valneva

Advancing Vaccines for Better Lives

Company Presentation – November 2019

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Valneva – Highlights and key information

- **Valneva is a biotech company** developing and commercializing vaccines for infectious diseases with major unmet needs
  - › > €100m product sales revenues[1]
  - › Cash flow positive[1]
- **Specializes in important, high value niches**
  - › Travel vaccines
  - › Technological competence on vector-transmitted diseases
- **Focused R&D programs in development including**
  - › the only Lyme disease vaccine in clinical development today
  - › a unique, differentiated chikungunya vaccine candidate
- **International footprint**
  - › Locations in EU and North America for Manufacturing, R&D, and Sales & Marketing

2018 Revenues: €113m
2019 Rev. Guidance: €125-135m
2019 Product Sales Revenue Guidance: €125-130m

Cash: €67.4m (as of Sep. 30, 2019)

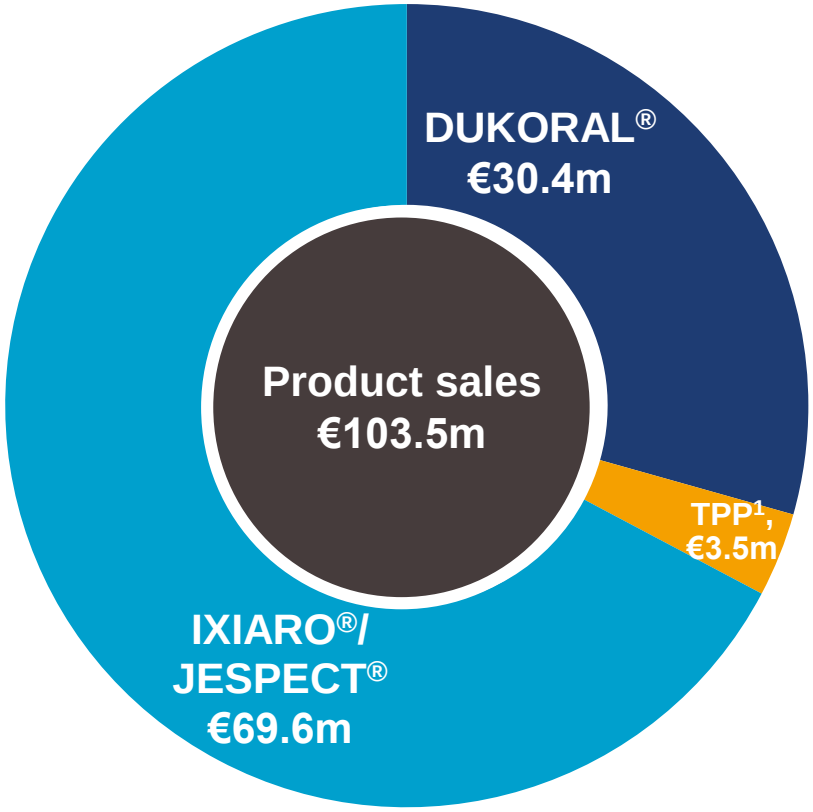
Ticker: EPA – VLA

1 In 2018: https://valneva.com/press-release/valneva-reports-strong-2018-results-expects-further-growth-and-major-pipeline-progression-in-2019/

Valneva's profitable commercial business funds R&D programs

Product sales growth 2017-2018 16% (CER);
Repeated double-digit sales growth expected 2018-2019

2018 Full-year results



Direct sales
81.2%

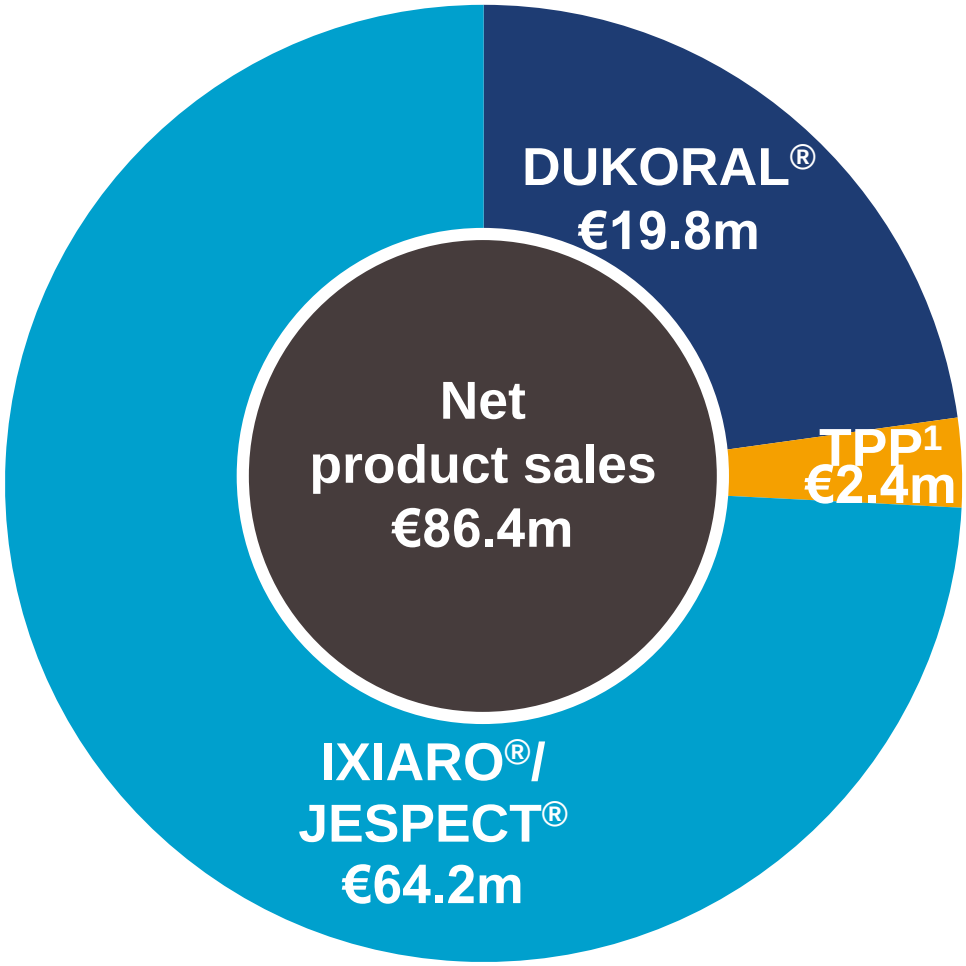
Gross
margin
60.7%

Cash
generated
€16.3m

Innovative R&D pipeline in areas of major unmet need

CER: *at constant exchange rates;* ***1*** *Third party products sold by Valneva's commercial organization;* ***2*** *Gross margin on product sales*

