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The commercial outlook for infectious disease vaccines

Data on sales, financing and major deals for vaccines for infectious diseases provide an outlook into the development of the commercial landscape for such products.

BioPharma Dealmakers

Vaccines were once generally regarded by the pharma industry as an area with relatively limited revenue opportunities. But with the success of products such as Pfizer's pneumococcal vaccines Prevnar and Prevnar 13—with combined sales of ~\$5.7 billion in 2016 according to data from EvaluatePharma—this perception has changed. Moreover, advances in vaccine technology and the need to combat emerging infectious disease threats such as Zika virus have provided further impetus to the field (see *BioPharma Dealmakers* B15–B17, June 2016). In this article, we highlight the development of the market and selected deals in the past two years for infectious disease vaccines as well as the level of early-stage financing for vaccine development in general.

Market set for growth

Data from EvaluatePharma on current and predicted future sales of vaccines against a selected group of infectious diseases that make up the bulk of the market indicate that growth is expected in the majority of areas (Fig. 1).

Overall, the highest-selling vaccines within the selected categories are pneumococcal vaccines, which are widely used in childhood vaccination programs. Between them, they are achieving sales of just over \$7 billion currently, and the forecasted level of sales in 2022 is similar. This sector is dominated by Pfizer's Prevnar products—Prevnar and its follow-up Prevnar 13—which are conjugate vaccines that contain polysaccharides from 7 and 13 different serotypes of

