8 Biopharma Trends and Top Startups to Follow in 2017

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Pharmaceutical industry is rapidly evolving, influenced by emerging novel technologies and recent advances in Life Sciences and Big Data analysis, new government policies and regulations, and a changing market conjuncture.

Let's review some of the most powerful trends that will dominate the industry in 2017 and promising biopharmaceutical startups riding their waves.

1. Gene editing: CRISPR/Cas9

Being one of the brightest scientific breakthroughs in years, a new targeted genome editing technology based on the CRISPR-Cas9 system, offers a huge promise for the future of medicine.

CRISPR (clustered regularly interspaced short palindromic repeats) refers to the system consisting of two key molecules: an enzyme Cas9 -- "molecular scissors" able to cut the two strands of DNA at a specific location in the genome; and a piece of pre-designed RNA sequence -- "guiding" RNA (gRNA), within a longer RNA scaffold. The role of the latter is to direct Cas9 "scissors" to the exact location in the DNA of interest and modify it as desired.

While CRISPR technology is still in its infancy with a number of serious issues to be addressed on the way, the discovery of the CRISPR/Cas9 gene editing approach has already transformed the biomedical research field forever. Compared to its "predecessors", such as zinc finger nucleases (ZFNs) and transcription activator-like effector nucleases (TALENs), the CRISPR-Cas9 system is simpler, preciser, and relatively cheaper, making it an ideal vehicle for "playing with genome". And it can be done in high-throughput screening formats.

With all the benefits CRISPR technology represents no wonder it has captured the attention of the popular media, the scientific community and top biotech investors. Over the last several years the number of Google search requests and research citations related to CRISPR have skyrocketed almost exponentially.

Some of the most well-established biotech startups in the field of CRISPR include:

Intellia Therapeutics: (IPO in 2016, highest post-money valuation ever for a pre-clinical biotech startup). Advances programs for in vivo and ex vivo therapies, the latter including HSC transplants and CARTs.

Editas Medicine (IPO in 2016) develops programs to treat eye diseases, uses engineered T-cells (e.g., CARTs) among other technologies.

CRISPR Therapeutics (IPO in 2016) works on a broad range of diseases including blood disorders, congenital heart disease, blindness, and cystic fibrosis.

Eligo Bioscience: The startup's advanced approach utilizes the idea of delivering CRISPR via phages to attack selectively nocive bacterial strains.

Other emerging players using CRISPR/Cas9 technology include: **Exonics Therapeutics** (neuromuscular diseases), **Agenovir** (viral diseases), **Poseida Therapeutics** (multiple myeloma, prostate cancer and beta-thalassemia), **Synthego**, **eGenesis**, and **Benchling**.

2. Immuno Oncology, CAR T cells

Surgery, chemotherapy and radiation therapy have long been the only major options for cancer treatment. Over the last decade a number of small molecule based targeted chemotherapies emerged, including imatinib (Gleevec®) and trastuzumab (Herceptin®) as standard treatments for a number of cancers. The existing medical arsenal, however, still appears to be very limited and inefficient in many cases, while being associated with dramatic side-effects.

A new hope comes from a paradigm shifting approach in biomedical research -- immunotherapy, and with rapidly expanding number of positive results in labs and in pre-clinics, grows the excitement of scientists, industry experts, and investors around the promising new possibility.

In short, immunotherapy is all about methods of stimulating person's own immune system to recognize and fight diseases. The most transformative thing about immuno oncology compared to "traditional" approaches is a highly targeted nature. While chemotherapy broadly targets all rapidly dividing cells, properly tweaked immune system targets only malignant cells -- without harmful side effects, and with higher efficiency.

With a number of existing strategies to influence the immune systems, such as using checkpoint inhibitors, vaccines, and monoclonal antibodies, it is chimeric antigen receptor (CAR) T-Cell therapy which deserves particular attention as a possible “big thing” in cancer treatment. In this approach a patient’s own immune cells (or cells from another donor) are removed and modified so that they can recognize and attack the patient's particular cancer. Thus engineered CAR T-cells are then grown in the lab to reach billions in numbers, followed by infusion back into the patient’s body.

The CAR T-cell technology already proved to be extremely promising in the case of hard-to-treat lymphoma and is considered an ultimate future of the immunotherapy field.