Strong operational performance for 9M 2019



Product sales growth
22% AER / 18% CER

Direct sales
86%

Gross margin²
65.2%

CER: At constant exchange rates; 1 Third party products sold by Valneva's commercial organization, 2 Gross margin on product sales

IXIARO®/JESPECT®

Only vaccine against Japanese encephalitis (JE) in US, Canada and Europe

IXIARO®/JESPECT®

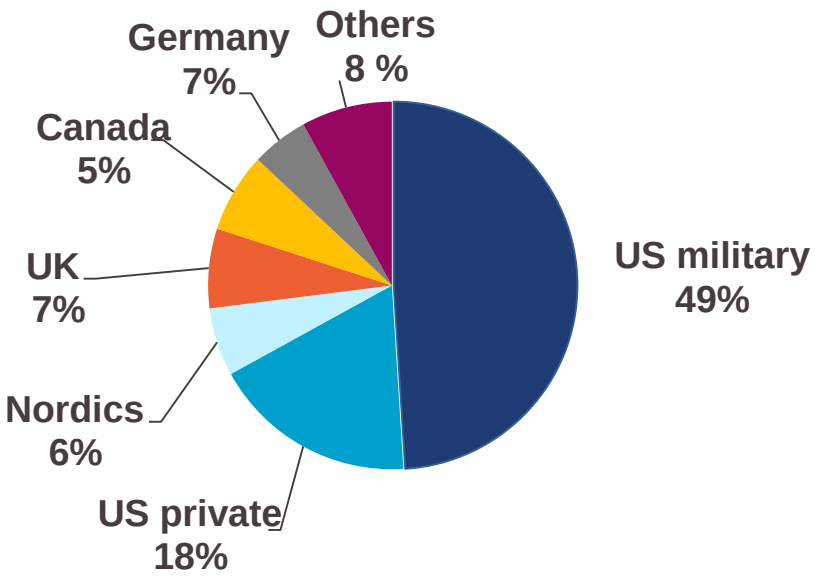
- **Designed to protect travelers and military against JE, the leading cause of viral neurological disease & disability in Asia**
- Indicated for active immunization against JE in **adults, adolescents, children and infants** aged two months and older[1]

Commercial position

- Currently, **no effective treatment for the disease**
- **The only approved vaccine available for US, EU and Canadian travelers**
- Supply agreement in place with US Military and strong track record of repeat contracts
- Limited competition - local producers exist in endemic regions and mainly serve public markets

IXIARO®/JESPECT®: US accounts for >65% of sales

9M '19 product sales analysis



Growth expected to be 20% CER[2] or more in 2019

1 *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. The currently available presentation for IXIARO® can be used in children from 3 years of age. Prior to availability of the new presentation, no attempt should be made to adjust the syringe volume or to administer a 0.25mL/3µg dose in children less than 3 years of age.;* ***2*** *CER: at constant exchange rates*

DUKORAL®

Only cholera (ETEC[1]) vaccine approved in EU, Canada and Australia

DUKORAL®

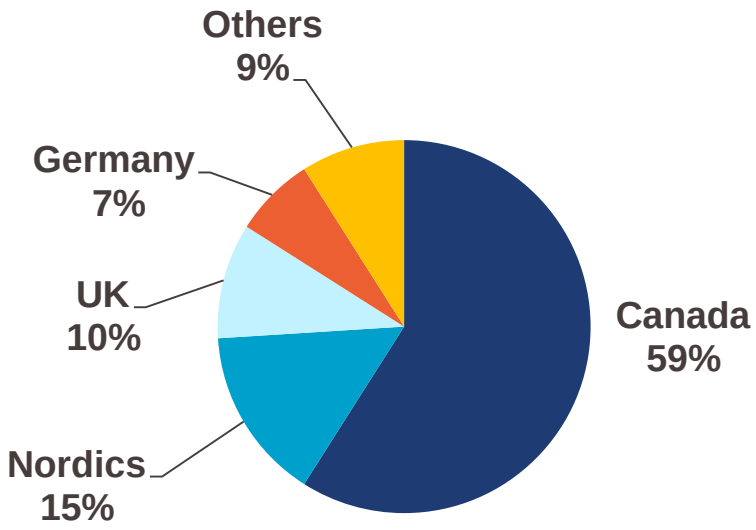
- **For the prevention of diarrhea caused by *Vibrio cholera* and/or heat-labile toxin producing enterotoxigenic *Escherichia coli* (ETEC)**[1]
- **Designed to protect adults and children** traveling to endemic areas

Commercial position

- In several markets, including EU, indicated for cholera only
- **Only approved cholera vaccine available for Canadian, European and Australian travelers**
  - ~3-5 million cholera cases, 100,000-120,000 deaths/year[2]
  - ~5-18 million reported ETEC cases/year[3] (ETEC is the most frequent form of traveler's diarrhea)
  - WHO pre-qualification widely used in other countries
  - Asian manufacturers predominantly serve local markets

