Industry corner: perspectives and controversies

From academia to industry: a road more travelled

In May 2014, I ‘left academia’ to ‘join industry’. Specifically, I left my position as Professor of Medicine, Cancer Biology and Pathology/Immunology/Microbiology; Director, Division of Hematology/Oncology at Vanderbilt University Medical Center; and Director, Personalized Medicine Center at Vanderbilt- Ingram Cancer Center in Nashville, TN, to head up early oncology drug discovery at the Pharma Research and Early Development unit of Roche, based in Basel, Switzerland. In my new role as the Global Head of the Oncology Discovery and Translational Area, I oversee activities spanning from target assessment to phase II clinical trials to leading discovery and clinical scientists, with the goal of developing new medicines for cancer patients. As I pass the three-year mark, I was invited to provide some thoughts about the transition.

Note that I highlight my experience in ‘big pharma’ as opposed to ‘small biotechs’, where the environment is different [1, 2].

One of the main questions I get asked is: ‘why did you decide to make the jump?’ For me, the answers are clear.

The first answer is personal. My father died of metastatic colon cancer when I was age 13. At that time—1981—the only systemic treatment option was 5-fluorouracil plus leucovorin, which had significant side-effects with minimal benefit [3]. I vowed to become a doctor and help cancer patients, but I had no clue as to how I would help them. Fast-forward to 2000–2014: as a medical oncologist, I took care of cancer patients on a 1:1 basis. As a professor, I taught and trained new physicians and scientists in oncology and cancer biology. And as a scientist, I contributed directly to the early development of many new therapies including not but limited to gefitinib [4–6], erlotinib [4–6], osimertinib [7], X-396 [8] and afatinib plus cetuximab [9, 10] for patients with lung cancer. Translational work on the link between somatic EGFR mutations and outcomes of patients treated with epidermal growth factor receptor tyrosine kinase inhibitors (EGFR TKIs) further demonstrated to me the power of precision medicine in the clinic [11]. The last two activities whetted my appetite to make an impact on an even greater number of cancer patients. Now, my full-time job is to develop new medicines to improve the quality and quantity of the lives of patients with cancer.

The second answer is professional. From my experiences as a principal investigator on clinical trials and as a translational researcher collaborating with scientists and physicians in industry, I was familiar with and appreciated the efforts of my colleagues on the other side. Thus, I intuitively knew that a move into industry would not diminish my role but would rather still allow me to continue to contribute significantly to the advancement of science and cancer care. I have found that my experiences as a physician–scientist are highly valued in industry, because I can leverage science to address patients’ unmet medical needs, using my first-hand knowledge from the bench to the bedside.

The third answer relates to the cancer field in general. Today, we have more tools than ever to interrogate cancers and understand them at the molecular level. Using methods in the laboratory (e.g. next-generation and single-cell sequencing, CRISPR/Cas9 gene editing, humanized mouse models, etc.) as well as in the clinic (e.g. detailed analysis of pre-, on- and post-treatment biopsies), we can rationally develop molecules in specific patient populations as much as the biology allows. Moreover, the pace of discovery has accelerated, with an explosion in targets (e.g. in cancer immunotherapy), technologies (e.g. chimeric antigen receptor T cells, engineered antibodies, gene therapy, etc.) and discoveries (e.g. targeted protein degradation by degronomids [12]). To take advantage of all of these tools and harness these rapid developments, one needs to have resources available. On a project by project basis, this is much more readily possible in industry.

In terms of the relative timing of such a transition, there are three main time periods when I could have made such a move: early in my career (i.e. immediately after fellowship), in mid-career (i.e. associate professorship), or after a measure of academic success (i.e. full professorship). In my case, I am sure that I would not have been able to achieve such a high-level position for my first job in the pharmaceutical industry without having had past successes.

I have experienced a number of key similarities between academia and industry. To select avenues of inquiry and evaluate programs and opportunities, researchers in both settings need to have a cutting-edge understanding of the scientific field. Both settings emphasize career development and offer opportunities to develop expertise. Just as in academia, industry supports the training of post-doctoral fellows (with academic advisors). Furthermore, in both settings, a high value is placed on scientific rigor. Finally, scientists’ projects need to undergo ‘review’ in both academia and industry, in order to determine which to fund and to evaluate progress.

One key difference relates to the factors that affect career advancements. For example, in academia, researchers must publish, preferably in ‘top journals’. By contrast, in industry, publication is regarded as a positive but is not required, in favor of activities that move molecules closer to the clinic. Nonetheless, scientists in industry still do publish, often in top journals.

