across all tested age groups
- Participants in the younger age group vaccinated with VLA2001 showed an overall safety profile comparable to the older age group
- VLA2001's tolerability profile was more favorable compared to the comparator vaccine AZD1222 (ChAdOx1-S) in participants aged 30 years and above

SARS-CoV-2 Neutralizing Antibody Levels (ND50)- IMM – VLA2001 Higher Than AZD1222 at Day 43



IMM includes all **randomized and vaccinated participants of the IMM subset** for the primary endpoint evaluation, **who were SARS-CoV-2 seronegative and have at least one evaluable post-baseline antibody titer** measurement after vaccination. Participants who met the case definition of **confirmed COVID-19** during the study are not **included in the IMM**.

GMT: Geometric Mean Titre, CI: Confidence Interval:
Note: [1] p-value and CI calculated using a two-sided t-test applied to log10 transformed data.

A final assay validation required by the MHRA to verify the integrity of the VLA2001-301 data remains ongoing and is a prerequisite for final submission of the clinical study report.

Immunogenicity Results – Primary Endpoint Met

SARS-CoV-2 Neutralizing Antibodies (ND50)- IMM – VLA2001 1.39 x AZD1222

Co-Primary Endpoint: Ratio of geometric mean titer (IMM population) of SARS-CoV-2-specific neutralizing antibodies, at two weeks after the second vaccination (i.e. Day 43) in adults aged 30 years and above.

Visit	Statistic	VLA2001 Age 30 and Above (N=492)	AZD1222 (ChAdOx1-S) (N=498)	Overall (N=990)
Day 1	n	492	498	990
	GMT (95% CI)	31.0 (31.00, 31.00)	31.0 (31.00, 31.00)	31.0 (31.00, 31.00)
	GMT Ratio (95% CI)			1.00 (1.00, 1.00)
	p-value [1]			NE
Day 43	n	492	493	985
	GMT (95% CI)	**803.5** (748.48, 862.59)	**576.6** (543.59, 611.66)	680.6 (649.40, 713.22)
	GMT Ratio (95% CI)			**1.39 (1.25, 1.56)**
	p-value [1]			**<.0001**

IMM includes all **randomized and vaccinated participants of the IMM subset** for the primary endpoint evaluation, **who were SARS-CoV-2 seronegative and have at least one evaluable post-baseline antibody titer** measurement after vaccination. Participants who met the case definition of **confirmed COVID-19** during the study are not **included in the IMM**.

GMT: Geometric Mean Titre, CI: Confidence Interval:

Note: [1] p-value and CI calculated using a two-sided t-test applied to log10 transformed data.

Immunogenicity Population, Table 14.3.1.1

High Proportion of Participants With Seroconversion in Terms of Neutralizing Antibodies – PP

Co-primary Endpoint: Seroconversion (PP population) (defined as 4-fold increase from baseline) of SARS-CoV-2-specific neutralizing antibodies, at two weeks after the second vaccination (i.e. Day 43) in adults aged 30 years and above.

Visit	VLA2001 (N=489) N(%)	AZD1222 (ChAdOx1-S) (N=498) N(%)	Overall (N=987) N(%)
Day 43			
Number of patients with eligible samples at visit	456	449	905
Participants with seroconversion (≥ 4- fold increase)			
n(%)	444 (**97.4**)	444 (**98.9**)	888 (98.1)
95% CI [1]	(0.954,0.986)	(0.974,0.996)	(0.970,0.989)
p-value [2]			0.0911

The Per-Protocol population (PP) will consist of the IMM population subjects who have no major protocol violations that impact the immune response.

[1] Exact 95% Clopper-Pearson confidence interval for proportion.

[2] P value or Two-sided CI is for the difference in proportions (VLA2001-AZD122) of Participants with seroconversion at each particular visit.

