Annual Business Report

2018

RISING

valneva


RISING
to the
challenge of protecting
the greater good

Important note: Please read the disclaimer on page 46

CONTENTS

Advancing vaccines for better lives

Valneva is a biotech company developing and commercializing vaccines for infectious diseases with major unmet needs. Our focused pipeline includes the most advanced Lyme disease vaccine in development today. Our vision is to contribute to a world in which no one dies or suffers from a vaccine-preventable disease.

5th
anniversary
in 2018

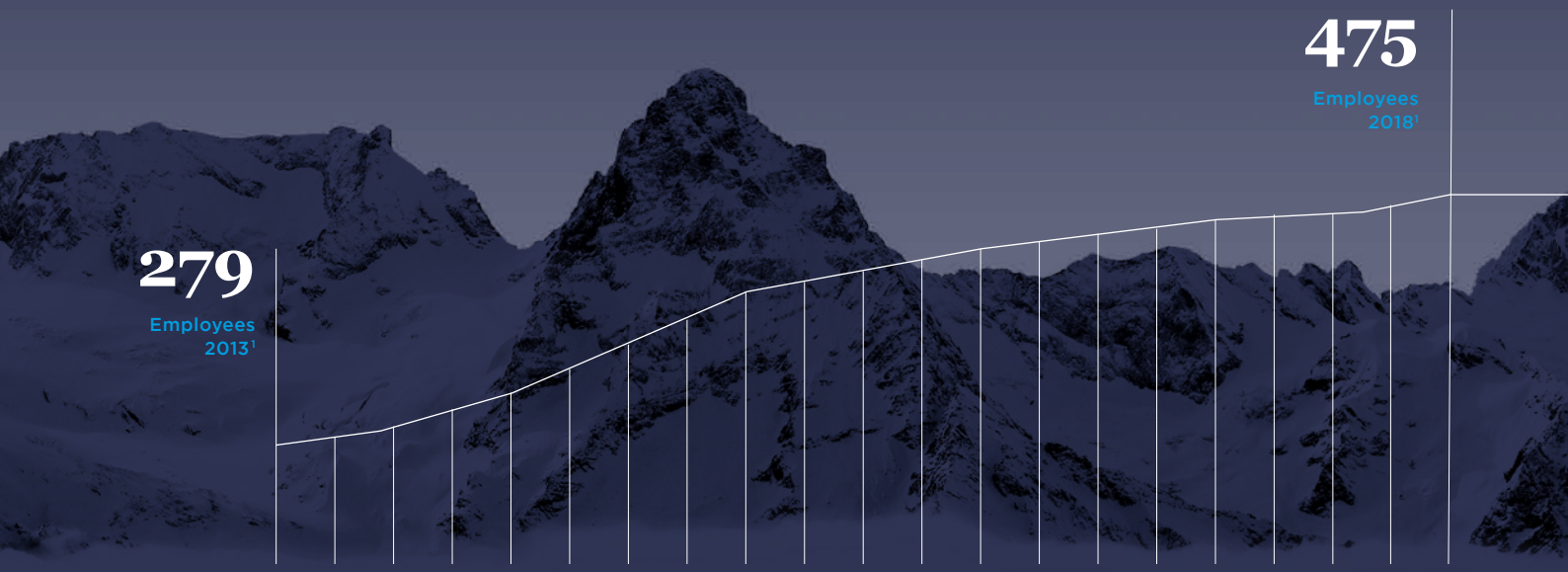
2
Commercial
Vaccines

Product sales
revenues exceed
€100M

3
Clinical
programs

Valneva at a glance

Valneva is a biotech company developing and commercializing vaccines for infectious diseases with major unmet needs



International footprint with approximately 480 employees in the U.S., Canada, Austria, Sweden, the UK and France

1 As of December 31 **2** As a result of the merger in May 2013 between Intercell AG and Vivalis SA to form Valneva SE, the Company's 2018 and 2013 results are not fully comparable. Vivalis SA's results were fully included in the income statement of 2013 while Intercell's results were only included for the seven month period starting from June 2013 **3** Including service revenues and license fees

Significant growth in the past five years since Valneva's creation

R&D investments 2013[2]

€ 21.4M

R&D investments 2018[2]

€ 25.3M

Product sales Revenues 2018[2]

Product sales Revenues 2013[2]

€ 23.2M

€ 103.5M

Total revenues[3] were €113 million in 2018

EBITDA 2013[2]

€ -11.8M

EBITDA 2018[2]

€ 13.1M

The Company's profitable commercial business funds

key

R&D

programs

Specialized in important, high value niches

- **Travel vaccines**
- **Technological competence in vector-transmitted diseaeses**

Focused R&D programs

including the most advanced Lyme disease vaccine in clinical development today

Dear Shareholders and Investors

We are very pleased to present our 2018 Annual Business Report following a dynamic year for Valneva.

In 2018, we met our ambitious financial targets while achieving the highest number of key research and development (R&D) milestones in Company history. This enabled us to raise €50 million in an oversubscribed placement led by blue-chip U.S. healthcare investors. Their investment supports our capital formation strategy, providing the capital needed to accelerate our key R&D programs. We are proud to continue investing in important vaccine development programs. Our aim is to address important unmet medical needs to make meaningful changes to the lives of people around the world. In the past year, we made significant progress with our unique, clinical-stage vaccine candidates against Lyme disease and chikungunya. Our prospects are becoming increasingly real and rewarding as these projects advance. Valneva's Management Board, together with its Supervisory Board, is committed to the Company's vision and strategy. The major progress that we made in the past year brings us closer to fulfilling our goals. The dedication of our highly talented workforce is crucial as we continue to execute our vision. Their contributions, and the confidence placed in us by Valneva's partners, investors and shareholders, create an environment for success. We thank them all for their support and aim to capitalize on the positive momentum of the past year in 2019 and beyond.

Thomas Lingelbach
President & Chief Executive Officer
Franck Grimaud
President & Chief Business Officer
David Lawrence
Chief Financial Officer
Wolfgang Bender
Chief Medical Officer
Frédéric Jacotot
General Counsel & Corporate Secretary

HIGH LIGHTS

March 2018

Valneva Reports Positive Phase 1 Interim Results for its Lyme Disease Vaccine Candidate VLA15

Valneva Initiates Phase 1 Clinical Study to Evaluate its Single-Shot Vaccine Candidate against Chikungunya

September 2018

Valneva Raises €50 Million in Oversubscribed Placement Led by US Healthcare Investors

October 2018

Valneva Announces FDA Approval of Accelerated IXIARO® Vaccination Schedule

November 2018

Emergent BioSolutions and Valneva Report Positive Phase 1 Results for their Vaccine Candidate Against the Zika Virus

December 2018

Valneva Initiates Phase 2 Clinical Development for its Lyme Disease Vaccine Candidate

Valneva Awarded FDA Fast Track Designation for Chikungunya Vaccine Candidate

January 2019

Valneva Announces New $59 Million IXIARO® Supply Contract with US Government

Valneva Reports Positive Phase 1 Interim Results for its Chikungunya Vaccine Candidate

Mid-Term

Strategy

Valneva's strategy stems from its vision to contribute to a world in which no one dies or suffers from a vaccine-preventable disease. We aim to become the leading vaccine biotech by combining the growth of our commercial business with the development of prophylactic vaccine candidates for diseases such as Lyme and chikungunya.