Currently, the leaders of the race in the CAR-T are big players like Novartis and Kite Pharma with their candidate technologies having good chances to get regulatory approval in 2017. The early stage companies are also active in the area of immuno-oncology with some of the most well-funded biotech startups being **Symphogen**, **CureVac**, **NovImmune**, and **Jounce Therapeutics** among others.

3. Microbiome

The microbiome trend is rapidly growing and can possibly become one of the major game-changers in the biopharmaceutical industry. Named in 2011 a “breakthrough of the year” by Science magazine, microbiome research has been receiving substantial amount of government funding and venture capital money lately. In fact, venture-capital investment in microbiome companies had grown since 2011 through 2015 by 458.5% to reach $114.5 million, and in 2016 alone the volume of venture funding in microbiome-related biotech startups exceeded $616.9 million.

Microbiota is the ecosystem of more than 100 trillion microorganisms living inside our body or on the skin, coexisting naturally with human organism and performing vital functions such as synthesis of vitamines, digestion and taking part in the immune system development. The versatility of genes of the microbiota -- microbiome -- attracts the increasing interest of research community and biotech companies as they try to develop new therapies or even find novel antibiotics using the understanding of how our own bacteria contribute to diseases, immune responses and the overall organism condition.

A great review of 20+ most active biotech startups in the field of microbiome has been published by CBinsight recently. Some examples include: **uBiome, Epibiome, Microbiome Insight, Metabogen**, and **CosmosID** (focus on genomics aspects); **C3J Therapeutics** (oral health); **Naked Biome, Azitra**, and **Xycrobe** (skin diseases); **Vedanta Biosciences, Symbiotic Health, Eligo Bioscience, Enterome**, and **Second Genome** (intestinal health).

4. Precision Medicine

Today's emerging field of precision medicine—previously referred to as personalized medicine—is a logical next step in the evolution of medicine, following a tremendous progress which has been made around genomics over the last few decades. The concept of precision medicine rests on the understanding that all patients are genetically diverse, and the variations in each person's genome can drastically affect how people respond to particular drugs and therapies.

One prominent example of this situation is AstraZeneca's Iressa (gefitinib) which was approved by FDA in 2003 as a therapy for non-small cell lung cancer (NSCLC) but later in 2005 the approval was withdrawn due to inefficiency of the drug for up to 90% of patients. It appeared, however, that the drug was, in fact, effective -- but only for patients having certain mutations in EGFR, a gene coding for a cell-surface protein receptor involved in cell signaling. Ten years later gefitinib was reapproved as a therapy for NSCLC — to be prescribed solely for patients with the relevant EGFR mutations, identified through special tests.

The above example somewhat illustrates the idea and power of precision medicine, but with that a necessity of integrating the diagnostics and biomarker development into the overall drug discovery and development process becomes apparent. It adds up an additional layer of complexity and cost for drug makers operating in a new "precision medicine paradigm".

Although there are obvious obstacles on the way of precision medicine "revolution", both technological and economical, the biopharmaceutical industry bets big on diagnostic-based targeted therapies. The Global Precision Medicine Market is estimated to grow at a cumulative annual growth rate (CAGR) of around 11.2% over the next decade to reach approximately $112.62 billion by 2025.

Apart from big players, a plethora of biotech startups are also trying to monetize on the precision medicine trend, including **Inform Genomics, Miramix, Population Diagnostics, GenomOncology**, and **Advanced Cell Diagnostics**, to name a few.

5. Antibiotics discovery

A growing rate of spread of multidrug resistance in bacteria have been making headlines recently, some even warning about the coming "post-antibiotics" apocalypse. The news about a woman who recently died in US from a "superbug" not responsive to any of the available antibiotics has just amplified the clamor around the topic.

While the public media is probably over-exaggerating the scale of the “catastrophe” (as usual), the problem of antibiotics resistance does exists and certainly requires coordinated and quick actions on the global scale - both in terms of government support, private financial stimulation and more effective ways of informing and educating the public about the proper use of antibiotics.

One of the reasons why the area of antibiotics research remained high and dry for so long is that antibiotics are not “attractive” products for big pharma from the business point of view, neither they are attractive for venture capital investors. It was estimated that only about 5% of all private venture investment in pharmaceutical R&D between 2003 and 2013 was for antimicrobial development.