\+ Per-Protocol Population, Table 14.3.2.1

VLA2001-301 Immunogenicity Conclusions – Endpoints Met

- The trial **met its co-primary immunogenicity endpoints** at two weeks after the second vaccination (i.e. Day 43) in adults aged 30 years and above
  - VLA2001 demonstrated **superiority** against AZD1222 (ChAdOx1-S) in terms of geometric mean titer for neutralizing antibodies as measured by live virus microneutralization assay. (GMT ratio=1.39, p<0.0001) (VLA2001 GMT 803.5 (95% CI: 748.48, 862.59))
  - VLA2001 demonstrated non-inferiority in terms of seroconversion rates (SCR above 95% in both treatment groups)
- At Day 43, 74.3% of a subset of study participants in the VLA2001 group had T-cells that were reactive against peptide pools spanning the full-length S-protein.
- In addition, in the VLA2001 group 45.9% had T-cells that were reactive against the N-protein and 20.3% against the M-protein.

Overall Clinical Data Conclusions

All Endpoints Achieved

- The trial met its co-primary endpoints. VLA2001 demonstrated:
  - **superiority** against AZD1222 (ChAdOx1-S), in terms of **geometric mean titer** for neutralization antibodies, as well as
  - **non-inferiority** in terms of **seroconversion rates** at two weeks after the second vaccination (i.e. Day 43) in adults aged 30 years and above.

- **VLA2001 was generally well tolerated**
  - The **tolerability profile** of VLA2001 was **significantly more favorable compared** to the **active comparator** vaccine.
  - Participants **30 years and above** reported **significantly fewer solicited adverse events** up to seven days after vaccination**, both** with regards to **injection site reactions**, and **systemic reactions**
  - Participants in the **younger age group** vaccinated with **VLA2001 showed** an **overall safety profile comparable** to the **older age group.**

- The **occurrence of COVID-19** cases (exploratory endpoint) was **similar between treatment groups** in the participants **30 years and above.**

- The **complete absence** of **any severe COVID-19 cases** may suggest that **both vaccines** used in the study **prevented severe COVID-19 caused by the circulating variant(s) (predominantly Delta).**

- **T-cell responses** analyzed in a **sub-set of participants** showed that **VLA2001 induced broad** antigen-specific IFN-gamma producing T-cells **reactive against the S, N and M proteins.**

VLA2001 ROUTE TO LICENSURE & DEVELOPMENT PLAN

VLA2001 – SARS-CoV-2 Clinical Development Plan

Ongoing

Ph1/2 VLA2001-201
- Extension for booster
- N= 77
- Age 18-55
- 6 Months follow-up

Ph3 VLA2001- 301a
- Adolescence
- Primary vaccination
- N= 660
- Age 12-17

Ph3 VLA2001-304
- Primary Elderly
- Single Arm Open Label
- N= 306
- Age 55+

Planned 2022

Ph3 VLA2001-301
- Primary Adults N=4012*
- **Extension for booster n=400**
- **Age 18-55+**

Ph3 VLA2001-321
- Pediatric
- N= 2200 Age 2-11
- Dose finding age 2-5
- Full dose age 5+