DUKORAL®: Canada accounts for over 55% of sales

9M '19 product sales analysis



Revenues to grow by up to 5% CER[4] in 2019

1 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; 2 WHO cholera factsheet February 2014; 3 Lundkvist J, Steffen R, Jonsson B. Cost-benefit of WC/rBS oral cholera vaccine for vaccination against ETEC-caused travelers' diarrhea. J Travel Med 2009; 16(1):28-34; 4 CER: at constant exchange rates

Lyme disease is a serious unmet medical need

VLA15 is the only vaccine candidate in clinical development today

1. **Multivalent vaccine (six serotypes) to protect against Lyme disease in N. America and Europe**
2. **Targets OspA of Lyme borrelia, preventing spirochetes from migrating through the tick's mid-gut – an established and proven Mode of Action for a Lyme disease vaccine**
3. **Safe and immunogenic with excellent boosterability in Phase 1 studies[1]**
4. **Currently in Phase 2 with clear development path for US and EU licensure; FDA Fast Track Designation granted**
5. **Semi-generic manufacturing process with three fusion proteins expressed in *e. coli* – Final industrialization for Phase 3 initiated**
6. **Addressing a very significant unmet medical need and market opportunity**

1 Valneva PR: Valneva Reports Positive Initial Booster Data and Final Phase 1 Data for its Lyme Disease Vaccine Candidate;

Overview of Lyme disease

Severe tick-transmitted infection with high prevalence in N. America & Europe

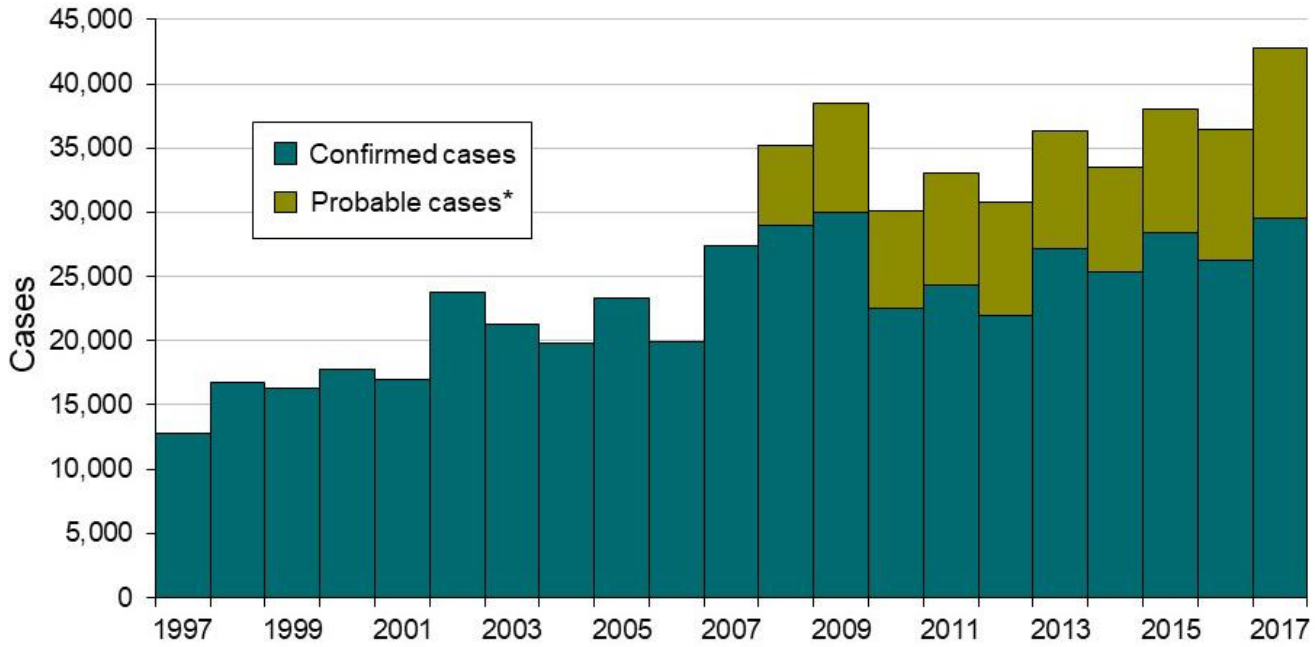
- Tickborne disease (Vector-Ixodes ticks)
- Caused by *Borrelia burgdorferi* spirochete (resides in gut of tick – migrates to salivary gland – enters host during feeding)
- Early signs and symptoms (3-30 days after tick bite) include flu-like sympthoms[1] and Erythema migrans rash[2]
- Left untreated, can spread to joints (arthritis), heart (carditis) and cause neurological problems
- Diagnosed by clinical symptoms, exposure to known endemic area, and lab tests
  - › Treatment: antibiotics (doxycycline, amoxicillin, or cefuroxime axetil)

1 *Fever, chills, headache, fatigue, muscle and joint aches, swollen lymph nodes;* ***2*** *Occurs in approx. 70-80% of infected persons.*

Lyme disease epidemiology

One of the fastest-spreading vector-borne illnesses in the Northern hemisphere

Annual Reported Cases of Lyme Disease in the US[1]



- **Lyme disease has seen a marked increase in reported cases, driven by:**
  - Climate change contributing to increased tick and host populations
  - Longer tick breeding seasons
  - Increasing awareness and healthcare follow-ups

Estimated Cases

- **~ 300,000 cases in US (p.a.)[2]**
- **~ 200,000 cases in EU (p.a.)[3]**
- Most-affected US regions:
  - 95% of US cases in 2016 occurred in Northern US states
- Key age Groups:
  - 17.3% of cases occur in 5-14 years
  - 36.6% of cases occur in 40-64 years

1 https://www.cdc.gov/lyme/why-is-cdc-concerned-about-lyme-disease.html; 2 https://wwwnc.cdc.gov/eid/artickle/21/9/15-0417_article; 3 Estimated from available national data. Number largely underestimated based on WHO Europe Lyme Report as case reporting is highly inconsistent in Europe and many LB infections go undiagnosed; ECDC tick-borne-diseases-meeting-report; 4 Climate change influences on the annual onset of Lyme disease in the United States; https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4631020/;

