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Keys to the kingdom

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What you need to know about your technology transfer office.

As an academic bioentrepreneur, you will face many challenges. At the very least, you must identify a novel and valuable life science opportunity, create a viable business model, build a team with technical and business acumen, manage resources and orchestrate partnerships, communicate your team's legitimacy to customers and stakeholders, as well as effectively 'pivot' as circumstances evolve (or, in other words, have the vision and courage to dramatically change your research or business strategy before your company runs into the ground)^{1,2}.

In addition, you will most likely have to negotiate with your university's technology transfer office (TTO) to license the intellectual property (IP) related to your research. Keep in mind that technology transfer regimes and policies regarding ownership of IP rights vary substantially across academic institutions for a variety of reasons. And that university TTOs in the United States and the United Kingdom govern themselves by different strategic and operational models³.

This administrative complexity and opacity in university technology transfer presents an extra obstacle to academic entrepreneurs who already face a multitude of technical and commercial hurdles before their discovery can reach the marketplace. The best way to overcome these issues is to be fully informed before initiating negotiations with your TTO. We hope the information in this article will better prepare you to meet these challenges.

Overcoming information asymmetries

Securing a license for your university discovery is an essential step in the quest to com-

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mercialize that discovery, and it can also help you raise capital and form strategic partnerships. You must therefore learn to effectively engage and negotiate with TTOs and determine reasonable deal terms (such as royalty rates and equity) for the technology at hand. First-time academic bioentrepreneurs frequently confront a deal-making process they do not completely understand, in part because final deal terms are often held confidential, making it difficult for outside observers to understand fair market terms. At the same time, bioentrepreneurs sometimes do not fully recognize how the interests of the TTO and university may diverge from their own. In fact, one postdoc we spoke to said, "Knowing what I know now about my university's licensing process, I might have considered a different university for my postdoc."

TTOs arguably benefit from information asymmetries in negotiations, whereas experienced bioentrepreneurs fear that disclosing details of prior deals could jeopardize their ongoing relationship with their TTO. Thus, they often stay silent on just how they got their asset outside the university walls.

Good advice can come from successful bioentrepreneurs or mentors within your network, but what to do if you don't have anyone like that to consult with? How will you know what constitutes a good deal? More generally, how can you gain better insight into the challenges you're about to face?

At the Oxbridge Biotech Roundtable, our mission is to facilitate connections between academia and industry to move ideas forward. To help answer questions about the bioentrepreneurial process, we collected anonymous qualitative data from bioentrepreneurs in the United States and the United Kingdom, and also spoke to TTO executives, heads of university innovation and entrepreneurship programs, venture capitalists and angel investors. The experiences of bioentrepreneurs reported here reveal that they have minimal structural bargaining leverage with their TTO. Because the TTO has full ownership of the technology, it approaches licensing with the risk perspective of an owner.

A daunting set of challenges

From these conversations, we've identified several key challenges for bioentrepreneurs in negotiations: a too-long licensing process, lack of business experience on the founding team, lack of funding, restrictive conflict of interest policies at universities and lack of access to experienced legal counsel.

Long negotiations. The length of the licensing deal negotiation process can become a major

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Box 1 The mature TTO

US TTOs are now devising novel strategies to deal with the bioentrepreneurs' equity split. Several apply antidilution provisions until the spin-out company has reached a sizable funding level (usually series A). There are a few surprising industry-wide fads in licensing, including a recent TTO trend of demanding undiluted equity percentages in the event of an IPO, sale or acquisition.

But it is unsurprising that US TTOs are leading the way, given that, on average, US TTOs are nine years older than their UK counterparts⁷. Still, at least two UK-based TTOs are now adopting models similar to these found across the Atlantic, suggesting that these policies may soon be implemented in equity deals with UK bioentrepreneurs.

problem for entrepreneurs. Of 13 US-based bioentrepreneur survey respondents, 53% said their negotiation process took longer than 6 months, and 38% cited the length of negotiation as a major pain point. One US-based entrepreneur said, "It took us 18 months to negotiate with the TTO. That is too long when time is critical to protect the invention, raise money and establish a company."