Another difference is how research ideas are generated and funded. Academic researchers use preliminary data to garner grants, while industry investigators use preliminary data to secure funds and expert resources to continue development of their molecules. In academia, grant applications typically undergo anonymous peer review, while in industry, very often the same committee of known senior experts participates in all reviews. In the former, academics ‘rebut’ criticisms through revised grants, while
in industry, scientific questions can be resolved through additional committee or 1:1 meetings. It should be noted that even in pharma, resources are not unlimited. Hence, funding of projects also involves a discussion of prioritization of the resources needed to move the project forward (e.g. determining how many people across the organization should support a particular project). In this context, commercial considerations are always evaluated, driving decisions that may differ from the goals and aspirations of academics.

A third difference is the big-picture motivation behind research programs that affects how projects are conducted. Academia focuses mainly on basic discovery for discovery’s sake, and the resulting publications inform the world of conceptual breakthroughs. By contrast, industry focuses on developing molecules into marketable drugs, and approvals from regulatory agencies are the major achievement, signifying that a new drug is indeed addressing a previously unmet medical need. In industry, this also means that we take a comprehensive view of the entire drug development continuum—from target assessment to biomarker identification to clinical development—even from the start of a project idea.

Finally, a major difference in industry compared with academia is the critical need for collaboration and teamwork across the whole organization. To successfully bring a new drug to market, many experts from multiple different fields are involved, many with whom academics do not even interact. Moreover, pharma operates in a highly regulated environment, which necessitates experts in a wide variety of areas, which is not always appreciated from the academic side. I was shocked to learn when I arrived at Roche that the approval of a drug that originated from our group involved >1200 people. Core project teams involve experts from areas including but not limited to discovery science, translational medicine, biomarkers, biostatistics, technical development, regulatory, commercial, clinical pharmacology, clinical development, clinical operations, clinical safety, project management, strategy and portfolio, and manufacturing. Each one of these areas has its own challenges: for example, in the realm of manufacturing an antibody, experts decide on the formulation (e.g. isosmolar? sucrose content? etc.), vial size, vial label, delivery methods and more. I never appreciated before how much ‘behind-the-scenes’ work it actually takes to deliver a medicine to a patient in the clinic.

Related to collaborations, it is also important to note the constructive interactions that pharma representatives have with regulatory agencies and academics. All sides are committed to developing new medicines for patients and often work closely together to achieve this goal. For example, the Food and Drug Administration (FDA) Breakthrough Designation was a result of close collaborations of the FDA with many stakeholders to expedite clinical development of new, potential ‘breakthrough’ drugs or treatments that show dramatic responses in early-phase studies [13].

My transition from academia to industry has been marked by a few surprises, some pleasant and some less so. I was pleasantly surprised and inspired by the dedication I found in industry to addressing unmet medical needs. Like me, the researchers and other professionals I met were passionate about and dedicated to improving the lives of cancer patients. I was also happy to see that I could continue my relationships with academia, funding agencies and nonprofit organizations through an academic appointment (as an adjunct professor), meetings (as an invited speaker or program committee member), journals (as an editor) and other activities including direct collaborations with academics in the laboratory and the clinic.

On the other hand, I have become more familiar with the reality that a great deal of published research is not reproducible [14–18]. Being a part of the scientific community, researchers in industry—not just pharma—rely significantly on the published literature to help determine avenues of inquiry. However, we often find that we are unable to confirm reported results in our own laboratories. Failure to reproduce such results leads to lost time and resources [19–24]. We collectively need to figure out how to address this challenge. Funding agencies, journals and groups like the Center for Open Science, among others, support efforts to understand and improve reproducibility in science [25–27]. This issue not only has an impact on life sciences industries; academic integrity is absolutely critical for support of the entire scientific enterprise from the public.

Finally, I knew that developing drugs was challenging, but living it first-hand has given me a greater appreciation of how truly tough it is. Today, developing a new drug takes more than 10 years from pre-clinical studies to regulatory approval and $1.4 billion in out-of-pocket costs (total cost = $2.6 billion) [28]. When we get a new molecule into the clinic for the first time, the chance of it getting launched is only ~10% [28–30]. The hurdles are many; at a high level, these include inability to show proof of mechanism or proof of concept, inability to find a safe dose and schedule, and inability to find a commercial development path forward. From 1827 to 2013, only 1453 new molecular entities were approved for use as therapeutics in the USA [31]. Thus, even with cutting-edge expertise, one needs patience, deep pockets, some serendipity and a high tolerance for risk and failure in industry.

Given the choice today, I would make the leap from academia to industry again. I do miss seeing patients and training new investigators, but I have a clear focus on early drug development. In industry, I have been able to retain many of the benefits of being in academia including an emphasis on scientific rigor and know-how and working with experts in multiple different disciplines. I also still interact with academic scientists in multiple ways. Hopefully, I will be able to look back in a few years and say that I directly helped to develop many new drugs that helped cancer patients live better and longer lives.

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References

17. Prinz F, Schlan t, Asadullah K. Believe it or not: how much can we rely on published data on potential drug targets?. Nat Rev Drug Discov 2011; 10(9): 712.

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