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The Role of Entrepreneurial Activities in Academic Pharmaceutical Science Research

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Abstract

Academic pharmaceutical science research is expanding further and further from the University setting to encompass the for-profit private company setting. This parallels the National Institutes of Health momentum to include multiple funding opportunities for University and private company collaboration. It has been recognized that the non-profit and for-profit combination research model can accelerate the commercialization of pharmaceutical products, and therefore more efficiently improve human health. Entrepreneurial activities require unique considerations in the University environment, but can be modeled after the commercialization expansion of the academic healthcare enterprise. Challenges and barriers exist to starting a company as an entrepreneurial faculty member, but the rewards to one's personal and professional lives are incomparable.

Introduction

Why is a Commentary in this area necessary?

If the United States' academic organizations have been creating protected intellectual property since the first U.S. patent issued in 1790 (United States Patent and Trademark Office), then why would it be necessary to discuss entrepreneurial activities in the academic pharmaceutical sciences in 2009? There have been some well-publicized stories about universities creating new drugs, e.g. the discovery of the beneficial effects of warfarin by the Wisconsin Alumni Research Foundation in 1945. One can even consider the 1967 licensing of Gatorade from the University of Florida to the Stokely-VanCamp Company a health care-related accomplishment. Depending on where one went to school, you also heard the recount of Nastech/Bristol-Myers Squibb's 1992 launch of Stadol after securing a license in 1983 from Anwar A. Hussain and the University of Kentucky Research Foundation. Many are also familiar with University of Kansas Professor Valentino J. Stella and the development of fosphenytoin.¹⁻³ These are all great examples of successful drugs that originated in academic labs, so the question still remains, why is it necessary to discuss entrepreneurial activities in pharmaceutical science? The answer appears to be that the current push in many academic settings is to embrace the idea of start-up companies as part of the University mission to improve the economic development status of the respective region where the entity resides. Although this may have been the case for some "less metropolitan" academic centers for many years, it has virtually enveloped the entire academic environment now, because of the depressed economic times that recently blighted many communities in the United States and around the world. Some Universities have even gone so far as to create

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new Faculty Entrepreneur Awards, such as that started at the State University of New York at Buffalo in 2008.

Entrepreneurial activity in the academic pharmaceutical science setting has traditionally been defined as intellectual property created in the University lab and either outlicensed to another company for development, or developed in the respective lab/start-up company of the principal investigator. Outlicensing seems to be a straightforward enterprise for most universities, and has worked relatively well in the hands of experienced technology transfer offices.⁴ However, economic conditions also affect the function of University technology transfer offices, as these are often the departments that receive cuts when budgets fall short of expectations. When budgets are limited for technology transfer offices, international patent applications can also be expected to be limited or completely eliminated in some cases. A lack of international protection can hurt the license value of any patent, but it is especially detrimental in the case of a pharmaceutical patent, where big pharma would like to recover the tens to hundreds of millions of dollars for the drug development process and make shareholders happy with world-wide marketing exclusivity. The outlicensing scenario can work well for many academics, because they can then often be involved in the development process of the intellectual property by being an advisor to the licensing company, or by being a member of the board of directors or scientific advisory board. These positions within the licensing company then allow the academic scientist to maintain a full-time University position and to not have to start a company of his/her own.

There are several universities that come to mind as the historical places where faculty start-ups are the norm, and not just for the few faculty members who decide to try something different. One effortlessly thinks of Stanford, Massachusetts Institute of Technology (MIT), the University of California System, and the North Carolina Universities of the Research Triangle, when wanting to describe entrepreneurial benchmarks. One notable mention is that these educational institutions also seem to be benchmark organizations for most aspects of pedagogy. However, out of this benchmark group, Colleges of Pharmacy only exist in the University of California system (UCSF, UCSD, and USC) and at the University of North Carolina. Traditionally it seems to have been engineering and information technology (IT) companies that have had multiple launches from Universities, as compared to medical center-based company launches from colleges of medicine and pharmacy. Granted the expense and regulatory pathway of drug development often astronomically exceeds that of applied engineering and IT invention commercialization, but it still seems that somehow there are those who still associate entrepreneurial activity in the collegiate medical and pharmaceutical science fields as unscrupulous as compared to the respectable field of physical science for profit. It hadn't appeared to matter whether or not university medical centers were trying to operate physician service clinics at a break-even or for-profit rate, or whether the centers were trying to supplement technology transfer offices with profits from spin out companies, there was still a previous general opinion that these medical centers should not be making a profit for any reason.⁵ Along this same line, there are still some academic scientists who believe that seeking patents and the income that might be generated is inappropriate. The problem with unpatented intellectual property is that the invention will never be commercialized, and therefore will never help improve human health. A few people have suggested that this issue can be solved by modifying the world's intellectual property and patenting system, as well as the regulatory drug approval process, to embrace models of nonprofit medical research.⁵ This is definitely a noble goal, however, worldwide change of this type would take cooperation across multiple sectors, and most of us don't have multiple decades to wait for new life-saving cures.

