

Q&A from “Taking a Drug from Idea to Market”

1. How do you decide the point at which side effects are acceptable or too dangerous/don't outweigh the benefits of the drug? What is the tolerance level for side effects? Is it a % of those in trial, degree of side effect etc.

LB: At Amgen, we have a structured benefit-risk management process. As part of this process we evaluate and characterize risks, including whether or not they can be prevented or mitigated. We then use largely qualitative scientific and medical judgment to decide whether the benefits of the treatment outweigh the risks. Our senior management in Research & Development is involved in the decision making process. There is no specific tolerance level since tolerance for risk is dependent upon the severity of the disease being treated, the amount of unmet medical need, and the magnitude of benefit for the treatment.

2. How do companies weigh profitability, overall need, rare disease drug development, and price of a drug. Also do the scientists drive the development or are they directed by the financial and business arm of the company?

LB: We develop therapeutic area strategies that define which disease areas we are most interested in. While these therapeutic area strategies do take into account the commercial market, they also consider things like where we have expertise, where is the greatest unmet medical need, etc. Based on these therapeutic area strategies, our research scientist then focus on developing drug candidates within those disease areas.

3. Given that a drug takes years to develop, what are the typical toll gates / criteria / triggers that determine when a drug should be taken to a certain milestone (say Ph I)

LB: At Amgen, we have portals that occur at different stages of drug development. The purpose of these portals is to assess our readiness for the next stage of development and to ensure that the product attributes based on emerging data are consistent with what we are aiming for.

4. How hard is it to find people who are willing to participate in trials?

LB: I think the level of difficulty is dependent on the disease area and how the study is designed. For example, I think there is a lot of willingness to participate in clinical trials for life-threatening diseases. But, things that make it difficult to find patients are if the trial has too many visits/procedures, if the eligibility criteria is too rigid, or if there are logistical issues to the patient participating (eg, the trial site is too far away).

5. Why are clinical trials so expensive? Is this the case for clinical trials in other countries as well?

LB: There are 3 main areas of cost in clinical trials. First, there are the resources or people who oversee the clinical trial at the sponsor or clinical research organization, second, there are the fees paid to the investigators and clinical sites to conduct the trial (enroll and treat patients), and third, there are the costs of the suppliers who contribute to the execution of the study. These vendors include laboratories, imaging analysis vendors, and randomization vendors, as examples. Many clinical trials are conducted in multiple countries. The costs of the investigator fees can vary across countries.

6. Who determines or how is it determined if a drug is over the counter or prescription?

LB: In the US, this is determined by the US FDA.

7. What are the considerations for determining a drug delivery method? Do you have any examples of creative or interesting drug delivery methods you or your company has created?

LB: Considerations include, but are not limited to: 1) whether it is a large or small molecule, 2) desired pharmacokinetic and pharmacodynamic characteristics, 3) patient population and others

8. In what ways has the use of biotechnology impacted the viability and speed of getting a drug to the market?

LP: Without innovation, we never would have taken drugs, antibodies or vaccines to the clinic as fast. Companies around the world have developed the technologies and know-how to produce these therapies fast and test them rigorously in the preclinical setting before moving into the clinic.

9. If there is evidence of reinfection for COVID, how successful will a vaccine be?

LP: In order to have a “successful” vaccine, at least two things are required: (1) an adequate immune response to prevent disease or prevent the progression of disease and (2) a durable response. We are reinfected by pathogens all of the time, so reinfection would not be a concern – in fact infection after vaccination may boost the immune response! However, if the question is whether a vaccine lasts long enough (i.e., durability), we do not have enough information yet.

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11. What made you all decide to go into your field of study?

LB: I was just so impressed by the caliber of the people that I was working with when I started working in the pharmaceutical industry. Also, I have always been fortunate to work in an environment where everyone around me wants everyone else to be successful, because that helps us get new medicines to patients more quickly.

12. What portion of your job includes outreach/public education of the science that you are doing? It seems as though connecting the dots between the lab and the public awareness of diseases/treatment is critical to build trust and improve success of treatment etc.

LB: One item I mentioned during my remarks is that I oversee the group at Amgen that is responsible for ensuring Amgen compliance with registering clinical trials and posting their results on publicly available websites, such as clinicaltrials.gov. These websites are excellent sources of information about ongoing clinical trials and new treatments for diseases.

LP: One of the things I do at Regeneron is to oversee many of our STEM programs. As scientific director of Regeneron’s science education efforts including the Regeneron Science Talent Search, research mentorship efforts, the International and Westchester Science and Engineering Fair and STEM teacher programs, I try to emphasize scientific knowledge and rigor so that the kids of today will be good science citizens of tomorrow.

13. How can a smaller company manage the complexity of regulatory with the FDA and internationally?

LB: The FDA has resources for small companies to help navigate the regulatory process. One of the best is the Small Business and Industry Assistance (SBIA):

<https://www.fda.gov/drugs/development-approval-process-drugs/cder-small-business-industry-assistance-sbia>

14. What role do other STEM professions, such as engineers, chemists or data scientists, play in the industry?

LB: Here are some examples: engineers design and test devices that are used to administer medicines, chemists make small molecule and other drug candidates, data scientists help us design clinical trials and evaluate information about our drugs in large data systems.

15. Dr. Bloss mentioned some countries also require additional local clinical trials. Could you speak a little more on bridging the differences in regulatory processes and translating therapies to populations in developing countries?

LB: There are a couple different approaches for obtaining the local clinical trial data that is required for certain countries. In many cases, we simply include patients from those countries in our global clinical trials, and then we do subgroup analyses to make sure the efficacy and safety of the drug is similar across different countries. In other cases, if for some reason patients in that country cannot join the global clinical trials, we do separate studies in those countries to evaluate the safety and efficacy of the product. We also do an ethnic sensitivity analysis. What this means is that we compare the pharmacokinetics, safety and efficacy of the drug between the local and global patient populations.

16. Given the variety of approaches to treating disease, (e.g. stem cells, traditional pharmaceuticals, immunotherapy, etc.) how are therapeutic approaches determined?

LP: There are whole companies focused on just one of the approaches listed above, and there are companies working on all of them. Technologies arise to address a particular question or disease and then great scientists think of other ways to use these technologies and how the technologies can be improved. Science really is built “on the shoulders of giants”, so the iterative process is always ongoing.

17. From a regulatory and translational perspective, what are the biggest hurdles for nature based therapies/ products?

LB: I do not have much experience with nature-based therapies, but if they are developed as pharmaceuticals, then I don't think the hurdles would be much different from what we experience with non-nature based therapies.

18. Can natural medicine be used? Why will doctors not talk about it as much? Will science start to study holistic medicine?

LP: “Natural medicines” are always being explored and studied. An example of these are antibiotics. Most antibiotics are found in places like soil. Frequently, however vitamins and extracts are typically not specific enough to develop for disease.

19. Dear Dr.Purcell, I am a Regeneron STS 2020 Scholar, also a Rickoid (RSI 2019). I was wondering, If you could talk a bit more about ways to apply for Internships at Regeneron.

LP: Please head to our website (www.regeneron.com) and click on “Careers” and search for the internship opportunities available.

20. Regeneron How has recent public spotlight on your companies impacted your work? Does it motivate or distract?

LP: To be perfectly honest, the team at Regeneron is so busy working to test new therapies across therapeutic areas, it really did not distract us. Our mission is to bring medicines to treat serious diseases, and we remain fully focused on that. However I do admit, that after 12 years of working at a company that nobody knew, it was interesting becoming a “household name”.