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NEXT BIG WAVE IN PHARMACEUTICAL INDUSTRY

Team Mavericks

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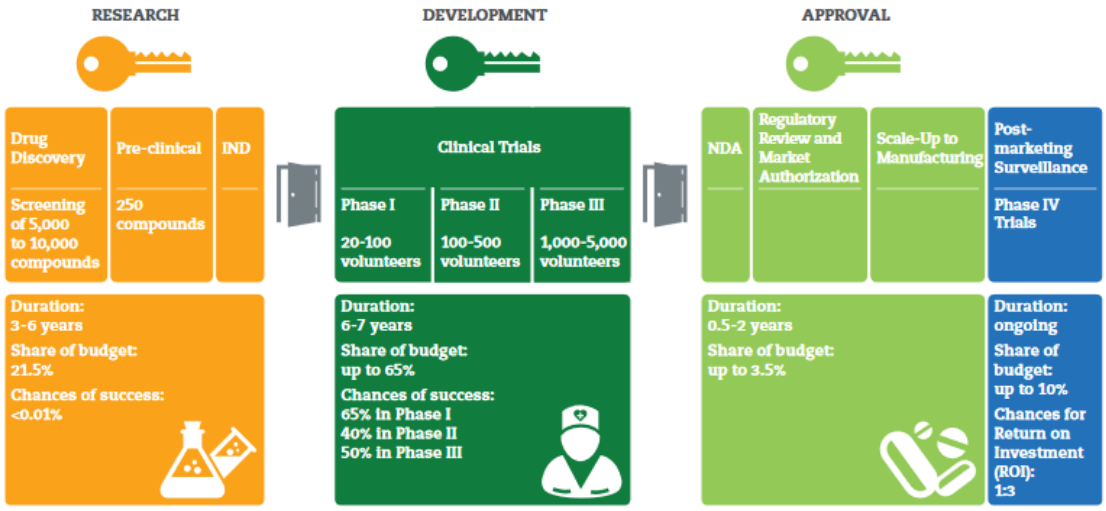
Pharmaceutical Industry

Relevance of the industry

The global market size of pharmaceutical industry is estimated to reach USD 1,430 billion by 2020, which includes 41% share by United States alone, followed by Europe (13%). The pharmaceutical industry is responsible for development, manufacturing and marketing of medications. Its importance in our society is inarguable. The drugs and vaccines against malaria is estimated to have saved 1.14 million African children's lives between 2011-15, immunization campaign reduced the number of deaths by 79%, between 2000 and 2014 in Africa.

It takes 10-15 years to develop a medicine/vaccine and launch in market. Global growth rate for the pharmaceutical industry will be 6.3% CAGR through 2022, amounting USD 1.12 trillion, up from the 5% CAGR of 2014-2020 period. In 2014, 5 out of 11 global R&D firms were pharma companies.

The R&D investment in the industry is too huge, it currently spends over USD 149.8 billion on R&D per year which is 5.5 times greater than that of the aerospace and defense industries, 1.8times more than software and computer services and 5 times more than chemicals industry. During 2011-15, the compound annual growth rate of global R&D spending was 1.7%, which will grow to 2.8% in 2016-22 period with overall spending of USD 182 billion in 2022. Top global companies in the R&D expenditure are Roche and Novartis (USD 8.5 billion), Pfizer (USD 7.7



billion), J&J (USD 6.8 billion) and Merck (USD 6.6 billion).

Summary

Pharmaceutical industry plays a vital role in developing new medicines and vaccines to prevent and treat disease, thereby saving the life of the patients suffering from chronic diseases. The uniqueness of the industry lies in converting fundamental research to innovative treatments. The

success of the pharma industry rests on continuous innovation to develop medicines for new, incurable or neglected diseases together with improving the existing treatments.

The ability of Artificial intelligence to speed-up the process and reduce the cost of drug development (drug - synthesis, testing, delivery) makes it an invaluable asset to Pharmaceutical industry. Assisting in the evaluation of complex simulation results, generating accurate models of target locations & molecules and decision on the type & quantity of dosage are few of the possible improvements. Utilizing AI along the development process makes few roles obsolete while providing opportunity for professionals with Computer Science experience.

The time taken to select the two or three specific molecules from the set of possible variants is cut-down drastically. Selection criteria for the molecules can be made heavily stringent as modelling highly selective molecules and the possible side-effects is facilitated. As per experts in the industry, finding the correct specimen for testing the molecule reduces the testing phase timeline and this is assisted by the running simulations on animal models and using AI to identify the most logical specimen to test the molecule. Drugs for very specific issues must be delivered, considering all the possible side-effects and dynamically changing body vitals. Apparatuses like micro needles evaluate the internal bodily conditions and this data can be used to decide on the type and quantity of dose.