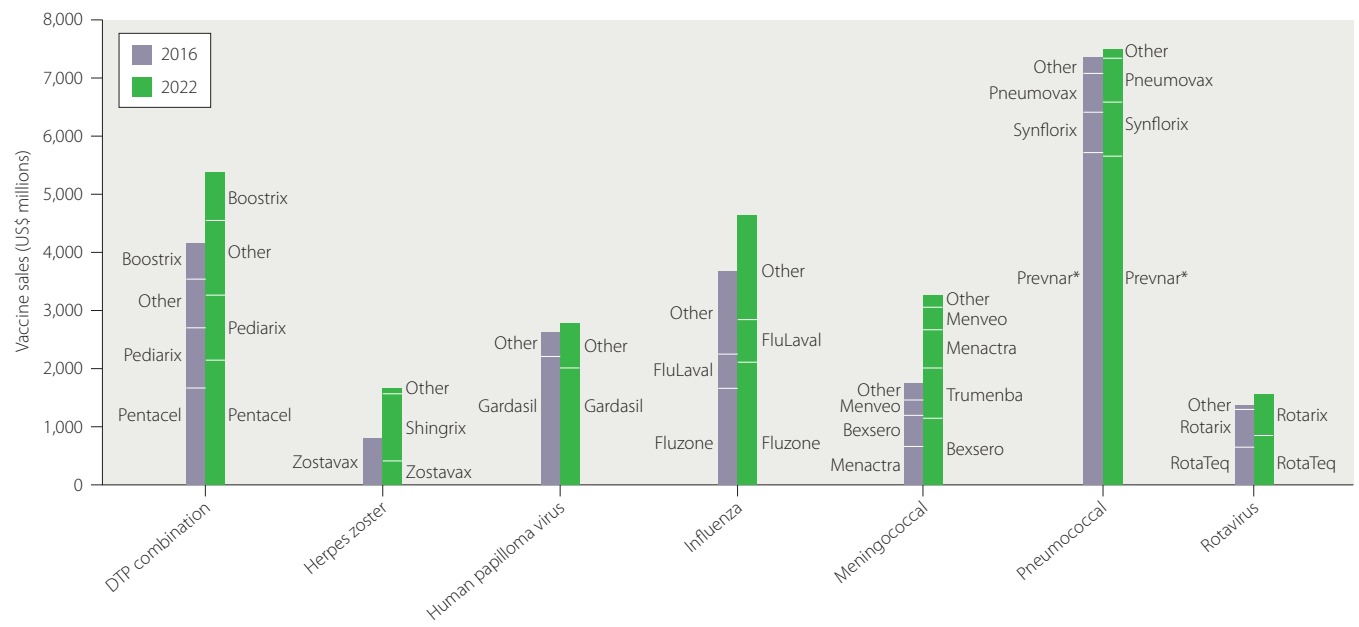


Figure 1: Global vaccine sales for selected vaccine categories in 2016 and 2022. 2016 sales are indicated by purple bars, and predicted sales for 2022 by green bars. DTP combination vaccines include vaccines against diphtheria, tetanus and pertussis (DTP) that also contain one or more components to provide protection against other infections, including hepatitis B, *Haemophilus influenzae* type B and/or polio. Meningococcal vaccines include meningococcal group A, C, W-135 and Y vaccines, meningococcal group B vaccines and meningococcal group C vaccines. Pentacel is a DTP, *Haemophilus influenzae* type B and polio vaccine. Pediarix is a DTP, hepatitis B and polio vaccine. Menactra and Menveo are meningococcal type A, C, W-135 and Y vaccines. Bexsero and Trumenba are meningococcal type B vaccines. *Sales included for both Prevnar and Prevnar 13. Source: EvaluatePharma, April 2017, Evaluate, www.evaluate.com

Table 1: Selected vaccine product licensing deals in the last two years

Deal Date	Primary company	Deal partner	Type of deal	Product indication	Status on deal date	Deal summary
September 2015	Daiichi Sankyo	AstraZeneca	In-licensing	Influenza	Phase 3	MedImmune—AstraZeneca's biologics research unit—grants an exclusive license to Daiichi Sankyo to develop and commercialize FluMist Quadrivalent in Japan.
April 2016	hVIVO	Imutex	Joint venture	Influenza, Zika and viral indications	Phase 2 and preclinical	hVIVO signs joint venture deal with the Seek Group to invest in the company Imutex for the development of vaccines against influenza and Zika.
June 2016	Astellas Pharma	University of Tokyo	In-licensing	Cholera, <i>Escherichia coli</i>	Phase 1	The Institute of Medical Science at the University of Tokyo, partners with Astellas Pharma to develop an oral vaccine against cholera and enterotoxigenic <i>E. coli</i> .
December 2016	Mymetics	Sanofi Pasteur	Out-licensing technology	Influenza	Preclinical	Mymetics Corp signs research deal to investigate the immunogenicity of influenza vaccines with Sanofi Pasteur.
October 2016	Sun Pharmaceutical Industries	International Centre for Genetic Engineering and Biotechnology (ICGEB)	In-licensing	Dengue fever	Preclinical	Sun Pharma signs deal with the ICGEB to develop a vaccine against all four serotypes of the dengue fever virus.
September 2016	Zydus Cadila	Takeda	In-licensing	Chikungunya fever	Preclinical	Takeda partners with Zydus Cadila to develop vaccine against chikungunya.
September 2016	LEUKOCARE	PaxVax	Out-licensing technology	Adenovirus infection	Preclinical	PaxVax will license LEUKOCARE's SPS formulation technology for the development of one of its live viral vaccine products.
April 2016	Orygen Biotecnologia	Protein Sciences	In-licensing	Influenza	Preclinical	Protein Sciences signs deal with Orygen Biotecnologia granting it an exclusive license to the Flublok influenza vaccine for Brazil.
December 2015	Janssen Pharmaceuticals	Bavarian Nordic	In-licensing	Human papillomavirus (HPV) infections	Preclinical	Janssen Pharmaceuticals to develop therapeutic vaccine for HPV infections in \$171 million deal with Bavarian Nordic.
December 2015	Yisheng Biopharma	U.S. Army Medical (USAMRIID)	Out-licensing technology	Ebola hemorrhagic fever (EHF)	Preclinical	Yisheng Biopharma collaborates with USAMRIID to develop a new vaccine against the Ebola virus.
September 2015	GlaxoSmithKline	Sinovac Biotech	Out-licensing technology	Measles	Preclinical	Sinovac signs deal to use GSK's measles seeds to develop a measles vaccine and combination vaccines for China.
July 2015	Immunovaccine	PharmAthene	Out-licensing technology	Anthrax	Preclinical	Immunovaccine enters licensing deal with PharmAthene to develop a recombinant protective antigen anthrax vaccine.
June 2015	Vaxxilon	Max-Planck Innovation GmbH—the technology transfer office of the Max Planck Society	In-licensing	Pneumococcal infections	Preclinical	Vaxxilon licenses rights to preclinical vaccine candidates from Max-Planck Innovation GmbH.

