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Accelerating vaccine R&D through collaboration

Recognizing that even broad, multidisciplinary teams need external support, GSK has formed over 115 partnerships to help develop vaccines for the future.

At GSK, R&D collaborations are underpinned by the simple concept that even the best teams can be improved. GSK seeks to combine the best science from inside and outside the company by including at least one external collaborator in every R&D project. This may lead to improvements that could advance the frontiers of vaccination.

The company has used this approach as the basis for a long-running review of how it performs its vaccine R&D. At the heart of the model is a deep commitment to internal expertise. With an R&D team of more than 2,000 scientists spread across three R&D centers in the United States, Belgium and Italy, and with 15 projects in clinical development, GSK is well equipped to take assets from early discovery through to late development and licensure. The achievements of the R&D team are consolidated by a manufacturing and commercial unit, which produces over 1.9 million vaccine doses a day for use in more than 150 countries. This unit has pioneered new models of tiered pricing, health economics and patient access, leading to improvements in global health.

Yet GSK leadership knows that even a broad, multidisciplinary team needs external support, as a vaccine can take more than 20 years to be developed. This thinking has led the company to form more than 115 active scientific collaborations with academic groups, funding bodies, consortia, biotechs and large pharmaceutical companies. These partnerships, which span from early research to late-phase development, are the backbone of GSK's efforts to develop the vaccines of the future.

A track record of collaborative success

GSK is confident that vaccine R&D programs work best when collaborators jointly meet scientific and technical challenges. In its projects, the company has applied a broad range of collaboration types. The thread connecting all of the approaches is a focus on bringing together the best people and securing their commitment to reach a common long-term goal.

An example of such a long-term collaboration is GSK's 30-year drive to develop a vaccine against malaria. The program had a big, early success in 1996 when a clinical trial of the malaria candidate vaccine RTS,S conducted in collaboration with the Walter Reed Army Institute of Research resulted in promising data. The PATH Malaria Vaccine Initiative joined the collaboration in 2001 and in 2009 GSK embarked on a phase 3 trial with the PATH Initiative and African scientists who ran the trial. Forming a public–private partnership enabled GSK to share expertise and spread cost and risk.

The candidate vaccine has now received a positive opinion from the Committee for Medicinal Products for Human Use of the European Medicines Agency, followed by a World Health Organization recommendation for a pilot implementation of the vaccine. These steps moved the vaccine closer to the point at which, when used in combination with other control measures, it will help reduce the number of cases of malaria, a disease that killed an estimated 438,000 people in 2015[1]. In advancing to this stage, the malaria candidate vaccine program has become a symbol of what collaborations can achieve.

Another example of successful collaboration has been reverse vaccinology, a technique—first formulated by a team led by Rino Rappuoli, GSK Vaccines chief scientist in conjunction with J. Craig Venter and investigators at the Institute for Genomic Research (TIGR), Rockville, MD, USA—that can reduce the time required for the identification of candidate vaccines and provide new solutions for those vaccines which have been difficult to develop. Reverse vaccinology could also allow GSK to develop new vaccines against diseases for which vaccines currently do not exist.

The company is taking a collaborative approach to other public health threats. When the Ebola outbreak began, GSK worked with the World Health Organization, the US National Institutes of Health and several European, US and African partners on a vaccine, resulting in a candidate that moved through phases 1 and 2 in 10 months. Typically, such work can take 10 years or more. This Ebola candidate vaccine was the result of another collaboration. The asset was discovered by the US National Institutes of Health and Okairos AG, a developer of vaccine platform technologies that GSK acquired in 2013. GSK has continued development of this candidate vaccine, taking it through adult and pediatric phase 2 trials.

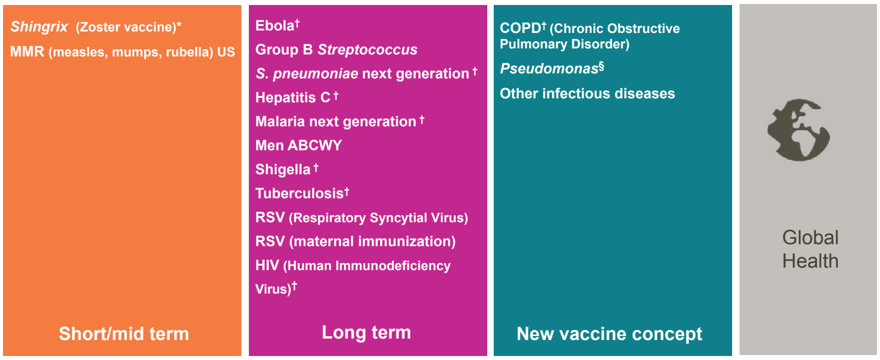
Recognizing that part of what made Okairos special lay in its agile and innovative culture, GSK designed an arm's-length relationship, allowing the transfer of Okairos's scientists to a newly created, GSK-independent biotech, now called ReiThera Srl. The model enabled the scientists to retain their autonomy and foster innovation while benefiting from the resources of GSK through an agreement.