You can prepare yourself before entering negotiations by consulting experienced bioentrepreneurs and making yourself aware of their deals at other institutions. You should also be able to clearly articulate how your business strategy is tailored to your technology and understand the socioeconomic impact of your technology. Also, be prepared to be patient.

Inexperience. The credibility of the entrepreneur is important when entering a partnership with the TTO. As stated by one US TTO official, "Our faculties are academia people. They lack the business experience and do not know what reasonable financial expectations or description policies are." A US-based TTO director told us that bioentrepreneurs often do not sufficiently research the market their product will be entering—information about which is needed by both the TTO and investors. This sort of behavior does the bioentrepreneur no favors, as licensing deals are more likely to be completed if the TTO is dealing with an experienced and well-prepared team. Any concerns, and the TTO may hedge with higher upfront costs, limited exclusivity or milestone-based payments.

You can counter all this by preparing an adequate business plan or strategy for your IP before approaching your TTO. To enhance your knowledge and build credibility, start networking and taking advantage of institutional resources—such as mentorship and entrepreneurship programs, competitions and incubators—as early as possible. Consider bringing aboard team members with prior experience in life science commercialization to improve your team's credibility. Having a seasoned, serial bioentrepreneur or experienced biopharma execu-

tive on your roster will enhance the perceived quality of the startup management team. As one UK-based venture capitalist remarked, "A management team is more important than the technology. Sometimes we see what we think is great technology but we just don't believe the management team can make anything of it."

Lack of funding. The most frequent problem cited by TTO officials in the United States and United Kingdom when deciding whether to close a licensing deal was a lack of investment or support for the startup in-licensing the asset. However, the need to secure funding before executing a license presents a seeming paradox, given that attracting funding often depends upon securing a prior licensing agreement. One solution in the United States has been the use of a license option agreement, which grants a prospective licensee a right to evaluate a patented technology and the option to enter into a full license agreement for the technology at some later point. Companies pay a modest fee to reserve the possibility (without incurring the obligation) of formally licensing the technology for a specified period. It can also be difficult to attract an experienced management team if your company has little professional investment, but having a clear business strategy and market research evidence can put you in a stronger position when approaching investors and potential hires. You should also research alternative option licenses and consider sourcing funding from abroad.

Conflict of interest rules. Particularly in the United States, university researchers who wish to pursue the commercialization of their technology often run afoul of conflict of interest policies. These exist to prevent academics from playing both sides of a technology licensing deal or devoting too much time to nonacademic obligations⁴. One US-based TTO representative was of the opinion that "the main pain point [in this process] is the inventor's divergence of interests and loyalty," because the situation calls for "negotiating against the institution and, in many ways, against themselves."

In this regard academics can run into difficulties as the TTOs represent the interests of the university (not the academic), yet the academic is technically an employee of the university. "Our policy is to never negotiate directly with the faculty," says a US-based TTO representative. This issue might be particularly prevalent in the United States because of increased numbers of entrepreneurial ventures and its stronger culture for litigation. To that end, our advice to you would be to reaffirm the need to seek advice before entering discussions with your TTO, and to always remember the TTO is seeking the best deal for the university not neccessarily for the academic or investors.

Experienced legal counsel. Finally, most bioentrepreneurs in our survey emphasized that retaining experienced legal counsel is invaluable during the negotiation process. Issues related to the quality of the complete IP package, including the scope, field of use and royalty stacking are important elements and are often a source of disagreement between founders and TTOs. As noted by a US-based survey respondent, "Entrepreneurs need to be careful of the quality of the IP they are getting from the TTO and should consult lawyers to vet it." You must also consider whether the patent arose from sponsored or collaborative research; when ownership of IP is assigned to multiple institutions, negotiations with multiple institutions for IP rights must necessarily ensue.