Products

Growing product sales revenues to €200 million and beyond

Valneva operates a successful commercial business, which continues to grow. Valneva aims to increase its product sales from €103.5 million in 2018 to over €200 million by 2022. Where possible our ambition is to add products to our commercial portfolio, leveraging our commercial and industrial infrastructure.

R&D

Investing in innovative R&D programs to meet unmet medical needs

Valneva's R&D team is committed to developing vaccine candidates in areas of growing medical need and providing innovative solutions for the benefit of both people and society. Our current R&D pipeline includes the most advanced clinical-stage vaccine to prevent Lyme disease, a tick-transmitted illness that is spreading widely in North America and Europe. Additionally, Valneva has vaccine programs against the mosquito-borne viral diseases chikungunya and Zika, neither of which can be effectively treated today.

In order to advance our two leading programs, Lyme disease (VLA15) and chikungunya (VLA1553), towards the next value inflection points, we expect to increase R&D investments significantly in the coming years.

Our approach is to fully develop products, alone, or via co-development and profit share, or through partnership agreements that will generate revenues in the form of milestone payments as well as royalties on future product sales.

Financials

Using proceeds from commercial business to invest in promising product candidates

One of Valneva's key strategic objectives is to be largely financially self-sustainable in its operations. Valneva generated €13.1 million of earnings before interest, tax, depreciation and amortization (EBITDA) in 2018, marking the third consecutive positive annual EBITDA result.

While we aim to achieve positive EBITDA for our business, Valneva is focused on generating long-term shareholder value and will therefore continue to invest in advancing its key R&D programs. This may result in a period of negative EBITDA in the mid-term, as R&D programs undergo costly late stage development.

2019

Outlook

Financial

Guidance

Double-digit product sales growth expected to continue in 2019: Valneva expects product sales revenues in 2019 of between €115 million to €125 million, representing 15–20% (CER[4]) year-on-year growth.

- Overall revenue is expected to be between €125 million and €135 million in 2019

Gross margin is expected to be above 60% and net operating margin, prior to R&D investments[5], is expected to be between 25% to 35%.

Valneva plans to invest €35 million to €40 million in R&D, notably in its Lyme disease and chikungunya vaccine candidates, in 2019.

Valneva expects to generate EBITDA of €5 million to €10 million in 2019.

Significant

R&D progress planned in 2019

Major confirmatory and supportive data points for Lyme disease vaccine candidate (VLA15):

- First booster data including final Phase 1 data[6] in Q1 2019 reported
- Determination of final doses and initiation of second Phase 2 trial mid 2019
- Further alignment with regulators on Phase 3 strategy

Development acceleration of chikungunya vaccine candidate (VLA1553):

- Valneva expects to report Phase 1 data (ungrouped) including first intrinsic human challenge mid 2019
- Alignment with regulators on potential route to licensure
- Readiness to progress into next clinical stage by end 2019

4 CER: at constant exchange rates **5** Net operating margin prior to R&D investment is calculated by excluding R&D expenses from the operating profit as recorded in the consolidated income statement under IFRS divided by total revenues
6 Valneva press release: https://www.valneva.com/en/investors-media/news/2019#309

Marketing & Distribution

With commercial operations in the U.S., Canada, UK, Scandinavia and Austria, combined with distribution partnerships, Valneva has a strong, specialized commercial capability for the successful distribution of its travelers' vaccines.

Building on the initial establishment of its own marketing and sales network in 2015, Valneva has developed a commercial presence in key travel vaccine markets. Countries served directly by in-house commercial operations currently represent over 80% of the Company's yearly product sales revenues.
Valneva has also continued to utilize its commercial organization to distribute third-party products, such as typhoid and influenza vaccines, and aims to potentially attract additional products to further leverage its commercial infrastructure.

The Company's commercial network is led by a seasoned management team with an average of more than two decades of commercial experience in the vaccine industry. Within its marketing strategy, the team works continuously to improve service and performance, including embracing digital technology, allowing Valneva to better connect with travelers, physicians and other health care professionals. Valneva places the customer at the heart of its activities and focuses on their needs for improved awareness, a deeper understanding of the travel health landscape, and tailor-made services to achieve their objectives.

A Strong Commercial Presence in Key Markets

US

Located northwest of Washington D.C. in Gaithersburg, Maryland, the commercial team in the U.S. focuses on the marketing and sales of IXIARO® to the U.S. military and in the private travel market. 2018 sales revenues generated by the U.S. team represented 39% of total product sales and 59% of overall IXIARO® sales.

Canada

The team in Canada is largely focused on marketing and distributing Valneva's IXIARO® and DUKORAL® vaccines, as well as third-party vaccines. Canada represents the single largest market for DUKORAL®, accounting for more than half of the vaccine's global product sales. 2018 sales revenues generated by the team in Canada represented 22% of Valneva's total product sales.

France

Valneva's Chief Business Officer as well as certain key business development staff are based in Nantes. Lyon is the intended location of our planned French commercial business, where key marketing staff are currently based.

Nordic Countries

Valneva's commercial team in the Nordics is well established. The team currently distributes Valneva's IXIARO® and DUKORAL® vaccines as well as third-party vaccines. 2018 sales revenues generated by the team in the Nordics represented 10% of total product sales.

UK

Valneva UK contributes to the sales of the Company's travel vaccines IXIARO® and DUKORAL®, in addition to selling third-party products. 2018 sales revenues generated by the UK team represented 8% of total product sales.

Austria

The team in Austria is also focused on the local marketing and distribution of IXIARO®, DUKORAL®, and third-party products. 2018 revenues from sales generated by the team in Austria represented 2% of total product sales.

Other

To ensure broad geographic access to IXIARO® and DUKORAL®, Valneva has partnered with leading global and local players through country-specific marketing and distribution agreements in countries where the Company doesn´t operate its own sales and marketing activities:

GlaxoSmithKline (GSK)	Germany, France	IXIARO® (DE, FR) and DUKORAL® (DE)
Seqirus (formerly BioCSL)	Australia, New Zealand	JESPECT® and DUKORAL®
Biological E	India and certain other Asian countries	JEEV®
Other partners	Italy, Spain, Portugal, Poland and certain Eastern European markets, Switzerland, Israel, the Asia Pacific region	IXIARO® and DUKORAL® JEVAL® in Taiwan

Japanese Encephalitis *Vaccine*

IXIARO® JESPECT®

Licensed in more than 35 countries

€ 60.0M
ANNUAL SALES 2017

€ 69.6M
ANNUAL SALES 2018

Aimed to protect travelers, military and populations in endemic regions against Japanese encephalitis

- An inactivated, alum-adjuvanted Vero-cell derived vaccine
- Indicated for active immunization against Japanese encephalitis in adults, adolescents, children and infants aged two months and older[7]

Key revenue drivers for 2019

- New supply contract with the U.S. government, Department of Defense, with $59 million in guaranteed revenues and potentially worth up to $70 million, in 2019 and 2020
- Further market penetration through reinforced product awareness notably in the U.S. private market
- Increased travel to endemic regions

Cholera (ETEC[8]) *Vaccine*

DUKORAL®

Established cholera (and ETEC[8]) vaccine

€ 28.5 M
ANNUAL SALES 2017

€ 30.4 M
ANNUAL SALES 2018

DUKORAL® is the only currently approved cholera vaccine available for European, Canadian and Australian travelers

The vaccine is an oral use formulation. DUKORAL® is indicated for active immunization against disease caused by *Vibrio cholerae* serogroup O1 in adults and children from two years of age who will be visiting endemic/epidemic areas. In Canada, the vaccine is indicated for the prevention of diarrhea caused by *Vibrio cholerae* (cholera) and/or heat-labile toxin producing enterotoxigenic *Escherichia coli* (ETEC)[8].