Such flexibility is evident in the breadth of collaborations in which the company is involved. Vaccine R&D teams at GSK are as comfortable collaborating with academic labs or small biotechs as they are teaming up with other large pharmaceutical companies for initiatives such as the Innovative Medicines Initiative projects BioVacSafe and FLUCOP. In BioVacSafe, GSK is working with 15 teams from universities, nonprofit organizations, large pharmaceutical companies and public bodies to develop tools that enable faster, more effective testing of vaccine safety. With funding from the European Union's Innovative Medicines Initiative and access to the best scientists in the region, the project stands to usher in an era of safer, more effective vaccines.

FLUCOP has similarly far-reaching implications. GSK has once again come together with other large pharmaceutical companies and a clutch of leading academic research centers, such as the University of Oxford, to solve one of the big challenges facing vaccine R&D. In the initiative, the collaborators are working to create standardized, validated serological assays for human influenza vaccines. GSK, which is leading one of the initiative's five work packages, is collaborating on assays that reliably detect antineuraminidase antibody responses—tools that could lead to more immunogenic vaccines.

GSK's vaccine development pipeline

GSK is working toward broad solutions aimed at protecting individuals against infectious diseases throughout their life (maternal, pediatric, adolescent, adult and elderly), wherever they live in the world: Global Health



*Shingrix is not approved for use by the FDA or EMA † In-license or other alliance relationship with third party §option-based alliance with Valneva

Guiding principles of collaboration

The many different types of collaborations in which GSK is active is a reflection of the range of challenges faced in vaccine R&D and the multitude of skill sets that are needed to tackle these problems. Although the goals and tasks vary significantly from collaboration to collaboration, a set of guiding principles shapes GSK's decisions about which projects to enter into and how to proceed once committed. Its method starts with putting the right people in charge of identifying collaborations. GSK, like all companies, is looking for the most promising ideas, strategic partners and technologies, but it is particularly well placed to identify such opportunities.

GSK's strength in spotting the most promising collaborations—and, as important, picking the right time to enter into one—is underpinned by its scientific expertise. Experts in vaccine R&D review and evaluate each opportunity. This science-led approach continues throughout each collaboration. During the process, key GSK scientists manage the relationship with the collaborator, ensuring there is two-way communication. Crucially, collaborator feedback is gathered and acted on, driving continuous improvement.

Collaborators with GSK can benefit from proximity to the resources, data and experienced researchers of the company's vaccines development team. In recent years, GSK has sought to infuse its internal R&D with some of the spirit of its partners, notably by working to foster an innovative, entrepreneurial outlook among our scientists. Setting up the internal innovation ecosystem has stimulated the rate of innovation within GSK while also leading to the creation of teams that bring the same passion and entrepreneurial zeal to collaborations as their partners in biotech and other research organizations.

What is at stake

Having set up an approach to internal and collaborative innovation capable of overcoming some of the biggest challenges in vaccine R&D, such as developing the first malaria vaccine candidate against a human parasite (*Plasmodium falciparum*), GSK is now keen to apply the model to new frontiers of research.

World-changing projects await that will involve using emerging technologies to understand how vaccines work and how they can be made more practical and effective. There will be more targeted alliances to develop adjuvants, antigen delivery methods and production process technologies (Box 1), as well as new and innovative vaccine candidates. Future challenges include better immunogenicity, lower reactogenicity, cross-protection, simplification of delivery and thermostability (Box 2). GSK is committed to external collaborations to maintain its vaccine R&D operation at the forefront of each of these fields, and it knows that this is how progress will happen fastest.

With GSK's long-term goal being to help improve health globally, continuously delivering better vaccines and protecting more people, accelerating R&D through collaboration is the essential enabler.

1. http://www.who.int/malaria/media/world-malaria-report-2015/en/

Box 1: Areas of interest for potential partnerships with GSK Vaccines R&D.

Fundamental and applied immunology
- Understanding host–pathogen interactions, understanding immune responses to infectious diseases and vaccines, and developing new protective antigens. New immunization strategies and technologies

New vaccine targets
- Discovering targets for infectious diseases (bacterial and viral diseases and diseases prevalent in the developing world) and noninfectious diseases

Adjuvants
- Developing new approaches to modulate the immune system and understanding the mode of action of adjuvants

Antigen delivery
- Developing nanoparticles and virus-like particles and investigating antigen stability. Vectors, RNA and new antigen-presentation platforms

Vaccine delivery
- Developing mucosal, oral, sublingual, nasal and intradermal delivery methods and devices; thermostability

New assessment technologies and analytical tools
- Miniaturizing clinical assays and making them faster and more robust, developing quality control and assurance assays. Biomarkers and the application of systems biology to (new) readouts

New production process technologies
- Process monitoring, process efficiency, simpler and faster antigen production. Alternative expression systems

Box 2: Future challenges.

Understanding how vaccines work
- Breadth, duration, cross-protection, reactogenicity/efficacy, etc.

Identifying new vaccine technologies to support:
- Enhanced efficacy (better immunogenicity, lower reactogenicity, cross-protection, etc.)
- Simplification (process, schedule, delivery, compliance, manufacturing, operations, etc.)
- Rapid-response vaccine platforms

Developing therapeutic vaccines against infectious diseases (prophylactic and therapeutic)

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