VLA15: Phase 2 – Optimizing dose and schedule

Observer-blind, randomized, placebo-controlled, Phase 2 studies conducted in the US and EU[1]

Phase 2
819 subjects in two studies
Primary objective: Safety and immunogenicity data four weeks after completed schedule
Secondary objectives: Long-term immunogenicity and safety data

- Study **VLA15-201** with run-in phase
- Study **VLA15-202**

VLA15-201 Run-in phase (completed June 2019[2])

- Conventional schedule, higher dose
- **3 adjuvanted dose levels**, placebo
- **120 healthy volunteers** (18 to 40 years)

90 µg w/ alum	30 subjects
135 µg w/ alum	30 subjects
180 µg w/ alum	30 subjects
Placebo	30 subjects

VLA15-201 (initiated June 2019[2]): Schedule 0, 1, 2 months

- **2 adjuvanted dose levels** (135 µg and 180 µg) chosen after run-in phase, placebo
- **453 healthy volunteers** (18 to 65 years)
- **9 sites in the U.S. and Europe**

VLA15-202 (initiated July 2019[3]): Schedule 0, 2, 6 months

- **2 adjuvanted dose levels** (135 µg and 180 µg) chosen after run-in phase, placebo
- **246 healthy volunteers** (18 to 65 years)
- **5 sites in the U.S.**

__1__ VLA15-201 only (ClinicalTrials.gov Identifier: NCT03769194); Phase 2 subjects are baseline seropositive (10%) or seronegative (90%); __2__ Valneva PR: Valneva Reports Successful Outcome of Phase 2 Run-In for its Lyme Disease Vaccine Candidate; __3__ Valneva PR: Valneva Initiates Second Phase 2 Study for its Lyme Disease Vaccine Candidate VLA15 ; VLA15-202 ClinicalTrials.gov Identifier: NCT03970733

Lyme disease vaccine candidate VLA15: Phase 2 on track

Patient recruitment for both Phase 2 studies completed September 2019

Process for a late stage development & commercialization partner initiated

Phase 2 on track to provide first data by mid 2020

- Initial Data: Day 85 after base immunization schedule expected mid 2020

Phase 3 could be initiated 2021/2022

- Two placebo-controlled Phase 3 efficacy studies are currently planned with 8000 volunteers each, based on current estimates of Lyme incidence rates in order to demonstrate efficacy of the vaccine in Lyme endemic regions in the U.S. and Europe

**Subject to development progress, regulatory concurrence and company funding*

Chikungunya is a major public health threat
VLA1553 is a unique, differentiated single-shot vaccine candidate

1. **Currently no preventive vaccines or effective antiviral treatments exist for chikungunya**
2. **VLA1553 is a monovalent, single dose, live attenuated[1] prophylactic vaccine targeting chikungunya virus neutralization**
3. **Excellent immunogenicity and safety in Phase 1 with first insight on efficacy[2]**
4. **Currently in Ph 1 (follow-up) – Acceleration directly into pivotal trial under evaluation; non-clinical work ongoing; FDA Fast Track Designation granted; PRV eligible**
5. **Full-scale drug substance manufacturing process established at in-house FDA licensed facility in Scotland – additional synergy with existing commercial infrastructure**
6. **Addressing a very significant market opportunity; up to $23.4 million (€20.3 million) awarded by CEPI**

1 CHIKV LR2006-OPY1 infectious clone was attenuated by deleting large part of gene coding nsP3 (alphavirus-replicase; 2 Valneva Reports further Positive Results for its Chikungunya Vaccine Candidate; Photo credit: James Gathany (source)

Chikungunya Phase 1 study (VLA1553-101) – Interim results

Excellent immunogenicity and safety profile up to Month 7[1]

Immunogenicity

- 100% Seroconversion Rate (SCR)[2] achieved at Day 14 after a single vaccination in all dose groups[1]
  - SCR fully sustained at 100% after six months[1]
- Single vaccination of VLA1553 is sufficient to induce sustaining, high titer, neutralizing antibodies[1]

Excellent immunogenicity profile after single vaccination

Safety

- Generally safe in all dose groups
- Well-tolerated in the low and medium doses
  - Superior safety profile, including viremia, in low and medium doses compared to highest dose
- Excellent local tolerability
- No Adverse Events of Special Interest (AESIs) up to Month 7[1]

Excellent safety profile in low and medium doses

1 Valneva Reports further Positive Results for its Chikungunya Vaccine Candidate; 2 SCR defined as proportion of subjects achieving a CHIKV-specific neutralizing antibody titre as NT_{50} ≥ 20; 3 As occurs with other live-attenuated vaccines