Key revenue drivers for 2019

- Continued market penetration through awareness campaigns directed at healthcare professionals and lay public, particularly in key markets such as Canada and the UK
- Increased travel to endemic regions

7 Age indication differs by territories **8** 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

DISEASES

About

JAPANESE ENCEPHALITIS

Japanese encephalitis (JE) is a potentially deadly infectious disease found mainly in Asia.

About 70,000 cases of JE are estimated to occur in Asia each year, although the actual number of cases is likely much higher due to under-reporting in rural areas.

The disease is transmitted by a mosquito-borne flavivirus related to the dengue, yellow fever, Zika and West Nile viruses. There is no cure for the disease, which highlights the importance of vaccination. About 1:25 to 1:1000 persons who are infected with the virus will develop symptomatic disease and inflammation of the brain. It is fatal in approximately 30% of individuals who show symptoms and results in permanent disability in half of the survivors.

According to the World Health Organization (WHO), 24 countries in Southeast Asia and the Western Pacific regions have endemic JE transmission, exposing more than 3 billion people to a risk of infection.

The WHO recommends strong prevention activities, including JE immunization in all regions where the disease is a recognized public health issue[9].

About

CHOLERA

Cholera is an acute diarrheal infection caused by ingestion of food or water contaminated with the bacterium *Vibrio cholerae*[10].

Cholera has a short incubation period (from two hours to five days) and is an extremely virulent disease that can cause severe acute watery diarrhea.

An estimated one to four million cholera cases and 21,000–143,000[10] deaths due to cholera occur every year.

According to the WHO cholera remains a global threat to public health and the WHO recommends immunization with currently available cholera vaccines in areas where cholera is endemic and in areas at risk of outbreaks.

About

ETEC

Enterotoxigenic *Escherichia coli* (ETEC) is an important cause of diarrhea in infants and travelers to underdeveloped countries or regions of poor sanitation. ETEC is estimated to affect about 11 million[11] travelers every year.

Similar to cholera, an enterotoxigenic *Escherichia coli* (ETEC) infection is usually transmitted through consumption of contaminated water or food.

The ETEC bacteria colonize the small intestine and cause severe diarrhea, dysentery, abdominal cramps and fever.

ETEC produce one or both of two enterotoxins, heat-labile enterotoxin (LT) and heat-stable enterotoxin (ST).

Heat-labile enterotoxin (LT) is structurally, pathophysiologically and immunologically similar to cholera toxin. This enterotoxin is neutralized by antibodies against cholera toxin B subunit[12].

9 WHO factsheet No 386 March 2014 **10** WHO Cholera factsheet, December 2017, http://www.who.int/mediacentre/factsheets/fs107/en
11 Lundkvist J, Steffen R, Jonsson B. Cost-benefit of WC/rBS oral cholera vaccine for vaccination against ETEC-caused travelers' diarrhea J Travel Med 200 9; 16(1):28-34
12 Isidean S.D, et al. A systematic review of ETEC epidemiology focusing on colonization factor and toxin expression. Vaccine 2011; 29:6167-78

Vaccine Candidates

We are dedicated to developing vaccines for infectious diseases with major unmet needs.

Infectious diseases are a leading cause of death and suffering in people worldwide. More people every year are visiting destinations that put them at a high risk for exposure to infectious diseases. Vaccination is the most effective method for preventing infectious disease and reducing its global burden[13]. Vaccines allow people to go about their daily lives without the fear of contracting a debilitating or deadly illness. In line with Valneva's mission to advance vaccines for better lives, the Company invests substantially in its development pipeline, including the most advanced Lyme disease vaccine in development today.

Valneva's R&D capabilities comprise all key functions needed to support the development of vaccines to licensure. Our global R&D operations, which encompass approximately 1/3 of our total employee base, are built on key R&D centers of excellence in Vienna (Austria) and Nantes (France).
Technical development functions at our manufacturing sites in Scotland and Sweden provide manufacturing support and operate dedicated manufacturing units for products used in clinical trials ("CTM-units").

Valneva's clinical portfolio

Underlining strong expertise in vector-borne infectious diseases
Our R&D portfolio primarily reflects our scientific, technical and clinical competencies in vector-borne infectious diseases and in both bacterial and viral vaccines.
We want to make a difference to people's lives by applying our innovative and pioneering science to address potential vaccine preventable diseases.

Three vaccines for infectious diseases with major unmet needs in clinical development, where no vaccines are currently available:

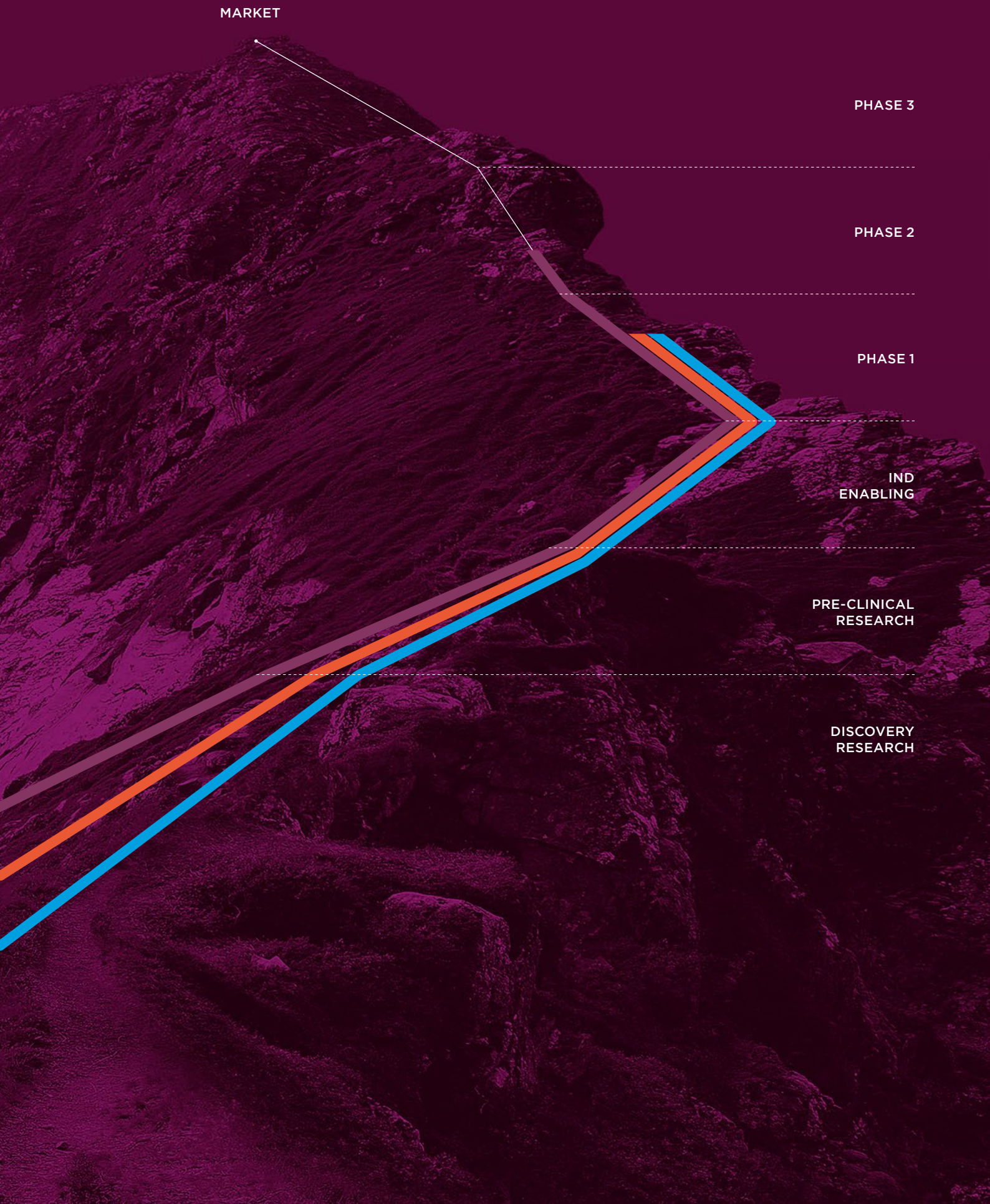
Product candidates

Lyme disease[14]

Zika

Chikungunya

13 Plotkin SL, Plotkin SA. A short history of vaccination. In: Plotkin SA, Orenstein WA, eds. Vaccines, 4th edn. Philadelphia: WB Saunders; 2004: 1-15
14 Based on a strategic alliance agreement signed in 2007, GSK has an opt-in right after Phase 2 on products developed by Valneva Austria GmbH


MARKET
PHASE 3
PHASE 2
PHASE 1
IND ENABLING
PRE-CLINICAL RESEARCH
DISCOVERY RESEARCH

Lyme Disease

LARVA | NYMPH | ADULT MALE | ADULT FEMALE

Not to scale

The most common vector-borne illness in the Northern Hemisphere [15, 16]

"The high incidence of Lyme disease is perhaps the greatest failure of contemporary public health in the United States and perhaps also in Europe, considering that we know the immunologic basis of control but have no licensed vaccine. A new vaccine would protect people of all ages from serious complications of this bacterial infection."

Stanley A. Plotkin, Emeritus Professor, University of Pennsylvania

Lyme disease is a systemic infection caused by *Borrelia* bacteria transmitted to humans by infected Ixodes ticks[17]. It is considered the most common vector-borne illness in the Northern Hemisphere. According to the U.S. Centers for Disease Control and Prevention (CDC), approximately 300,000 Americans[15] are diagnosed with Lyme disease each year with at least a further 200,000 cases in Europe[16].

Early symptoms of Lyme disease (such as a gradually expanding erythematous rash called *Erythema migrans* or more unspecific symptoms like fatigue, fever, headache, mild stiff neck, arthralgia or myalgia) are often overlooked or misinterpreted. Left untreated, the disease can disseminate and cause more serious complications affecting the joints (arthritis), the heart (carditis) or the nervous system.

The medical need for vaccination against Lyme disease is steadily increasing as the disease footprint widens[18]. Currently no Lyme disease vaccine is available to protect humans from this devastating illness.

Currently the only active vaccine program in clinical development against Lyme disease

VLA15 is a multivalent, protein subunit vaccine that targets the outer surface protein A (OspA) of *Borrelia*, one of the most dominant surface proteins expressed by the bacteria when present in a tick. It is intended for preventative, active immunization against Lyme disease in adults and children aged two years and older, aiming for protection against the six most common types of *Borrelia* that cause Lyme disease in North America and Europe.

The vaccine is designed to confer protection by raising antibodies that prevent *Borrelia* from migrating from ticks to humans after a bite. The target population for VLA15 includes individuals at risk living in endemic areas, people planning to travel to endemic areas to engage in outdoor activities and people at risk who have a history of Lyme disease (as infection with *Borrelia* does not confer protective immunity against all pathogenic *Borrelia* species).

VLA15 demonstrated a favorable safety profile in its Phase 1 clinical trial of 179 subjects[19], where no safety concerns were associated with the vaccine in any treatment group[20]. VLA15 was also immunogenic in all doses and formulations tested, with good OspA-specific IgG antibody responses against all OspA serotypes[21]. To evaluate the benefit of a booster dose, 64 subjects across the two higher dose groups from Phase 1 received a booster in the period 13 to 15 months after their initial primary immunization. These single re-vaccinations resulted in a significant immune-response.

The VLA15 program was granted Fast Track designation by the US Food and Drug Administration (FDA) in July 2017[22].

Phase 2 study initiated in December 2018

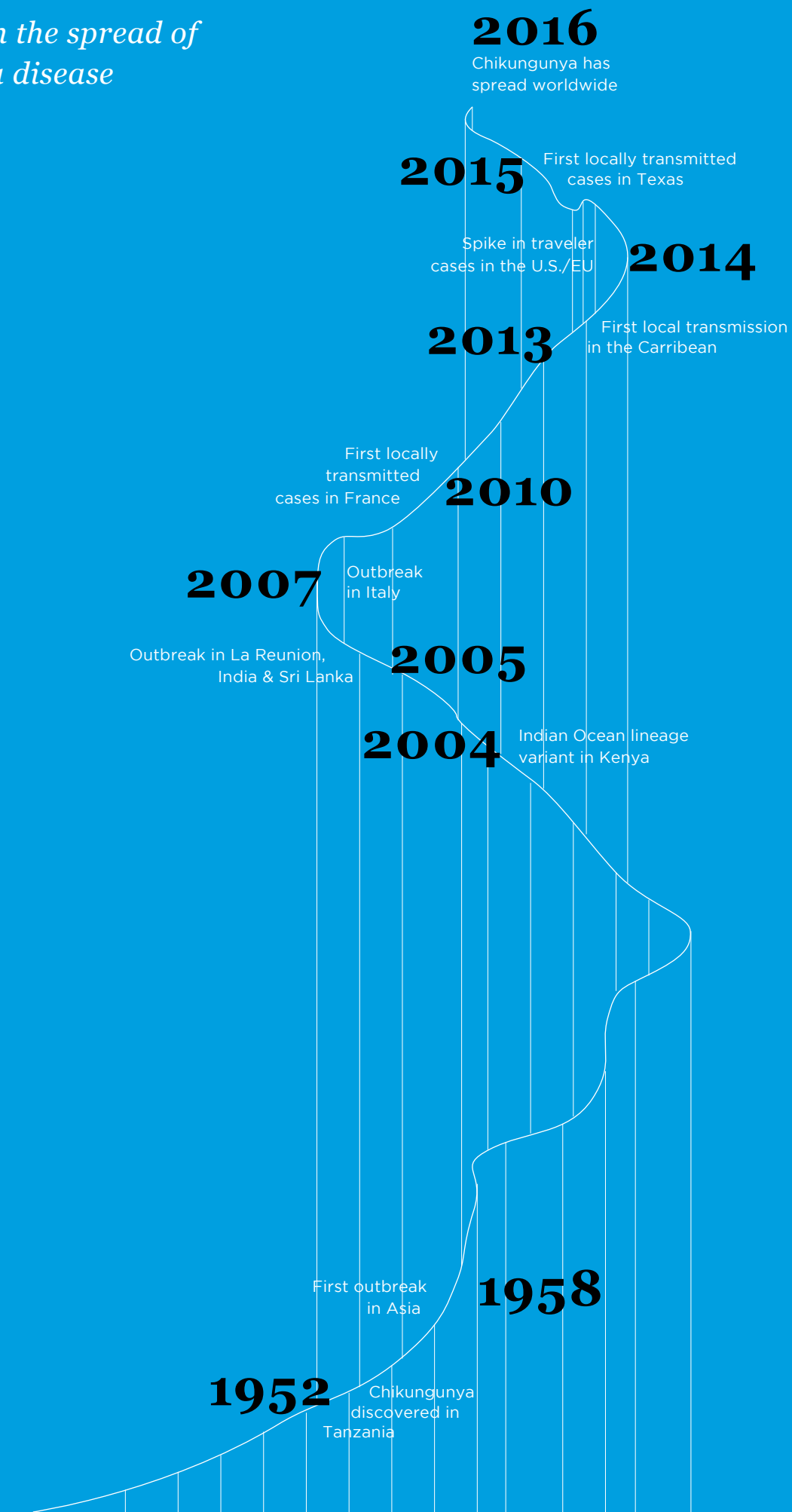
Valneva initiated[23] the first of two planned, parallel Phase 2 studies of VLA15, which are being conducted in the U.S. and Europe.