Core team members and their functionality

Assume a small R&D team for a pharma company. There are three primary teams, drug synthesis team (chemists), drug testing team (biologists) and drug delivery team (biologists, physicists and chemists). Each team has a managing lead, three specialists and at least two technicians. Managing lead of each team generally has a doctorate in his specialization and takes care of the decisions and project details of the team. He portrays as the team leader during inter-team discussions and makes sure the necessary pre-requisites and requirements are available to the team. Specialists are individuals who work on the core activities of the team. Based on the requirements, they decide on the type of tests to conduct and analyse the corresponding reports to progress in the activity they are working on. Technicians take care of the non-critical and usual activities in the lab.

There is heavy usage of computers to analyse the data obtained from various experiments and in multiple cases, special equipment for conducting experiments uses computer to operate and obtain results. Each team uses computational power in a peculiar way. Synthesis team uses computations to identify and analyse the structure of molecules and assesses the corresponding utility of the molecule in the development process. Testing team primarily records the possible side-effects on both animal and human test subjects. Identifying the correct specimen in early stage is necessary to development a drug with low side-effects and high specificity. Delivery team needs to understand and analyse the physical, chemical properties of the molecule to decide on the mode of delivery to the patients. Test can be performed on special equipment to identify the

possible issues that arise when the drug is consumed in conventional ways. After the complete analysis, a specific type and quantity of dosage is decided.

AI in development process changes the way activities are done in the development process. AI assisted simulations can be performed to identify or create molecules based on the structures & reactivity of both molecule & target site in the body. The simulations forecast the synthesis on possible auxiliary reactions and helps them in selecting different molecule based on the potency of the reactions. Once the molecule is synthesized, AI helps in identifying the correct specimen model and simulations can be done to reduce the number of specimens being used for the testing of the drug. Dosage size and time is decided based on the physiological conditions of the patient and making sure that there are no adverse results is essential. Designing the final consumable is made using AI to decide the number and quantity of buffers.

Industry pain points & Value proposition

In 2015, 56 new medicines were launched while more than 7000 compounds were at different stages of development, this gap indicates the research hurdles drugs must overcome before the compounds can be developed into safe and effective medicines. The cost of developing a successful medicine, today, is USD 2.6 billion compared to USD 179 million in 1970s which is due to the various technical, regulatory and economic challenges faced by R&D pipelines. The screening for potential chemical and biological compounds takes extensive work, *on average 5000-10000 compounds are screened.* The extensive testing of the compound is to test its efficacy and safety: takes *on average 5 to 10 years.* Companies experience huge investment's loss (i.e. R&D expenditure that doesn't turn into a market accepted medicine) as the R&D in pharmaceuticals has high failure rate. The molecules in initial phase seem promising and the surety of their success is confirmed only during preclinical and clinical trials, thus the investment loss increases further if the failure is identified at later stages, as each stage has its own investment associated with it.

Identifying the adequate protein for a disease, proving the concept, making optimized molecule, carrying the preclinical and clinical safety trials are all essential but they drag the process of drug development too far. To examine the chemistry of whether a drug might bind to a protein or genes or RNA, drug companies can now use artificial intelligence to accelerate the process. The biological systems can also be probed to get clues about how a drug can affect a patient's cells or tissues.

Nowadays, a single disease may not be the same in every patient, hence patients need to be considered as an individual, instead of a category or community. Patients with similar disease on the same therapy might have different needs and non-adherence reasons. Care has become more individualized and by collecting digital health records and deploying data mining over it, AI can provide real time solution by creating customized drugs as per the individual's need. The development costs will not be much different if the R&D process is kept the same.

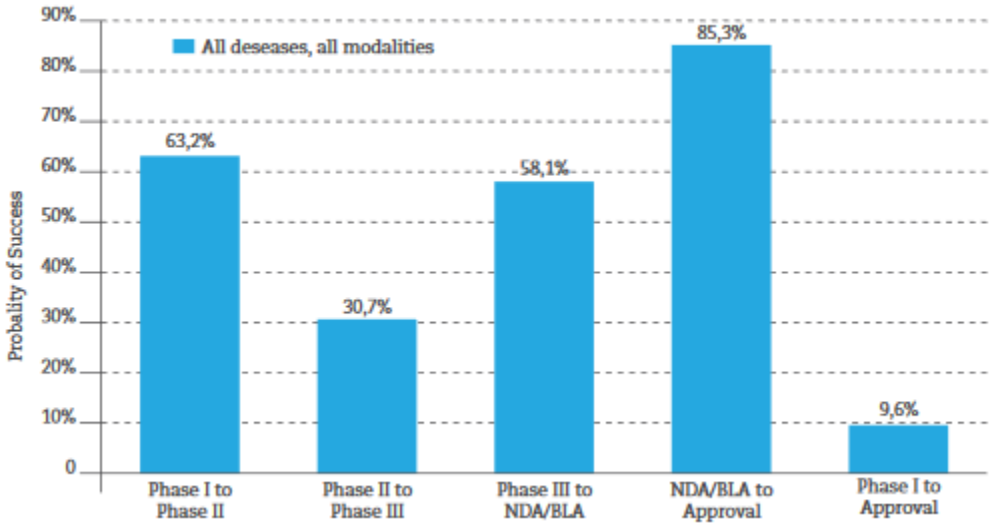
In the current drug development process, only 9.6% of the therapies can pass from Phase 1 clinical trials to the FDA approval. With the usage of artificial intelligence, the failure rate can be minimized as the seamless molecule selection and target site to test has already been ensured. AI with the help of big data analysis can also draw insights of genetic and chemical information from the public databases.