Competitive analysis of clinical stage chikungunya vaccine candidates

	Emergent (Paxvax)'s Phase 2[1]	Themis' Phase 2[2]	Valneva's Phase 1[3]
Vaccine candidate	Virus-like particle (VLP) vaccine VRC-CHKVLP059-00-VP VLPs composed of E1, E2, and capsid proteins from CHIKV strain 37997.	Measles-vectored Chikungunya vaccine (MV-CHIK), Live-recombinant vaccine: CHIKV (La Reunion strain 06-46) structural genes C, E3, E2, 6K, and E1 in measles virus vector (Schwarz vaccine strain).	Monovalent, single dose, live-attenuated vaccine candidate with cross-protection potential against globally circulating strains (pre-clinical evidence)
Route of administration	2 vacc. of 20 µg, Day 0 & 28, i.m.	1 or 2 vacc. of MV-CHIK (10^4 or 10^5 TCID50/dose), Day 0 & 28, i.m.	Single-shot of either $3.2x10^3$, $3.2x10^4$ or $3.2x10^5$ $TCID_{50}$/dose, i.m.
Development stage	Phase 1 (NCT03028441) in the U.S. completed Phase 2 (NCT02562482) in the Caribbean completed: 2 vaccinations, 3 doses, 2 schedules Phase 2 (NCT01489358) at NIH completed	Phase 1 (NCT03028441) completed, Phase 2 (NCT02861586) in EU completed (Reisinger et al. 2018) Phase 2 (NCT03635086) in UK, formulation finding in UK (active, not recruiting) Phase 2 NCT03101111 in Puerto Rico (completed) Phase 2 in Puerto Rico in pre-exposed adults (recruiting) (NCT03807843)	Phase 1 in U.S. (NCT03382964) completed (manuscript in preparation)
Key findings	Seroconversion occurred in 74% to 98% of subjects within 7 days after one dose	Up to 100% seroconversion rate achieved after two injections (86.4% to 100.0%, depending on dose and administration schedule). (applied threshold 1:10)	100% Seroconversion Rate (SCR) achieved at Day 14 after a single vaccination in all dose groups. (applied threshold 1:20)
Duration of protection	Immune response was persistent through the six-month visit, including the one-dose regimen	… responses to the vaccine were durable up to 6 months after one or two immunizations	SCR fully sustained at 100% after 6 months Single vaccination is sufficient to induce sustaining, high titer, neutralizing antibodies
FDA/EMA Status	FDA Fast Track May 2018 EMA PRIME designation Oct 2019	FDA Fast Track Feb 2019 EMA PRIME designation Jun 2018	FDA Fast Track Dec 2018
Timing Phase 3	2020	Q4 2019	Acceleration into pivotal trial under evaluation (Phase 3 start planned Q2 2020)
Manufacturing	Produced in human embryonic kidney VRC293 cells (suspension-adapted serum-free cell line derived from HEK-293)	Produced in Vero cells	Full-scale drug substance manufacturing process established at in-house FDA licensed facility Product is lyophilized, longer at optimized storage conditions (i.e. 2-8°C).

__1__ PR Emergent BioSolutions Announces Interim Results From Phase 2 Study Evaluating CHIKV-VLP, Chikungunya Virus Vaccine Candidate (Link) + Detailed study results Emergent/Paxvax' Phase 2 clinical trial results (Link), __2 PR__ Themis Bioscience Publishes Compelling Phase 2 Results for Lead Vaccine Candidate against Chikungunya Fever in The Lancet (Link) + Themis' Phase 2 clinical trial results: (Link), __3__ PR Valneva reports further positive results for its chikungunya vaccine candidate (Link),

Chikungunya vaccine candidate VLA1553 progressing rapidly

Up to $23.4m / €20.3m awarded by CEPI for late-stage development of VLA1553

- Accelerate regulatory approval for use in regions where outbreaks occur
- Support WHO prequalification to facilitate broader access in lower/middle income countries

Further Phase 1 results for single-shot chikungunya vaccine candidate reported

- Day 28 safety and immunogenicity after single dose
- Viremia data at Days 3, 7 and 14 post-vaccination
- Month 6 safety and immunogenicity data providing information on antibody persistence
- Month 7 re-vaccination safety, immunogenicity and viremia data as early indicator of efficacy

Additional non-clinical experiments ongoing to support EoP2 FDA meeting Q1 2020

- Mosquito transmission studies (complete)
- NHP study addressing biodistribution (complete)
- Passive transfer study in NHPs to develop correlate of protection using human sera from VLA1553-101 (will complete Q4 2019)

Aiming for accelerated pathway into Phase 3 in the U.S., subject to FDA approval*

** Subject to development progress, regulatory concurrence and company funding*

2019 product sales guidance raised following strong 9M results

All other guidance confirmed despite GSK SAA termination impact

	2019 9 Month Results	2019 9 Month Results Excluding GSK SAA termination impact	2019 Guidance
Product sales revenues	€86.4m	-	**€125m - €130m**
Total revenues	€81.4	€92.1	€125m - €135m
R&D investments	€23.2m	-	€35m - €40m
Gross margin	65.2%	-	> 60%
Net operating margin[1]	32.4%	-	25% - 35%
EBITDA	€3m	€13.7	€5m - €10m

1 *Net operating margin is based on the P&L for the Commercial Products segment including an allocation (56%) of G&A costs from Corporate Overheads and Amortisation of Intangibles related to IXIARO®*

Corporate Governance and Shareholder Structure

Management Board

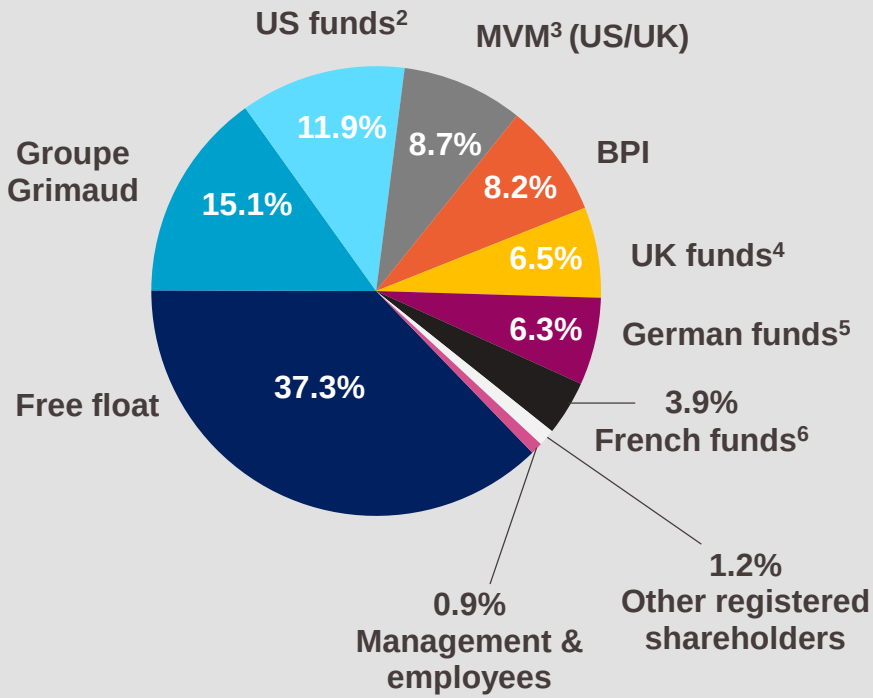
- **Thomas Lingelbach**, *President & CEO*
- **Franck Grimaud**, *President & CBO*
- **David Lawrence**, *CFO*
- **Wolfgang Bender, MD, PhD**, *CMO*
- **Frédéric Jacotot**, *General Counsel & Corporate Secretary*