The overall Phase 2 objective is to determine the optimal dosage level and schedule for use in Phase 3 pivotal field efficacy studies, based on immunogenicity and safety data.

Valneva expects to announce interim Phase 2 data in 2020.

15 As estimated by the CDC, https://www.cdc.gov/lyme/stats/humancases.html **16** 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 **17** Stanek et al. 2012, The Lancet 379:461–473 **18** 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 **19** Valneva press release: https://www.valneva.com/en/investors-media/news/2018#282 **20** No differences in the safety profile were observed for the adjuvanted groups compared to the non-adjuvanted treatment groups **21** IgG levels were substantially higher after three immunizations (Day 84) compared to after two (Day 56) **22** Valneva press release: https://www.valneva.com/en/investors-media/news/2017#270
23 Valneva press release: https://www.valneva.com/en/investors-media/news/2018#303

Key events in the spread of chikungunya disease



Chikungunya

A mosquito-borne viral infection spreading in the Americas and Europe

Chikungunya is a mosquito-borne viral disease caused by the chikungunya virus (CHIKV), a *Togaviridae* virus, transmitted by *Aedes* mosquitoes.
Clinical symptoms include acute onset of fever, debilitating joint and muscle pain, headache, nausea and rash, potentially developing into long-term, serious health impairments. Chikungunya virus causes clinical illness in 72–92% of infected humans around four to seven days after an infected mosquito bite. Complications resulting from the disease include visual, neurological, heart and gastrointestinal manifestations; fatalities have been reported (case fatality rates of 0.1% to 4.9% from epidemics)[24] in elderly patients at higher risk. Chikungunya outbreaks have been reported in Asia, Africa, the Americas and recently (2017) in Europe. As of 2017, there have been more than one million reported cases in the Americas[25] and the economic impact is considered to be significant (e.g. Colombia outbreak 2014: $73.6m[26]). The medical and economic burden is expected to grow as mosquitos, the primary vectors of CHIKV, continue to further spread geographically. There are no preventive vaccines or effective treatments available and, as such, chikungunya is considered to be a major public health threat.

Chikungunya vaccine VLA1553

A potential single-shot vaccine against a severe, growing threat
VLA1553 is a monovalent, single dose, live-attenuated vaccine candidate for protection against chikungunya. The vaccine candidate is designed for prophylactic, active, single-dose immunization against chikungunya in humans over one year old. The vaccine aims for long-lasting protection and an anticipated safety profile similar to licensed vaccines for active immunization in adults and children. The target population segments are travelers, military personnel and individuals at risk living in endemic regions. VLA1553 is based on an infectious clone (CHIKV LR2006-OPY1) attenuated by deleting a major part of the gene encoding the non-structural replicase complex protein nsP3, aiming for protection against various chikungunya virus outbreak phylogroups and strains[27].
In pre-clinical development, a single-vaccine shot was shown to be highly immunogenic in vaccinated non-human primates (NHP) (*cynomolgus macaques*) and showed no signs of viremia after challenge[28]. In NHPs, VLA1553 induced a strong, long lasting (more than 300 days) neutralizing antibody response comparable to wild-type CHIKV infections combined with a good safety profile.

The program VLA1553 was granted Fast Track designation by the FDA in December 2018[29].

Phase 1 interim results

Valneva reported positive Phase 1 interim results for its chikungunya vaccine candidate VLA1553 in January 2019[30].
The primary objective of VLA1553-101 Phase 1 study was to assess the overall safety and immunogenicity profile 28 days after a single vaccination across three dose levels. The interim results showed an excellent immunogenicity profile and an acceptable safety profile after a single vaccination with a 100% seroconversion rate[31] achieved at Day 28 in a pooled analysis[32] of all vaccinated groups. Results also showed 96.5% of subjects achieved at least a 16-fold increase in antibody titres and a high geometric mean titre, fully supporting VLA1553's differentiated target product profile.
The Phase 1 clinical trial is a randomized, observer-blinded, dose-escalation, multi-center study.
It is conducted in the U.S. and investigates three different dose levels of VLA1553 in 120 healthy adults vaccinated with a single-shot immunization. The trial design includes the investigation of antibody persistence and an additional vaccination using the highest dose of VLA1553 at 6 and 12 months. This re-vaccination will serve as an intrinsic human viral challenge, aiming to demonstrate that subjects are protected from vaccine-induced viremia thereby indicating potential efficacy of VLA1553 early in clinical development.
Final data from the trial are expected to be available mid 2019.

24 WHO, PAHO **25** PAHO/WHO data: Number of reported cases of chikungunya fever in the Americas – EW 51 (December 22, 2017)
26 Cardona-Ospina et al., Trans R Soc Trip Med Hyg 2015 **27** Hallengärd et al. 2013 J. Virology 88: 2858-2866
28 Roques et al. 2017JCI Insight 2 (6): e83527 **29** Valneva press release: https://www.valneva.com/en/investors-media/news/2018#304
30 Valneva press release: https://www.valneva.com/en/investors-media/news/2019#305 **31** SCR was defined as the proportion of subjects achieving a CHIKV specific neutralizing antibody titre of NT50≥20 **32** The Phase 1 study continues blinded with re-vaccinations to potentially obtain a first indication of efficacy, the interim results were therefore not analyzed by dose group but through a pooled analysis of all dose groups

Zika

A mosquito-borne disease associated with birth defects

The Zika virus is a mosquito-borne flavivirus that was first discovered in 1947. The first human cases were detected in 1952. Since then, outbreaks have been reported in tropical Africa, Southeast Asia, the Pacific Islands, and, in 2015, in the Americas.