Did the delayed entrepreneurial activity in the healthcare enterprise cause a slow-down in academic pharmaceutical science entrepreneurial activity?

Slowly the academic healthcare enterprise has had to learn how to be more capital efficient, but still continue to be a leader in patient care, education and research. Since entrepreneurial activity seemed to generate revenue to support other applied science entities of the University system, more programs and alliances that are not strictly non-profit have been appearing in the academic healthcare enterprise. Ways of dealing with the unique challenges and barriers to entrepreneurial activities in the medical center setting have been developed so that the medical center mission can be maintained in the presence of the new and competitive nature of healthcare. Therefore, it is possible that pharmaceutical science departments which reside inside medical center Colleges of Pharmacy have more slowly begun to accept entrepreneurial activities as grand opportunities, as compared to the progress of their more expeditious engineering counterparts on campus.

The largest industry in America, healthcare, hasn't generally appeared to adopt entrepreneurship as readily as some other industries. There is a substantial amount of literature published in this area, and one good example is from Phillips and Garman in the 2006 edition of the *Journal of Health and Human Services Administration*.⁶ Four barriers to entrepreneurship in healthcare are described, including structural, economic, organizational, and behavioral. The structure of academic health centers has been set up to provide service, education, and research for the primary purpose of patient care, and other activities are thought to detract from the primary patient care mission. Economically it is difficult to divert funds from third party payers to activities other than patient care. Non-profit healthcare organizations have difficulty meshing with for-profit entities. Lastly, healthcare organizations have an expected culture, policies plethora, and behavior that often do not nurture an entrepreneurial risk-taking, uncertain, personal initiative-driven environment.

Disruptive innovation has been a large force that has caused change in healthcare centers. Christensen et al. described disruptive innovation as “cheaper, simpler, more convenient products or services that start by meeting the needs of less demanding customers.”⁷ Building relationships between non-profit and for-profit patient services is even more important as healthcare costs increase.⁸ Intrapreneurial activities generate less risk than entrepreneurial activities, as intrapreneurial activities would be directly related to the healthcare organization mission. For example, one might consider the translational research movement to be an intrapreneurial activity of the academic healthcare center, but in the entrepreneurial world one might call those clinical trials. It is possible that the intrapreneurial translational research effort may have a few more academic endpoints measured or statistically evaluated, but in many cases the study can still be called a clinical trial of some type. However, it is easier to overcome barriers when clinical research is viewed to be consistent with the existing mission of the organization.⁹ It can be viewed as a different type of organizational problem when clinical research is part of the mission, but a clinical trial is not able to be completed due to resource limitations.

Challenges and Barriers

Why is venturing into this area exhilarating and exasperating?

A brief look at how entrepreneurship has improved society—A couple hundred years ago Thomas Jefferson reminded society that “A little rebellion now and then is a good thing, and as necessary in the political world as storms in the physical.” He also said that “The best society is the one composed of the greatest number of entrepreneurs.” The founding fathers of the United States obviously shared enthusiasm for entrepreneurial activity. Another great historical example of entrepreneurial attitude is the early Soviet/

Russian manned space program that began just over one hundred years ago.¹⁰ These Soviet engineers developed space travel from the first spacecraft design sketch, to the first dog in space, to the first human in space, to the first human extravehicular activity in space.¹⁰ Meanwhile back on the ground in the United States, entrepreneur Henry Ford was busy making the Model T the most popular car in the country. Whilst a few years after the United States space program finally surpassed the Soviets and put the first man on the Moon, Bill Gates was considering leaving Harvard to start Microsoft. About a decade after that Oprah Winfrey formed Harpo Productions, then one more decade brings the timeline to Larry Page and Sergey Brin founding Google, and in the current decade the most successful entrepreneurs still remain to be determined. These are all examples of an exhilarating entrepreneurial atmosphere that many people dream about, but very few actually decide to attempt.