Supervisory Board

- **Frédéric Grimaud** (France), *Chairman*
- **Lisa Shaw-Marotto** (US), *Vice Chairperson, Chair – Nomination & Compensation Committee*
- **James Sulat** (US), *Chair – Audit Committee*
- **Anne-Marie Graffin** (France)
- **Alexander von Gabain, Prof., PhD** (Austria)
- **Balaji Muralidhar, MD, PhD** (UK)
- **Sandra E. Poole** (US)

Stock Information

- Primary listing = Euronext (Paris)
- Number of ordinary shares: 90.9m
- Shareholder structure[1]:



1 Estimates as of September 2019, based on ordinary share capital; 2 Combined positions of 11 U.S.-based funds managed by Deerfield Partners, Armistice Capital, Artisan Partners L.P., New Leaf, General American, Granite Point and others; 3 Funds managed by MVM Life Science Partners; 4 Combined positions of Highclere, AXA Investment Managers Ltd. and Abingworth LLP; 5 Combined positions of DWS Investment, Apus Capital, Apo AM, Lupus alpha, Medical Strategy, Hauck & Aufhäuser, CD-Ventures and Deutsche Apotheker; 6 Combined positions of 9 France-based funds managed by CDC Entreprises Valeurs Moyennes, AXA Paris, Tocqueville Finance, AG2R, PRO BTP, Chaussier Gestion and others.

Upcoming newsflow

Valneva to attend forthcoming chikungunya VRBPAC[1] meeting

Lyme partnering process

Lyme disease vaccine candidate VLA15: Phase 2 execution on track for initial data mid-2020

Chikungunya vaccine candidate VLA1553: progressing towards potential accelerated development strategy; aiming for EoP2 FDA meeting Q1 2020

New IXIARO® contract with the U.S. Department of Defense in H1 2020

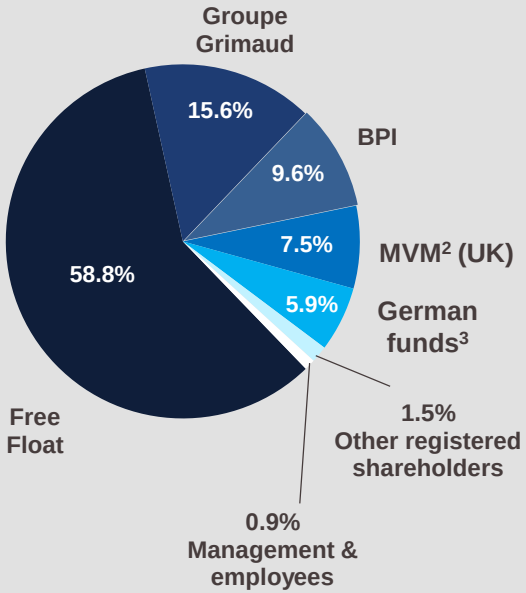
1 https://www.fda.gov/advisory-committees/advisory-committee-calendar/vaccines-and-related-biological-products-advisory-committee-november-8-2019-meeting-announcement

Appendices

VLA continuously strengthening its institutional shareholder base with blue-chip healthcare investors

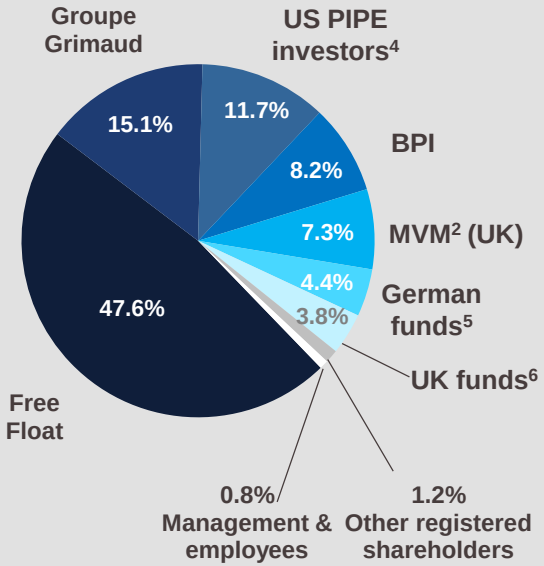
January 2018

- Number of ordinary shares: 77.6m
- Shareholder structure[1]:



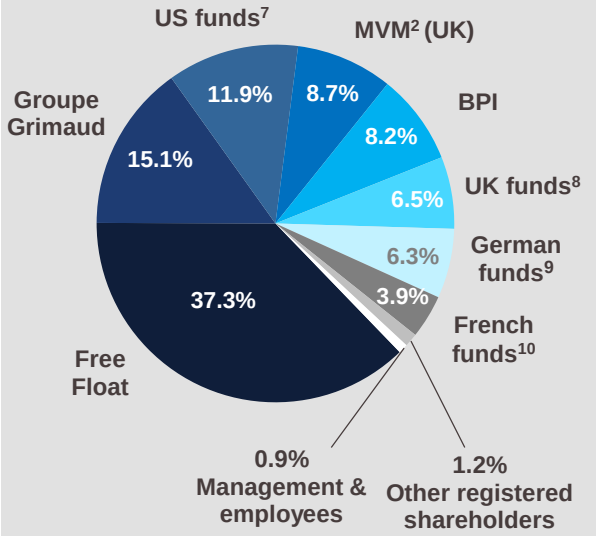
October 2018

- Number of ordinary shares: 90.9m
- Shareholder structure[1]:



September 2019

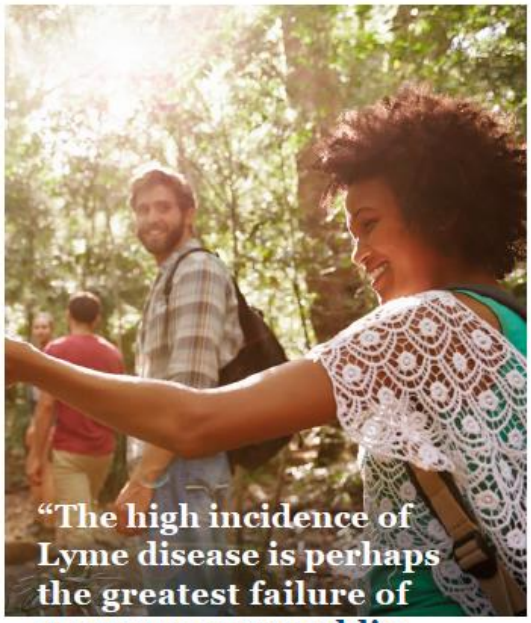
- Number of ordinary shares: 90.9m
- Shareholder structure[1]:



1 Estimates based on ordinary share capital; 2 Funds managed by MVM Life Science Partners; 3 Combined positions of 10 Germany-based funds managed by Apus Capital, Apo Asset Management, Lupus alpha, CD-Ventures, SK Vermögensverwaltung, Hauck & Aufhäuser, and others; 4 Combined positions of U.S.-based participants in Valneva's September 2018 private placement; 5 Combined positions of Apus Capital, Lupus Alpha, Apo Asset Management, CD-Ventures, and Medical Strategy; 6 Combined positions of Highclere and Abingworth, LLP; 7 Combined positions of 11 U.S.-based funds managed by Deerfield Partners, Armistice Capital, Artisan Partners L.P., New Leaf, General American, Granite Point and others; 8 Combined positions of Highclere, AXA Investment Managers Ltd. and Abingworth LLP; 9 Combined positions of DWS Investment, Apus Capital, Apo AM, Lupus alpha, Medical Strategy, Hauck & Aufhäuser, CD-Ventures and Deutsche Apotheker; 10 Combined positions of 9 France-based funds managed by CDC Entreprises Valeurs Moyennes, AXA Paris, Tocqueville Finance, AG2R, PRO BTP, Chaussier Gestion and others.

Vaccination against Lyme disease

Justification for a Lyme vaccine



- Vaccination with OspA has been proven to work in the past (Lymerix®, ImuLyme®)

- **Disproven postulate[1], restrictive recommendations and corporate decisions resulted in there being no Lyme vaccine available for humans since 2002**

- **Delayed or inadequate treatment can lead to disabling sequelae**

- **Disease footprint widens[2]**

- **Direct medical costs in the US estimated up to $1.3 billion[3] – indicating an attractive health economical benefit**

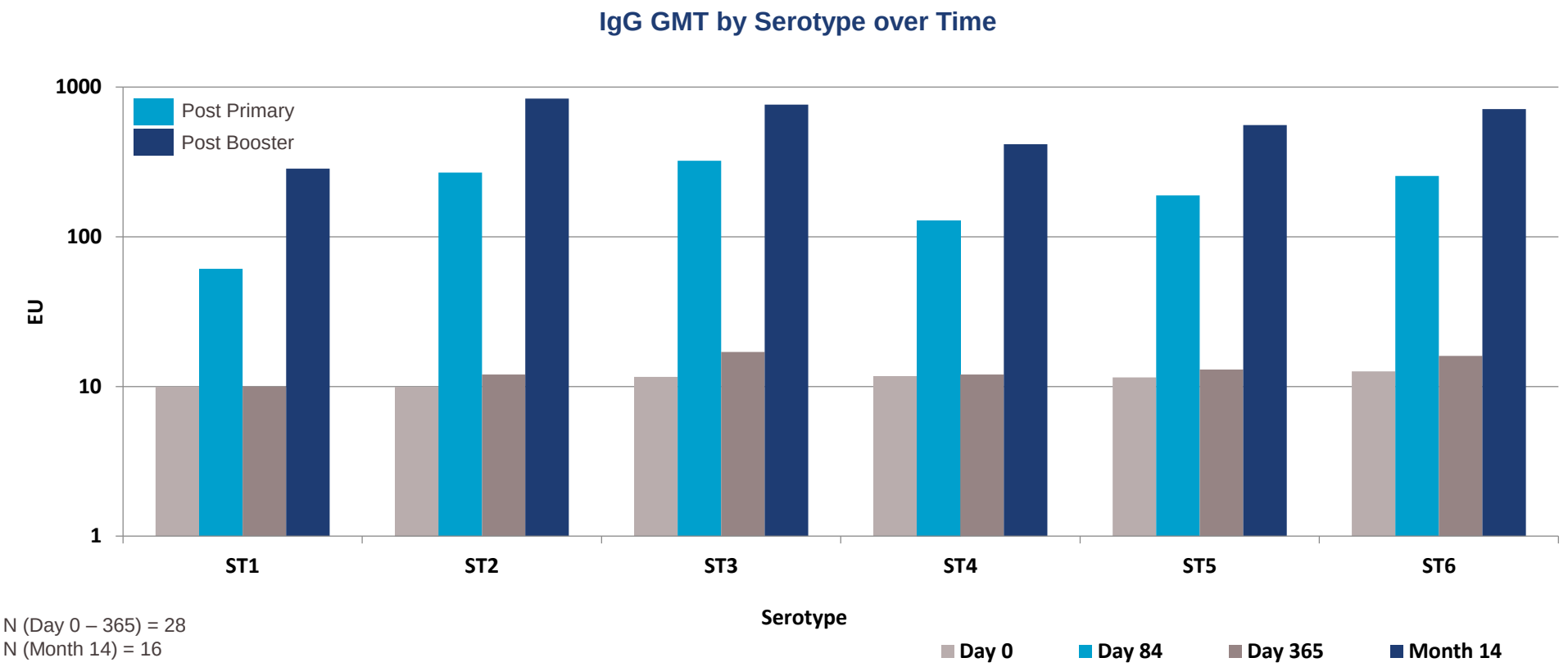
- **Other preventive measures have not been shown to work on a public health scale**