According to the WHO, there is scientific consensus that ZIKV is a cause of microcephaly and Guillain-Barré syndrome. Since 2013, 31 countries and territories have reported cases of microcephaly and other central nervous system malformations associated with ZIKV infection.

Zika vaccine VLA1601

An inactivated vaccine candidate partnered with Emergent BioSolutions

VLA1601 is a highly purified inactivated vaccine candidate against the Zika virus, developed using the same manufacturing platform as Valneva's IXIARO® (JESPECT®) JE vaccine. In pre-clinical development, VLA1601 demonstrated excellent purity and had an overall biological, chemical and physical profile comparable to the commercially produced JE vaccine. Valneva has an established manufacturing process in its dedicated clinical JE vaccine facility. In July 2017, Valneva granted U.S. company Emergent BioSolutions Inc. an exclusive worldwide license for its Zika vaccine technology. The agreement includes predefined post-Phase 1 opt-in rights for Emergent.

Interim results of the Phase 1 clinical study

Valneva and its development partner Emergent BioSolutions reported positive interim results for the Phase 1 study evaluating VLA1601 in November 2018[33].
The vaccine candidate met the study's primary endpoint showing a favorable safety profile in all doses and schedules tested. VLA1601 was also immunogenic in all treatment groups and induced both dose- and schedule dependent neutralizing antibodies against the Zika virus with the kinetics expected for an inactivated, alum-adjuvanted whole-virus vaccine. Seroconversion rates (SCR) reached up to 85.7% on day 35 (interim analysis of data up to day 56). The final analysis at day 208 after first vaccination is expected in the second quarter of 2019 and will include additional immunogenicity data.

33 Valneva press release: https://www.valneva.com/en/investors-media/news/2018#300
34 Provisional Data as of January 2, 2019, https://www.cdc.gov/zika/reporting/case-counts.html


Number of confirmed Zika cases in the U.S.
(2015–2018)34
5460
Travel
231
Locally transmitted
55
Sexual transmission and other routes

Manufacturing site

Solna

Sweden

Manufacturing site

Livingston

Scotland

Dedicated GMP facilities

Vienna

Austria

MANUFACTURING & SERVICES

Valneva's global manufacturing network includes three in-house operations to cover the internal and external production of clinical and commercial products.

Valneva provides state-of-the-art manufacturing according to Good Manufacturing Practice (GMP) guidelines, including quality assurance and control capabilities for the production and release of commercial and clinical trial products. We extend our manufacturing network through partnerships with various contract manufacturing organizations (CMOs), providing specific services within the different supply chains of our clinical trial and commercial products.
Dedicated internal resources manage these CMOs, assuring the quality oversight and a highly efficient supply chain management needed to ensure the on-time delivery of our products.
From the process sustainability and quality assurance points of view, vaccine manufacturing is considered to be extremely demanding. The high quality standards of Valneva's production facilities are regularly and rigorously verified by our partners and by multiple regulatory authorities including the FDA, the Swedish Medical Products Agency (MPA), the UK Medicines & Healthcare products Regulatory Agency (MHRA) and the Austrian Agency for Health and Food Safety (AGES), as well as through qualification verification, audits and inspections.

Valneva also leverages its capabilities in product development and clinical trial materials manufacturing with third parties.

- Technical development (process and assay development for viral and bacterial vaccines)
- Clinical immunology assay development and sample testing services
- Clinical manufacturing
- In-vivo testing for pre-clinical proof of concept (PoC), immunogenicity and safety assessments
- General facility services
- Clinical strategy and operations for clinical-stage vaccine programs

Manufacturing Site

Valneva's FDA approved manufacturing site in Livingston located just outside Edinburgh is currently dedicated to drug substance production for our viral vaccines.

The site includes the dedicated commercial manufacturing unit for the drug substance of the Company's leading commercial product, IXIARO®/ JESPECT®.
An additional fully segregated, multi-purpose clinical trial material manufacturing facility provides a flexible platform for process development and the drug substance production of viral products intended to undergo clinical investigations. This facility has been used for the production of clinical trial materials for the Company's Zika and chikungunya vaccine candidates.

Manufacturing Site

Just outside Stockholm is Valneva's manufacturing site in Solna. The site has a long tradition of vaccine manufacturing connected to Sweden's state-owned vaccine institute.

The multi-purpose bacterial drug substance GMP facility is producing the various substances needed for the Company's second commercial product, DUKORAL®. The site also comprises facilities for the formulation, filling and packaging of DUKORAL®.
A fully segregated, multi-purpose clinical trial material manufacturing facility (CTM Unit) provides a modern platform for process development and for the bulk production of cell-culture viral products intended to undergo clinical investigations.
In 2018, Valneva entered into a three-year collaboration and manufacturing agreement with Hookipa Pharma Inc., for which Valneva Sweden will provide analytical services, develop process scale-up and produce GMP clinical trial material to support the development of Hookipa's immunotherapies.

Dedicated GMP facilities

Co-located with Valneva's development center in Vienna (Austria), the Company operates GMP laboratories and facilities for the testing and quality control of Valneva's commercial and clinical stage vaccines.

Those facilities comprise multiple in-vitro quality control (QC) labs, a dedicated laboratory for clinical serology, a state-of-the-art facility for in-vivo release testing (i.e. for IXIARO®/JESPECT®) and are regularly inspected by regulatory bodies, including the FDA.

Supervisory Board

Our commitment to corporate governance underpins the trust that our investors, employees and institutions have in us. We maintain our efforts to build confidence as we continue to grow.

As part of Valneva's two-tier corporate governance system, the Supervisory Board, acting in the interests of the shareholders, participates actively in reviewing the Company's strategic options and setting direction together with the Management Board.

Frédéric Grimaud (F)
Chairman of Valneva's Supervisory Board, Representative of the Company's largest shareholder, President and CEO of Groupe Grimaud

James Sulat (US)
Vice-Chairman of the Supervisory Board & Chairman of the Audit Committee, former CFO for Chiron, CEO of Maxygen

Ralf Clemens, MD, PhD (D)
Chairman Scientific Committee, Member of Board of Trustees International Vaccine Institute IVI, member GHIT scientific selection committee, member CEPI scientific committee, Advisor Bill & Melinda Gates Foundation, former Head/Senior Vice President Vaccine Development at GSK, Novartis and Takeda

Alain Munoz, MD, PhD (F)
Chairman of the Nomination & Compensation Committee, Board member of Hybrigenics SA, Supervisory Board member of OxThera AB, Zealand Pharma A/S, former Vice President of International Product Development at Sanofi

Anne-Marie Graffin (F)
Member, Managing Director of SMAG Consulting, Supervisory Board member of Nanobiotix SA, Board member of Sartorius Stedim Biotech SA, former Vice President at Sanofi Pasteur MSD

Alexander v. Gabain Prof., PhD (A)
Member, Chairman of the trans-European innovation consortium, EITHealth, former Vice-President of the Karolinska Institute, Co-founder of Intercell