AI releases the absolute dependence on few core physical activities and provides an opportunity to substitute using modelling & simulations. There would be a reduction in the total number of required technicians and specialists as many of the activities performed by them can be devoted to AI. This creates an avenue for computer scientists and data analysts to enter pharma R&D laboratories. A pressure on managing lead to be technically proficient is also generated as their daily team composition will be different. Super computers and deep learning software find opportunity to exist in the labs usually filled with chemical and biological equipment.

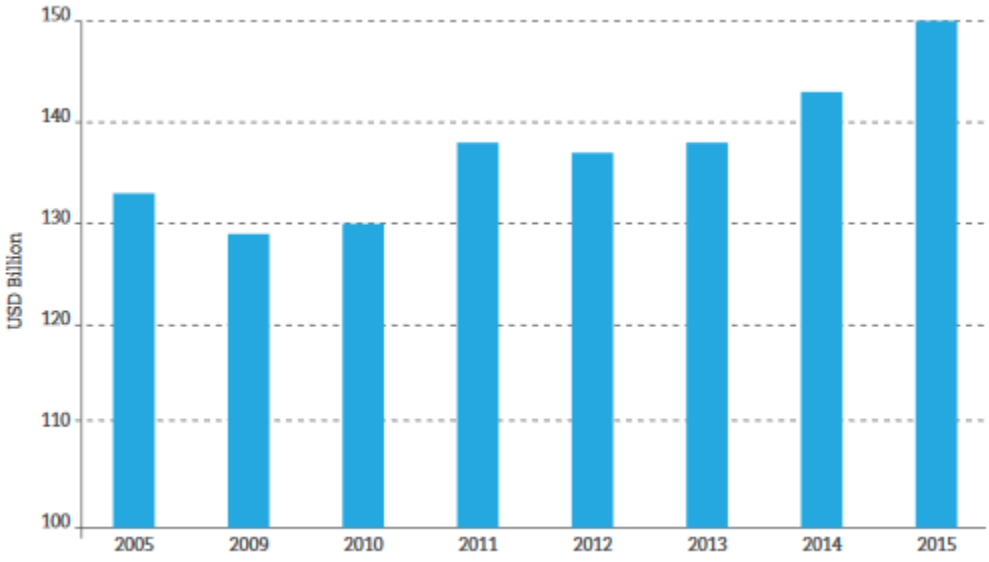
"The development of full artificial intelligence could spell the end of humans but the advances in AI have made life easier for many, including himself." ~ Stephen Hawkins

APPENDIX

- Phase transition success rates and the Likelihood of Approval for All Medicines and Modalities



- Pharmaceuticals R&D spending



- The number of trials failed to meet the primary and secondary efficacies

Phase III Failures: Lack of Efficacy

THERAPEUTIC AREA	NUMBER OF TRIALS	PATIENTS ENROLLED	AGENTS/COMBINATIONS TESTED
CARDIOVASCULAR *Indications studied: acute coronary syndrome, acute heart failure, atherosclerotic disease, cardiovascular cell damage*	6	**58,759**	darapladib, evacetrapib, losmapimod, otamixaban, serelaxin
ENDOCRINE/METABOLIC *Indication studied: diabetes*	4	**38,066**	aclerastide, aleglitazar, basal insulin peglispro[a], saxagliptin
ONCOLOGY *Indications studied: breast cancer, castrate-resistant prostate cancer, colorectal cancer, leukemia, non-small cell lung cancer, lymphoma, ovarian cancer, uveal melanoma*	18	**19,856**	alisertib, cabozantinib, dacomitinib, enzastaurin, etirinotecan pegol, ganetespib + docetaxel, iniparib, lapatinib + trastuzumab, MAGE-A3, motesanib, onartuzumab, ramucirumab, selumetinib + dacarbazine, trebananib + paclitaxel, True Human™ antibodies[b], vintafolide, vosaroxin + cytarabine
PULMONARY *Indication studied: chronic obstructive pulmonary disease*	1	**16,485**	fluticasone furoate + vilanterol
CENTRAL NERVOUS SYSTEM *Indications studied: Alzheimer's disease, depression, schizophrenia*	5	**9,140**	bitopertin, edivoxetine, pomaglumetad methionil, solaneumab
AUTOIMMUNE *Indications studied: ankylosing spondylitis, Crohn's disease, systemic lupus erythematosus*	4	**3,378**	apremilast, tabalumab, vercirnon
TOTALS	**38**	**145,684**	**34 AGENTS/COMBINATIONS**

[a]Program terminated due to focus on other drugs in portfolio and to assess effects on liver fat.
[b]Phase III trial terminated due to insufficient number of per-protocol patients available for primary endpoint analysis and protocol violations

Source: PAREXEL Analysis

Table 1. Phase III trials during 2012-2015 that failed to meet primary or secondary efficacy endpoints.

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