1 Steere et al. CID 2011: 52 (Suppl3) S259; 2 New Scientist, Lyme disease is set to explode and we still don't have a vaccine; March 29, 2017 https://www.newscientist.com/article/mg23431195-800-lyme-disease-is-set-to-explode-and-you-cant-protect-yourself/ ; 3 Adrion, E. et al PLOS ONE Feb 2015

Lyme Phase 1 study (VLA15-101) – Immunogenicity

GMT for highest adjuvanted dose group between 61 (ST1) and 269 (ST2), substantial booster effect

IgG GMT of Highest Adjuvanted Group (90µg + Alum) Before and After Primary Series and Booster Dose



N (Day 0 – 365) = 28
N (Month 14) = 16

Chikungunya: Vector prevalence and disease outbreaks

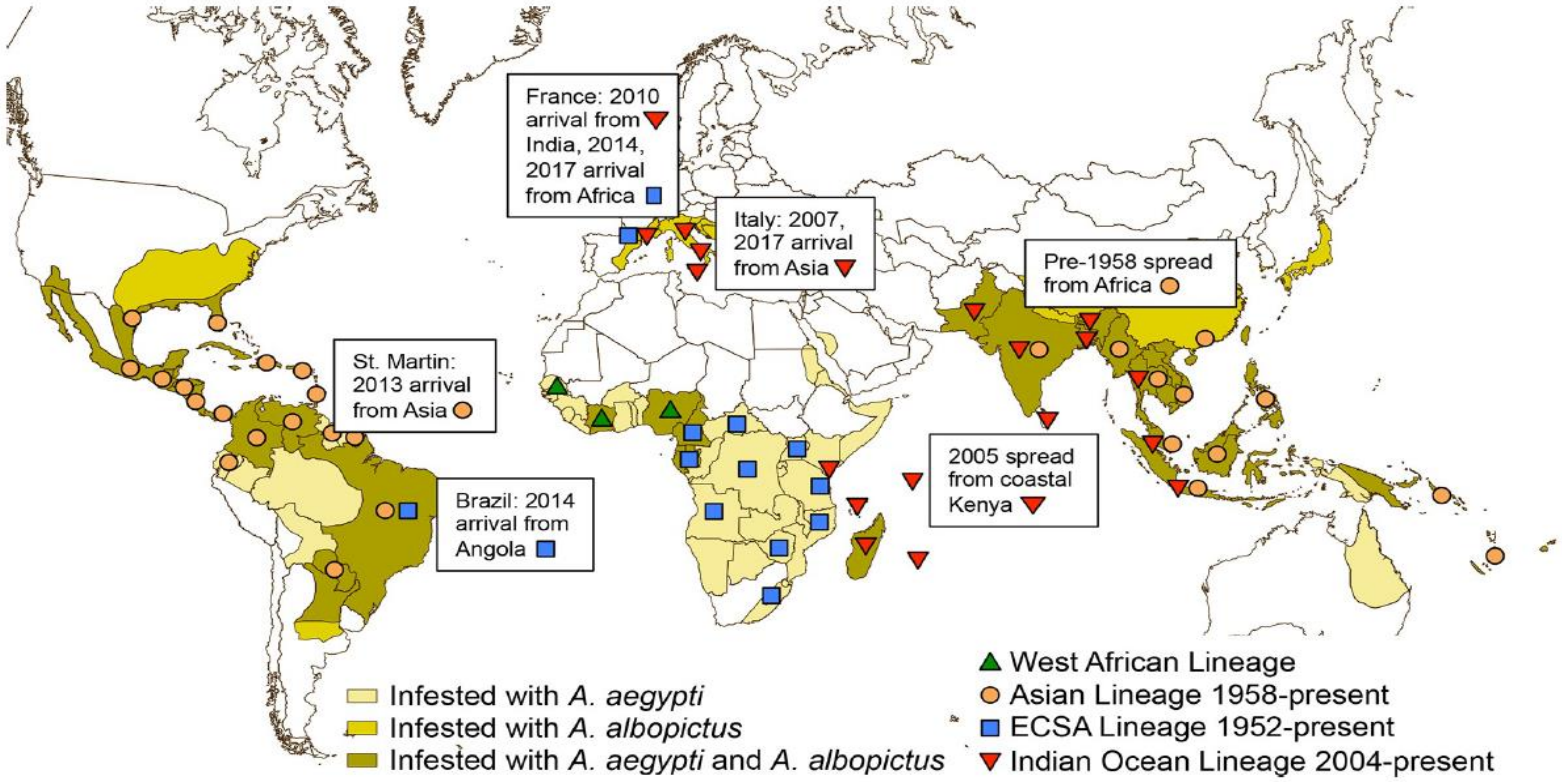


Fig 1. World map with countries where autochthonous (locally initiated) chains of CHIKV transmission have been identified. Data from World Health Organization (http://www.who.int/emergencies/diseases/chikungunya/en/) and Pan American Health Organization (https://www.paho.org/hq/index.php?option=com_topics&view=article&id=343&Itemid=40931&lang=en). CHIKV, chikungunya virus.

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Thank you
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