Balaji Muralidhar, MD, PhD (UK)
Member, Partner at MVM Partners LLP, former member of Bain Capital's Healthcare Deal team

Lisa Shaw-Marotto (US)
Member, President of Executive Perspective Consulting LLC, former Vice President Marketing at Merck & Co

Maïlys Ferrere for bpifrance Participations SA (F)
Member, Director of Large Venture Investments at bpifrance, France's state-owned investment bank

Sandra E. Poole (US)
Member, Chief Operating Officer at LogicBio Therapeutics, former Executive Vice President, Technical Operations at ImmunoGen, Senior Vice President Biologics Manufacturing at Sanofi Genzyme

Thomas Lingelbach
President & Chief Executive Officer
CEO of Intercell since 2011/Managing Director for Novartis Vaccines & Diagnostics Germany/Vice President of Global Industrial Operations at Chiron Vaccines/more than 25 years in the vaccine industry

Frédéric Jacotot
General Counsel & Corporate Secretary
VP Legal & IP and General Counsel of Valneva since September 2013/Former Division Counsel at Abbott/30 years as a legal expert in the pharmaceutical industry

David Lawrence
Chief Financial Officer
CFO of vaccine biotech company Acambis/ Vice President Finance, Business Development and Strategy at Chiron Vaccines/ Vice President Finance GSK/Non-executive and advisory experience/30 years of experience in vaccines and Life Sciences

Franck Grimaud
President & Chief Business Officer
CEO and co-founder of Vivalis since 1999/ Formerly responsible for Groupe Grimaud's development in Asia/25 years in Corporate Business Development and Life Sciences

Management Board

Valneva's Management Board is a highly dedicated international team, with diverse backgrounds, experience, expertise and skills.

Wolfgang Bender, MD, PhD
Chief Medical Officer
Senior international positions at various large Life Science companies including Novartis, Takeda, Pfizer and Hoechst/Experiences in scientific-medical affairs, drug development and general management of vaccines and pharmaceuticals/more than 30 years of experience in Life Sciences

Our Corporate Social Responsibility Approach

We have defined long-term responsible business commitments, which reflect global health needs and sit across four key focus areas.
Our four pillars are the foundation for our Corporate Social Responsibility (CSR) approach.
We naturally devote attention to our first pillar, Protecting Lives. The second pillar covers Acting Ethically, both in R&D and in business.
Our third pillar focuses on our employees, or more specifically, Developing our People.
Respecting the Environment by preventing pollution, managing waste and controlling energy consumption represents our fourth pillar.

Protecting

Lives

Valneva is engaged in the development and commercialization of innovative vaccines against infectious diseases with high unmet medical need with the aim of protecting the lives of people around the world.

Valneva's commercial vaccines address two life-threatening diseases: Japanese encephalitis, or JE, and cholera. Approximately 70,000 new cases of JE are recorded every year, while an estimated three to five million cases of cholera are recorded annually.
Valneva is continuously expanding its marketing and distribution network to ensure global availability of its products.
The Company has entered into agreements with Biological E. (India) and Adimmune (Taiwan) to make its Japanese encephalitis vaccine available in these countries, where the disease is endemic.
As new infectious diseases emerge worldwide, our role is to develop lifesaving vaccines to address global health needs. In 2018, Valneva dedicated more than 20 % of its revenues to R&D, working on clinical candidates to prevent diseases for which no preventative interventions or treatments currently exist, including Lyme disease and the chikungunya and Zika viruses.

Acting

Ethically

As we conduct research designed to develop new healthcare solutions, we continually examine our practices and processes from an ethical standpoint and ensure compliance in an ever-evolving regulatory environment.

Valneva has set up an in-house committee, the Research & Development Operational Committee (RDOC), which meets every month to carry out a thorough review of our R&D pipeline.
To ensure respect for ethics across our R&D activities, we monitor and audit our processes with our quality control and quality assurance procedures as we continuously seek to improve them.
Our approach to business ethics and our commitment to preventing corruption have shaped the Valneva Code of Conduct and our Anti-Bribery and Anti-Corruption Policy. Both apply to all Supervisory Board members, Management Board members, directors and all employees of Valneva worldwide.

Developing our

People

Our employees are our single largest asset

Valneva's success stems from the dedication and expertise of approximately 480 employees. Valneva is an international and multicultural company who prides itself on offering its workforce the opportunity for personal growth and development. Our culture is marked by enthusiasm, innovation and strong execution, which creates a unique identity.
Valneva promotes equal opportunity and maximizes our talent. A management review and personal development plan are in place for all of our employees. Our learning initiatives are driven by the need to develop job-related expertise and to reinforce leadership and communication competencies.
As a global company that respects all cultures, we are convinced that the rich diversity of our workforce and the talents they offer make us more innovative, effective and competitive.

Respecting the

Environment

Aware that the environment we live in directly affects people's health, we feel that we have a responsibility as a vaccine company to reduce our own carbon footprint and manage our waste and consumption.

We aim to use natural resources efficiently to minimize the environmental impact of our activities and products during their lifecycles. We integrate sustainable operations and supply chains, innovative products and packaging, and environmental sustainability into our business decision process. A policy for waste separation, recycling and monitoring has been adopted at Valneva. We highlight the importance of this policy as a major priority for all sites. It consists of four key areas:

1. Formal environmental management system based on strict procedures and compliance with regulations
2. Pollution prevention and waste management
3. Improvement of energy consumption management
4. Information and training programs on environmental protection, health and safety

The United Nations Global Compact

In line with its CSR approach, Valneva supports the United Nations Global Compact and incorporates the UNGC's ten principles into its strategies, policies and procedures.

UN GLOBAL COMPACT
WE SUPPORT

Supporting the Baan Dek Foundation

To reinforce its involvement in offering access to healthcare, Valneva continued its official sponsorship of the Baan Dek Foundation, a Thai-registered foundation that aims to foster children's education, health and safety in Thailand. In 2018, the Baan Dek Foundation supported over 1,000 vulnerable children throughout 50 communities in Chiang Mai.

Baan Dek
FOUNDATION

Local community engagement

Valneva also supports social engagement at the local level. Valneva believes in the importance of social engagement and encourages its employees to participate in charity events and volunteer in their local communities. Several initiatives took place in 2018 to raise money for local charities and to support educational institutions in the communities where we work.

Other sponsorships

Valneva supports the Encephalitis Society, an international charity that envisions a world aware of encephalitis, its consequences and the support available. The Encephalitis Society works with survivors and family members affected by the condition and drives the largest encephalitis awareness campaign – World Encephalitis Day.

ENCEPHALITIS SOCIETY
The brain inflammation charity

"2018 has been a significant year for Valneva. We broke the €100 million threshold for product sales, made significant progress in R&D and successfully executed a strategic capital raise as part of our capital formation strategy. 2019 is already off to an excellent start with the new IXIARO® supply contract with the U.S. Department of Defense and positive Phase 1 interim results for our chikungunya vaccine candidate. We are excited about continuing to execute our strategy and unlocking shareholder value."