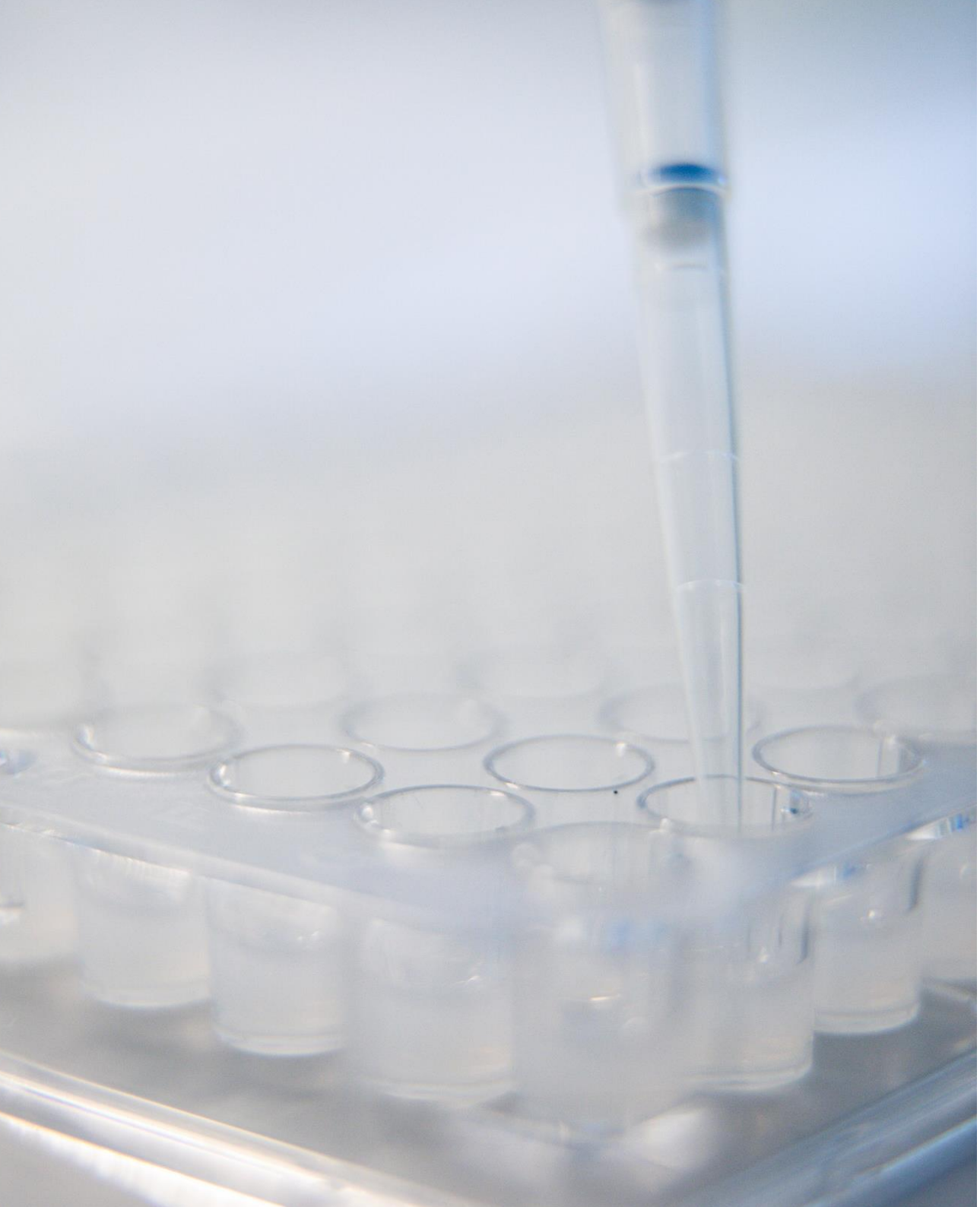
Ph3 VLA2001-3XX
- Booster study: N=200
- Age 12+
- Threshold based and min. 6 months after primary or infection

* Primary Adults VLA2001-301 ongoing

VLA2001: Route to Licensure

- **Valneva to submit Cov-Compare data to UK Medicines and Healthcare products Regulatory Agency (MHRA)**
  - Rolling submission with MHRA commenced in August 2021[1]
  - Final submission to MHRA anticipated for November
  - Potential initial approval expected by year-end
- **Valneva plans to submit data package to the European Medicines Agency (EMA)**
  - Pre-submission discussions with EMA ongoing
  - 306 elderly participants in the VLA2001-304 trial already enrolled[2] to collect additional data for the EMA package
  - Cov-Compare endpoints aligned with EMA

1 Valneva Commences Rolling Submission to MHRA for its Inactivated, Adjuvanted COVID-19 Vaccine ; **2** Valneva Completes Recruitment of Elderly Participants in Phase 3 Trial of its Inactivated COVID-19 Vaccine



CLOSING REMARKS

Thank you
Merci
Danke
Tack

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