Influence of organizational social structure, new vs. established—Research studies on innovative organizations, like entrepreneurial start-ups, have been completed in order to determine which features of the organization helped shape the short-term inventive success versus the long-term sustainability.^{11,12} Not surprisingly, the features linked to the success of a new versus an established organization are incompatible.¹¹

New and different organizations have problems, but there are also advantages to this structure. The personal characteristics of the founder influence the new organization's makeup, including vision, imperfections, and genius. An individual can rarely have a major influence in an established institution that has developed a structure to decrease the impact of a single personality, e.g. a conventional committee system.¹¹ Entrepreneurs find survival in established institutions uncomfortable because more restrictions and structure are created. Survival of start-up enterprises depends heavily on quick decision making and ease of directional changes. Unfortunately for many entrepreneur-types, their direct supervisors in an institutional setting may be polar opposites in terms of risk tolerance, which may stifle the entrepreneur's professional potential.

Expansion of an organization is a difficult challenge, no matter what the type of organization. For example, when a company is taken public from a private start-up stage, new investors may be much more conservative in their decision making processes than the founding entrepreneurs. This type of situation may cause initial unrest in the organization direction, but it is apparent that both types of personalities are needed in order to make organizations grow successfully.^{11,13} This seems to expand on the Collins philosophy of not only “getting the right people on the bus”, but “getting the right people on the bus at the right time”.¹³ Therefore, the right people may actually be the wrong people, depending on the stage of growth of the institution. This personnel hiring challenge can be exhilarating or exasperating, most often depending on the success rate of putting together the right team while maintaining impeccable timing.

Managing in the whitespace after decades of training in the traditional blackspace—Once one has put together an olympic pharmaceutical research team at exactly the right time, the next challenge is how to manage all these talents. Most people trained in the pharmaceutical sciences have never had any formal personnel management training, so when faced with their initial management responsibilities they revert back to how they were trained and managed by their mentors. Most scientists have been trained in large institutional settings where traditional blackspace management is prevalent. The blackspace tasks deal with formally recognized goals, planning, budgeting and management.¹⁴ This blackspace largely encompasses the activities of most universities where all the academic researchers are trained. Unfortunately or fortunately, depending on one's point of

view, entrepreneurial activities incubate in the whitespace. The whitespace has few rules, unclear authority, no budgets, and haphazard strategy.¹⁴

Successful whitespace managers drive innovation, start new enterprises, and identify new market opportunities. An entrepreneurial academic researcher working for a blackspace manager needs support and monitoring in order to maximize and develop the enterprise so that the entrepreneur and the institution can both benefit. Management in the whitespace requires one to find creative ways to get tasks completed, and measure progress and recognize accomplishments in non-traditional ways. One unusual challenge for the whitespace manager is the need to establish legitimacy.¹⁴ An academic researcher operating in the blackspace does not need to prove to the institution that he/she deserves support. Conversely, the academic entrepreneur may spend the first few years of the start-up convincing the institution and the investors that he/she has the expertise and reputation needed to make the enterprise successful. The academic entrepreneur who can build a qualified research team to help legitimize the value of the company is usually the most successful.

Resource management is always an issue, no matter what the assignment.¹⁵ The whitespace manager often finds that there is a need to utilize whatever resources he/she can get, rather than the traditional blackspace need to utilize what he/she thinks he/she needs after outlining a detailed budget. Creativity and determination frame the whitespace resource management universe.¹⁴ In a world of dwindling resources, blackspace managers may perceive the entrepreneur as a competitive threat to those very same resources. Maintaining transparency of the entrepreneur's company milestones, as well as sharing the rewards and credit for completion of those milestones with the academic institution, can help alleviate competition concerns. Eventually, if the entrepreneur is fortunate, the start-up organization will grow large enough to require blackspace management.

Conflict of interest—Maintaining a very good conflict of interest policy that is not overly cumbersome is a challenge that needs to be taken very seriously. More refined and structured conflict of interest committees have been growing at universities in order to manage the entrepreneurial academic enterprise.¹⁶ It is certain that these entrepreneurial financial conflicts of interest can be managed, just as the patient care financial conflicts of interest have been managed. One curious fact that doesn't seem to be recognized by many of those in charge of conflict of interest committees is that everything a start-up pharmaceutical company does eventually has to be reviewed by the FDA in order to generate product approval and revenue. Generation of pharmaceutical research from a non-business NIH research grant is usually only eventually peer reviewed for publication, without the onerous FDA regulatory hurdle. The point being that it seems much more likely that someone would be able to get away with academic research fraud before they could commit drug product approval fraud. Yet academic for-profit pharmaceutical drug development creates mountains of conflict of interest paperwork, while non-profit academic research goes without extra scrutiny.