David Lawrence, CFO

35 "Grant income" was reclassified from the position "Revenue and Grants" and included in "Other income/expense" for periods starting Jan 1, 2018. The comparable period was adjusted accordingly to maintain the comparability

€ in thousand
(except per share amounts)

	Year ended December 31, 2018	2017
Product sales	103,476	92,619
Revenues from collaborations, licensing and services	9,559	12,672
Revenues[35]	**113,035**	**105,291**
Cost of goods and services	(44,448)	(45,979)
Research and development expenses	(25,291)	(23,356)
Marketing and distribution expenses	(20,930)	(17,875)
General and administrative expenses	(16,932)	(15,545)
Other income and expenses, net[35]	4,004	4,240[1]
Amortization and impairment of fixed assets/intangibles	(3,177)	(10,731)
Operating Profit / (Loss)	**6,261**	**(3,954)**
Finance income	178	72
Finance expenses	(4,209)	(8,678)
Result from investments in associates	1,122	–
Profit / (Loss) before income tax	**3,351**	**(12,560)**
Income tax	(88)	1,078
Profit / (Loss) for the period	**3,264**	**(11,482)**
Earnings / (Losses) per share *for profit/loss for the period attributable to the equity holders of the Company, expressed in € per share*		
– basic	0.04	(0.15)
– diluted	0.04	(0.15)

€ in thousand	At December 31, 2018	2017
ASSETS		
Non-current assets	**103,934**	**105,895**
Intangible assets	44,891	48,468
Property, plant and equipment	37,997	38,374
Equity-accounted investees	1,122	–
Other non-current assets	17,236	17,368
Deferred tax assets	2,689	1,686
Current assets	**125,972**	**83,448**
Inventories	22,727	19,931
Trade receivables	11,259	17,622
Other current assets	10,261	7,840
Cash and cash equivalents	81,725	38,055
TOTAL ASSETS	**229,907**	**189,343**
EQUITY		
Capital and reserves attributable to the Company's equity holders	**143,186**	**92,669**
Share capital	13,638	11,638
Share premium and other regulated reserves	297,720	252,934
Retained earnings and other reserves	(171,435)	(160,421)
Net result for the period	3,264	(11,482)
LIABILITIES		
Non-current liabilities	**43,777**	**59,000**
Borrowings	40,070	54,097
Non-current contract liabilities, other liabilities and provisions	3,707	4,903
Current liabilities	**42,944**	**37,674**
Borrowings	17,529	17,399
Trade payables and accruals	13,325	9,527
Current tax liability	1,406	322
Tax and employee-related liabilities	8,643	7,531
Current contract liabilities, other liabilities and provisions	2,041	2,896
TOTAL LIABILITIES	**86,721**	**96,674**
TOTAL EQUITY AND LIABILITIES	**229,907**	**189,343**

€ in thousand	Year ended December 31,	
	2018	2017
CASH FLOWS FROM OPERATING ACTIVITIES		
Profit/(loss) for the year	3,264	(11,482)
Depreciation and amortization	6,828	11,141
Impairment	–	3,568
Share-based payments	1,887	811
Income tax	88	(1,078)
Other adjustments for reconciliation to cash generated from operations	1,559	6,330
Changes in working capital	3,955	4,199
Cash generated from operations	**17,580**	**13,489**
Income tax paid	(1,273)	(660)
Net cash generated from operating activities	**16,306**	**12,829**
CASH FLOWS FROM INVESTING ACTIVITIES		
Purchases of property, plant and equipment	(2,874)	(2,890)
Proceeds from sale of property, plant and equipment	76	–
Purchases of intangible assets	(297)	(1,148)
Purchases of financial instruments	–	(94)
Interest received	178	72
Net cash generated from (used in) investing activities	**(2,917)**	**(4,060)**
CASH FLOWS FROM FINANCING ACTIVITIES		
Proceeds from issuance of common stock, net of costs of equity transactions	49,286	(43)
Disposal/(Purchase) of treasury shares	(23)	(104)
Proceeds from borrowings, net of transaction costs	1,481	11,104
Repayment of borrowings	(15,571)	(16,415)
Interest paid	(4,165)	(4,980)
Net cash generated from/(used in) financing activities	**30,945**	**(10,438)**
Net change in cash and cash equivalents	**44,334**	**(1,670)**
Cash at beginning of the year	33,545	35,267
Exchange gains/(losses) on cash	(795)	(53)
CASH AT END OF THE YEAR	**77,084**	**33,545**
CASH AND CASH EQUIVALENTS AT END OF THE YEAR	**81,725**	**38,055**

Financial Review

Product sales revenues (on an AER[36] basis) in 2018 increased to €103.5 million from €92.6 million in 2017, representing year over year growth of 11.7%.

IXIARO®/JESPECT® product sales contributed €69.6 million to revenues in 2018 compared to €60.0 million in 2017, representing over 15% growth. The increase was mainly driven by strong demand in the U.S. and in Canada. DUKORAL® sales contributed €30.4 million to the 2018 product sales, representing growth of 6% compared the year 2017, largely driven by strong sales performance in Canada.

Valneva's total revenues[37] (on an AER[36] basis) in 2018 increased to €113.0 million compared to €105.3[38] million in 2017.

As a result of sales growth, improved margins and reduced amortization and impairment charges, Valneva realized an operating profit of €6.3 million in 2018 compared to an operating loss of €4.0 million in 2017. EBITDA in 2018 was €13.1 million, compared to an EBITDA of €10.8 million in 2017. EBITDA is calculated by excluding depreciation, amortization and impairment charges from the operating profit as recorded under IFRS.

Liquid funds on December 31, 2018 stood at €81.7 million compared to €38.1 million on December 31, 2017 and consisted of €77.1 million in cash and cash equivalents and €4.6 million in restricted cash.

36 AER: actual exchange rates **37** Including service revenue and license fees **38** "Grant income" was reclassified from the position "Revenue and Grants" and included in "Other income/expense" for periods starting Jan 1, 2018. The comparable period was adjusted accordingly to maintain the comparability

Product Sales Revenues

€ 115 M – € 125 M

R&D Investments

€ 35 M – € 40 M

Total Revenues

€ 125 M – € 135 M

EBITDA

€ 5 M – € 10 M

Financial Outlook

Contact information

Investor Relations & Corporate Communications
France: T +33-2-2807-3710
Austria: T +43-1-206 20-1116
communications@valneva.com
investors@valneva.com
www.valneva.com

VALNEVA SE
Campus Bio-Ouest
6 Rue Alain Bombard
44800 Saint-Herblain, Nantes area, France

VALNEVA SE
Gerland Plaza Techsud
70, rue Sant-Jean-de-Dieu
69007 Lyon, France

VALNEVA AUSTRIA GMBH
Campus Vienna Biocenter 3
1030 Vienna, Austria

VALNEVA SCOTLAND LTD.
Oakbank Park Road
Livingston EH53 0TG, Scotland

VALNEVA SWEDEN AB
SE–105 21
Stockholm, Sweden

VALNEVA CANADA INC.
3535 Saint-Charles Blvd., Suite 600
Kirkland (Québec) H9H 5B9, Canada

VALNEVA UK LTD
Centaur House, Ancells Business Park
Ancells Road / Fleet
Hampshire GU51 2UJ, United Kingdom

VALNEVA USA, INC.
910 Clopper Road, Suite 160S,
Gaithersburg, MD 20878, United States

Credits

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