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Deal Date	Primary company	Deal partner	Type of deal	Product indication	Status on deal date	Deal summary
May 2015	Soligenix	Hawaii Biotech	Out-licensing technology	Ebola hemorrhagic fever (EHF)	Preclinical	Soligenix along with the University of Hawaii and Hawaii Biotech collaborate to develop a heat-stable subunit Ebola vaccine.
May 2015	GeneOne Life Science	Inovio Pharmaceuticals	In-licensing	Respiratory tract infections	Preclinical	Inovio partners with GeneOne Life Science for immunotherapy development of Inovio's DNA-based MERS vaccine, INO-4500.
February 2017	Affinivax	Astellas Pharma	Out-licensing technology	Pneumococcal infections	Research	Affinivax signs deal with Astellas to develop and commercialize a vaccine targeting <i>Streptococcus pneumoniae</i> .
February 2017	CEVEC Pharmaceuticals	NewLink Genetics		Zika virus	Research	NewLink Genetics gains license and rights to Cevec's CAP technology to develop Zika vaccine.
January 2017	Synthetic Genomics	Johnson & Johnson		Infectious diseases	Research	Agreement to develop RNA-based therapies for cancer and infectious diseases.
October 2016	Heat Biologics	University of Miami	Out-licensing technology	Zika virus	Research	Heat Biologics and University of Miami collaborate to develop a Zika vaccine.
September 2015	CureVac	International AIDS Vaccine Initiative (IAVI)	Out-licensing technology	HIV	Research	CureVac's RNAactive technology will deliver immunogens from IAVI to help develop a vaccine against AIDS.
February 2015	Moderna Therapeutics	Institut Pasteur		Infectious diseases	Research	Using Moderna's mRNA platform, Institut Pasteur will discover and develop drugs and vaccines.
January 2015	Moderna Therapeutics	Merck & Co. (known as MSD outside the United States and Canada)	Out-licensing	Undisclosed targets	Research	Merck signs licensing and collaboration deal with Moderna's infectious disease-venture Valera to develop five mRNA-based therapies and vaccines.

CMV, cytomegalovirus; HSV, herpes simplex virus; HPV, human papilloma virus; MERS, Middle East respiratory syndrome; SARS, severe acute respiratory syndrome. Source: EvaluatePharma, April 2017, Evaluate, www.evaluate.com and company press releases.

Streptococcus pneumoniae, respectively. The other major products are GlaxoSmithKline's (GSK) Synflorix (a conjugate vaccine that contains polysaccharides from 10 serotypes) and Merck & Co's Pneumovax (a vaccine that contains polysaccharides from 23 serotypes), which had sales of \$680 million and \$640 million, respectively, in 2016.

The market for vaccines against shingles (also known as herpes zoster), which is caused by the varicella zoster virus, is predicted to have the highest percentage increase of the markets analyzed—108% by 2022. The market is currently dominated by Merck & Co's Zostavax, which was approved by the US Food and Drug Administration (FDA) back in 2006 and had sales of \$780 million in 2016. However, its sales are predicted to drop with the anticipated market entry of GSK's Shingrix (Fig. 1), which is currently under review by regulators in the United States and Europe. Shingrix differs from Zostavax in that it is a recombinant subunit vaccine, and not a live, attenuated virus vaccine, and clinical trial data indicate that it may offer greater protection in older patients. Merck & Co's Varivax vaccine against chickenpox, which contains a lower dose of the same attenuated varicella zoster virus as Zostavax, was the leading attenuated virus vaccine product in 2016 with sales of \$820 million, and is predicted to maintain this position in 2022.

The meningococcal vaccines market is also set to grow substantially. The current leading product is Sanofi Pasteur's Menactra, a meningococcal group A, C, W-135 and Y vaccine, with sales of \$650

million in 2016. Close behind is GSK's Bexsero, a meningococcal group B vaccine gained through GSK's \$20 billion asset-swap deal with Novartis over 2014–2015, which had sales of \$530 million in 2016. Its sales are projected to grow to almost \$1.2 billion in 2022, but competition from Pfizer's meningococcal group B vaccine Trumenba is increasing. Trumenba's sales are predicted to jump from \$88 million in 2016 to \$820 million in 2022, in part due to its recent approval by the European Medicines Agency (EMA).