Intellectual property segregation—The segregation of university and start-up company intellectual property is another challenge that one is usually not prepared for by graduate school. Very little intellectual property and patent coursework is taught to pharmaceutical science graduate students, yet almost 100% of them will be involved in contributing to patents in industry and academics. Some universities do not allow a faculty member to have separate intellectual property from the institution, but others allow faculty-owned intellectual property (IP) with certain restrictions. If one is at an institution that allows separate IP, then the key to maintaining segregation is having separate sets of laboratory

notebooks for company and academic labs, as well as duplicate research equipment and space for both facilities.

Marketing and business development from the “ivory tower”—So now that the entrepreneur has picked the perfect people at the perfect time, learned how to manage with limited resources, and proven to everyone that the venture is worthwhile; the next challenge is to become an expert marketing and business development team leader. Again, most pharmaceutical science researchers who have taken the traditional PhD graduate program curriculum have never had any formal marketing training. However, just as academic health centers have learned to move towards private enterprise marketing strategies, the entrepreneur can also gather enough information to function in this realm as well.¹⁷ In fact, the academic health center economic development departments and marketing experts have begun to partner with entrepreneurs in order to share their expertise. After all, a good marketing strategy and business development program are important to the success of the start-up company headed for growth and the potential for blackspace management.

Discussion

Inspire entrepreneurial attitude and innovation

Despite all the challenges and barriers to entrepreneurial activities in academic pharmaceutical research, multiple successful pharmaceutical companies are slowly developing out of academic centers. The competitive edge of the University is production of knowledge, and part of this knowledge production should be in applied research towards pharmaceutical development. This doesn't mean that everyone in academic pharmaceutical science will abandon faculty duties and run out to start a company, but for those who are interested, it should be a real and validated opportunity. If universities do have such great IP, then that intellectual resource should be used to differentiate an institution from the benchmark competition by developing some of that IP with faculty creativity. After all, new ventures in the forms of new Colleges of Pharmacy and Medicine are appearing all over the country to compete with the more established programs. Indeed innovation can be disruptive, but innovation should not be stifled and excluded from the rest of the University mission, and at some point disruptive innovation may trump the benchmark competition.

Be opportunistic and entrepreneurial by creating resources

Resources that can be allocated to economic development should pay off in the University setting. Although the typical start-up pharmaceutical company return on investment timeframe can be multiple years, the payoff of an FDA approved drug with a good pharmaceutical marketing partner is bigger than any other sector. Resources for start-up companies can come in many forms, including business management expertise, outsourcing services, accounting assistance, payroll management, insurance plans, retirement plans, equipment leasing, equity investments, and space availability, just to name a few.

Benefit the educational mission (student, faculty and staff)

Everyone in the academic institution can benefit from start-up company presence. Students benefit by having first-hand knowledge of how a company runs on a global scale. The start-up experience is different than doing a large pharma internship, as most large pharma positions only provide a small piece of training in a focused area, rather than intimate knowledge of how to get a drug or device to market. Educating students in the areas of resource allocation, regulatory affairs, business management, and the patent process will give them a broader background and a competitive edge for career advancement.

Faculty members benefit by getting first-hand experience at directing pharmaceutical development operations. The faculty entrepreneur is now more than just an established researcher focusing on one human health problem, he/she becomes a diversified expert in the FDA approval process and the proof-of-concept research required prior to the approval process. This faculty entrepreneur can now train students in the development process at a much higher level than a general textbook overview. If one believes that those who can't do teach, then this solves the problem by creating those who can do and teach.

Staff at the University can also benefit from the learning experience of start-up company operation. Whether these staff hold administrative or technical positions is of no consequence, as education in the operations aspects of both areas provides opportunity for career diversification and evolution.

Conclusions

Welcoming the disruptive innovation of a start-up pharmaceutical company into the academic environment has many advantages, including a distinctive impact on the research and educational missions of the University. This new introduction of the private sector into the non-profit sector can raise questions; however, research data exists in other sectors concerning the best ways to solve resource, management, and conflict of interest issues. The commercialization of the healthcare enterprise can provide a good model to mimic, as far as oversight and support for entrepreneurial activities. The challenges and rewards of the academic entrepreneurial lifestyle appeal to many faculty members, and this opportunity can be integrated and monitored in the University environment. Universities and entrepreneurs benefit in many ways from a well-designed economic development initiative, and this initiative helps to not only stimulate the economy, but accelerate development of products to improve human health.

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