Antibiotics have strict prescription limits, short period of treatment course, they are relatively cheap and they might become inefficient anytime due to developed bacterial resistance therefore becoming useless and not marketable. Economics is one of the reasons why we have not seen any new classes of antibiotics developed for about 30 years, while the bacteria constantly evolve.

The situation is changing for the better, however, and the trend of biopharma “coming back” to antibiotics discovery will be continuing in 2017. The main drivers for the revived interest are the new stimuli created by the governments and private organizations over the last several years. Examples in US include the GAIN (Generating Antibiotic Incentives Now) Act of 2012 and a more recent qualified infectious disease product (QIDP) designation for antibiotics and antifungals, which provides new candidates with priority review and five additional years of market exclusivity when approved. Further support could come from the 21st Century Cures Act approved by the House in July 2015, which includes the Antibiotic Development to Advance Patient Treatment (ADAPT) Act that permits FDA to approve antibacterial drugs to treat serious or life-threatening infections based on small clinical trials.

One recent example of a large-scale public-private collaboration aimed at curbing multidrug resistance is a recent formation of CARB-X -- The Combating Antibiotic Resistant Bacteria Biopharmaceutical Accelerator. It was launched by three U.S. government agencies and the Wellcome Trust, a U.K. nonprofit organization and it expects to spend up to $450 million over the next five years to support new research and biotech startups involved in antibiotics discovery.

The increasing need for new antibiotics and new incentives available for business stimulate new biotech startups to emerge. Some of the recent examples include **Forge Therapeutics** (small molecule inhibitors of LpxC, a zinc metalloenzyme in gram-negative bacteria), **Cidara Therapeutics** (immunotherapy platform to fight bacterial infections), **Visterra** (antibody-drug conjugate therapy), **Tetraphase Pharmaceuticals**, and many other promising biotech startups focusing on antibiotics.

6. Artificial Intelligence (AI) and Machine Learning

A true scientific revolution has been happening in data science over the last several years with an exponential progress in the area of machine learning and artificial intelligence. Here is a brief review of how the field of machine learning emerged and developed into what it is today.

The AI and machine learning advances have already been in practical use for some time in many industries, including smart cars, natural language processing (NLP), image recognition, smart online search and recommendations, fraud detection, financial trading, weather forecasting, personal and data security, and chatbots, to name a few. The biopharmaceutical industry, however, is just beginning to adopt the new computational technologies, though quite rapidly.

Numerous AI-based startups, focusing on different aspects of drug discovery and development, diagnostics and clinical research, have emerged over the past several years. Deals to healthcare-focused AI startups went up from less than 20 in 2012 to nearly 70 in 2016. Some examples include **Atomwise, BenevolentAI, NuMedii, Insilico Medicine, Envisagenics, Deep Genomics**, and **BergHealth**.

7. Medical cannabis

Last but not least, there is a huge potential now for Cannabis, in all of its forms. The legalization of marijuana in the United States sparked a growing interest of investors who now turn their focus to the small — but rapidly expanding — medical marijuana industry. It is estimated that the global market for medical marijuana could reach $50 billion by 2025.

With all the controversy and rising concerns around marijuana legalization, the trend is nevertheless poised to grow rapidly and is now hard to ignore.

While US now is the biggest market for medical-grade cannabis, Israel is pushing hard to position itself as a global player in this rapidly-growing area of biopharmaceutical research. It is reported that about 120 research programs are active in Israel, including clinical trials looking at the effects of cannabis on autism, epilepsy, psoriasis, and tinnitus.

Some of the biotech startups focusing on marijuana research are listed here.

8. Focus on R&D outsourcing

In a world of exponentially growing knowledge, increasingly sophisticated technologies and an unstable economic environment, biopharmaceutical companies are increasingly betting on mergers & acquisitions, partnerships and R&D outsourcing business models with academia and CROs to harness the most value out the new possibilities. Companies collaborate actively and even launch open innovation initiatives to increase competitiveness and stay on the cutting edge of technological progress.

Please, leave your comments below and suggest other important trends shaping the future of biopharmaceutical industry and research.