A range of influenza vaccines are being marketed and developed by the most companies in the field, and sales of these vaccines are predicted to increase by ~25% from 2016 to 2022. Sanofi Pasteur's

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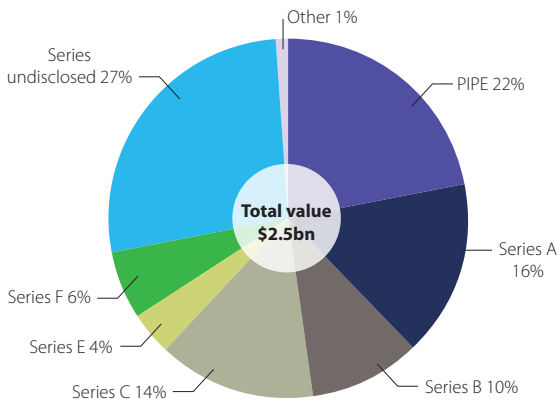


Figure 2: Venture funding for vaccine companies over the past two years. Data include funding for companies that are developing vaccines in general, not just those for infectious diseases. PIPE, private investment in public equity. Source: EvaluatePharma, April 2017, Evaluate, www.evaluate.com

Fluzone is the leading product in this category with sales of ~\$1.7 billion (almost 50% of the market) in 2016, which are forecast to grow to \$2.1 billion in 2022.

Other notable products within the analyzed data include Merck & Co's human papilloma virus (HPV) vaccine Gardasil for cervical cancer prevention, with 2016 sales of \$2.2 billion, and the recently approved pioneering dengue vaccine, Sanofi Pasteur's Dengvaxia, for which sales are forecast to grow substantially to \$670 million in 2022.

Vaccine dealmaking

Among the most substantial merger and acquisitions (M&A) and licensing deals in the vaccine area in recent years are two that saw Novartis exit the field. Following on from its \$20 billion asset swap with GSK (announced in 2014 and completed in 2015), which

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included all the non-influenza segments of Novartis's vaccines unit, Novartis announced the sale of the remaining influenza vaccines business to Commonwealth Serum Laboratories (CSL) for \$275 million in 2014. Once the deal was completed in 2015, CSL created Seqirus by wrapping in the company's existing flu vaccine subsidiary, bioCSL.

Selected product deals over the last two years involving infectious disease vaccine products in development are shown in Table 1. In total, there were almost 50 deals made; the majority were at the preclinical stage, and many deals did not disclose a value. One of the highest-value deals in the field overall with a disclosed value was Pfizer's \$130 million acquisition of GSK's quadrivalent meningococcal ACWY vaccines Nimenrix and Mencevax, which was announced in June 2015.

One specific vaccine technology area in which there has been substantial deal activity in the past two years is mRNA vaccines for both infectious disease and immuno-oncology applications. Moderna Therapeutics, which is developing products based on its mRNA platform in a wide range of therapeutic areas, has signed several deals specifically for infectious diseases (Table 1; see also *BioPharma Dealmakers* B3–B4, September 2016). The company recently announced its first human proof-of-concept data for its platform from a phase 1 trial of an mRNA vaccine against influenza. Two other leading mRNA companies, BioNTech and CureVac, have also been active dealmakers in the past two years (Table 1; *Nat. Biotechnol.* **35**, 193–197, 2017).

Early-stage financing

Data from EvaluatePharma on venture financing for vaccine companies overall, including areas beyond infectious diseases, show that more than \$2 billion has been raised over the past two years (Fig. 2) and also highlight the resurgence of interest in vaccines in oncology (see *BioPharma Dealmakers* B6–B7, March 2017). For example, two companies developing neoantigen vaccines have attracted substantial investment: Gritstone Oncology raised \$102 million in series A funding in 2015 and Neon Therapeutics raised \$125 million in two funding rounds in 2015 and 2017. Among financings related to infectious disease vaccines, CureVac raised \$140 million in funding in 2015 and 2016 for the development of its portfolio of mRNA vaccines, which include vaccines for influenza, rotavirus, respiratory syncytial virus and HIV, as well as cancer vaccines.

