

# Executive Summary

**V**accines—standardized biological preparations that harness the immune system to develop specific defenses against pathogens—have been a mainstay of medical intervention since before rational chemotherapy was developed. If humankind has managed to erase deadly and debilitating endemic diseases such as smallpox worldwide, and if eliminating polio has become a realistic hope, this is almost exclusively due to widespread and systematic deployment of vaccines. The list of diseases that used to kill uncounted scores of European and US children less than a century ago, but are now so rare in these areas that many physicians fail to diagnose them, is even longer.

Development of vaccines has gone a very long way from the crude but trailblazing preparations used in the late 19th and early 20th centuries to today's engineered multivalent recombinant antigens, advanced adjuvants, and codon-optimized DNA vaccines, many of which are delivered using sophisticated formulations or devices. Today the vaccine market generates sales of \$25 billion per year. And yet, even in 2011 vaccination is available for no more than 26 out of the hundreds of infectious diseases known to affect humans. There is still a lot to do for vaccine developers, and it does not stop with prevention any more: Therapeutic vaccines are slowly emerging, and for a pharmaceutical industry that used to be addicted to small molecules and is now swaying

in the pincer grip of blockbuster patent expiries and its own innovation crisis they might well be the Next Big Thing.

This report provides an analytical snapshot of the current state of the vaccine industry, the state of its development efforts as per October 2011, and an outlook to 2020. After a brief first chapter that reviews the basic facts that are important in vaccinology, we move to Chapter 2 which deals with the major task of vaccines: prevention of infectious diseases. A thorough overview of vaccine-preventable diseases is given, with a special focus on human immunodeficiency virus (HIV), hepatitis C, and influenza. We use the case of a potential HIV vaccine (pursued for decades with very limited success) for a case analysis of how the first vaccine for a previously “unvaccinable” major infectious disease could fare, on the market and in terms of epidemiological impact, assuming several scenarios. The major corporate players on the market, and vaccine specialist companies including those developing or selling vaccines for “weaponized” biological agents such as anthrax, are reviewed as are the international organizations and the charities, which play the dominant role in making standard vaccines accessible to the developing nations. Attention is given to emerging tropical viral diseases (such as Dengue and West Nile virus) which are increasingly spreading to the temperate zones of the globe, driven by climate warming, migration, and tourism to the tropics. A special section of this second

chapter is devoted to the challenge of tropical parasitic diseases—malaria, but also schistosomiasis. Opposition to vaccination, a popular phenomenon that has persisted for the past 150 years under various guises, is also discussed.

The following chapter is dedicated to therapeutic vaccines that target chronic infectious diseases such as HIV and hepatitis C infection, but also non-infectious conditions with massive immune system involvement such as asthma and allergy, type 1 diabetes, multiple sclerosis, psoriasis, arthritis, and transplant rejection—but also Alzheimer's disease and periodontitis. A special section addresses efforts to develop therapeutic vaccines for conditions that most people would not consider targets for this type of intervention: smoking, cocaine abuse, obesity, cachexia, and age-related macular degeneration (a sight-destroying retinal condition that has much in common with cancer).

Therapeutic cancer vaccines are covered in Chapter 4. This part of the report reviews the paradigms of active immune intervention in cancer and the problems it faces. It discusses all cancer vaccines currently known to be in Phase III clinical trials, and gives a cross-sectional overview of products that are in Phase I or II.

Chapter 5 provides perspectives for vaccine development and the direction which the markets are likely to take to 2020. Bioinformatics, molecular simulations and “*in silico* immunology” will be the most important developmental drivers—which are actually very similar to those identified in our recent Insight Pharma Report, “Engineering Next-Generation Therapeutic Proteins: Trends and Markets to 2020.” There will be limited “universalization” of vaccines in the sense that emergent strains (*e.g.*, the influenza seasonal strains, but probably not the pseudospecies developing in HIV-infected individuals) will be better addressed than today. Polyvalent vaccines (which address several known serotypes of an infectious agent, or several different agents as is the case

in pediatric vaccines) might not become much more polyvalent than they are today: The human immune system is not designed to handle too many concurrent antigenic stimuli.

Our best estimate for the growth of the preventive vaccine market to 2020 calls for a CAGR of 5–7%, with a fuzzy upper limit that could go as high as 9% under optimal conditions which (among other things) assume increased involvement of the WHO and various charities such as the Gates Foundation, and no second global economic recession during the current decade.

In support of this analysis we have conducted a four-part online survey in which experts on Cambridge Healthtech Institute's list of experts in the life science industry were offered participation. The survey, which was carried out in late September and early October 2011, covered preventive vaccines for infectious diseases in general (6 questions, 91 respondents), influenza vaccines (3 questions, 93 respondents), HIV and HCV vaccines (8 questions, 55 respondents), and cancer vaccines (7 questions, 330 respondents). Participants could choose which parts of the survey they wanted to answer. All questions were multiple-choice. Analyses of the responses, which offer unique insights into industry sentiment concerning vaccine development to 2020, can be found throughout this report.

Vaccines are a huge field which merits several focused reports on several of the chapter subjects that have been chosen here, *e.g.*, on influenza vaccines, HIV and hepatitis vaccines, and therapeutic cancer vaccines. This report offers a cross-sectional overview of the entire vaccine theatre as it presents itself today, and as it is projected to develop during the remainder of the present decade. The results of these projections are encouraging. Preventive vaccines will continue to develop, technically and in terms of market coverage, offering a solid high single-digit percent growth rate for preventive vaccines until 2020.

Some segments of this market—in particular, biodefense vaccines but also vaccines for tropical diseases—are less predictable because they depend on politics more than on market forces. However, we believe that the uncertainty is almost exclusively in the extent of growth, not in a risk of market shrinkage, in these segments.

That the therapeutic cancer vaccine segment of our questionnaire drew by far the most respondents is no accident. Cancer chemotherapy traditionally advances in incremental steps, and progress is dominated by new adjuvant regimens and second- and third-line therapies; each of these new elements tends to extend survival only marginally, and although we have seen the effect mounting over the decades there are relatively few breakthroughs. The last drug classes that have offered such breakthroughs (at least for certain types of tumors) were anti-angiogenic drugs and kinase inhibitors. Standardized cancer vaccines, which work by harnessing the patient's immune system, should offer a completely new therapeutic angle. Most importantly, they would be best suited to prevent tumor recurrence once a complete remission has been achieved by initial therapy—which would open an entirely new perspective for cancer survivors, and a completely new market as well. A 10–15% share of the tumor therapy market by 2020 does not seem unreasonable from today's perspective, but there are too many unknowns in their developmental situation to make a reasonable estimate.

From the pharmaceutical industry perspective, vaccines of any type offer a solid growth perspective at a time when small molecules seem unable to sustain the growth on which the industry has mostly relied. It is only logical that the industry's focus is now shifting toward advanced protein drugs (which we have fully addressed in the recently published Insight Pharma Report, "Engineering Next-Generation Therapeutic Proteins: Trends and Markets to 2020"), the most exciting of which are antibody-derived constructs. The resurgence of the interest in vaccines

is part and parcel of this renewed focus on the human immune system, which is still a frontier in many respects.