Bioentrepreneurs often fail to appreciate the opportunity cost to the TTO in outlicensing. If a technology is licensed to an ineffective team (particularly with an exclusive license), the university forgoes any success or revenue it may have received from licensing the technology to a better organized industry partner. Moreover, universities have limited resources and manpower to protect IP, and, for this reason, prefer to license technology to teams they believe are well prepared to commercialize it. This conundrum has been termed the "keys to the kingdom" problem, in that a risk-averse university TTO may choose to wait indefinitely rather than hand over the 'IP keys' to a poorly prepared team.

Do our differences define us?

A notable disparity between the United Kingdom and United States is the availability of funds for academic startups. Our survey respondents felt that UK bioentrepreneurs are less able to secure early-stage funding than their US counterparts. "Companies that would struggle to raise \$100,000 in the United Kingdom could easily get \$1 million to \$2 million in the United States," said a UK-based TTO representative. This may be due to the



University	Guideline university equity share (%)	Guideline type
University of Wisconsin-Madison ^b	0	No ownership of IP claimed by university
Massachusetts Institute of Technology ^b	5	Max.
Washington University in St. Louis	5	Max.
Carnegie Mellon University	6	Max.
University of California ^c	10	Max.
Stanford University ^b	10	Max.
Rockefeller University	15	Max.
University of North Carolina	15	Min.
City University of New York	20	Max.
Oklahoma State University	20	Max.
North Carolina State University	25	Max.
University of Washington ^c	33	Not stated as negotiable
Texas State University	40	Min.
Illinois State University	50	Not stated as negotiable
New York University ^c	50	Not stated as negotiable
University of Maryland	50	Negotiable
University of Texas ^b	50	Not stated as negotiable
Missouri State University	60	Negotiable
University of Illinois	60	Not stated as negotiable
Texas A & M University	63	Negotiable
Indiana State University	65	Negotiable
University of Rochester ^c	65	Max.
Cornell University	67	Not stated as negotiable
Georgia Institute of Technology	67	Not stated as negotiable
Iowa State University	67	Negotiable
Emory University	67	Not stated as negotiable
University of Utah	67	Max.
Georgetown University	70	Max.
Marshall University	70	Negotiable
University of Massachusetts ^c	70	Not stated as negotiable
University of Pennsylvania	70	Not stated as negotiable
Brown University	72	Not stated as negotiable
California Institute of Technology	100	Not stated as negotiable
Northwestern University ^c	Not specified in policy	•
Princeton University ^c	Not specified in policy	
Harvard University	Not specified in policy	
Johns Hopkins University	Not specified in policy	
Penn State University	Not specified in policy	
Purdue University	Not specified in policy	
Tufts University	Not specified in policy	

a61% (39 of 63) US universities researched specified a guideline percentage for the university's share of equity in a spin-out company using university IP. Full table with references are provided in Supplementary Table 1. The authors have made their best efforts to find the most up-to-date, publicly discoverable, online policy documents. ^bUniversities ranked highly in gross licensing revenue but lacking information specific to life sciences in ref. 6. ^cUniversities named in ref. 6.

less-established venture capital network of biotech investors in the United Kingdom and/ or higher expectations for success on the US side of the Atlantic. However, UK university spinouts can develop a network with investors and incubators abroad. Our advice to you would be to network at conferences attended by entrepreneurs and venture capitalists, and reach out to seasoned bioentrepreneurs who are often very willing to help novice bioentre-

preneurs with advice and further introductions. Many of these events are often free, and even held on academic campuses. UK academics can seek support from US incubators, which also support and help other non-US high-tech companies, which is useful for developing a peer group that includes not only academics but also other entrepreneurs. (Although these differences exist today, TTOs are changing as they expand and grow; see **Box 1**.)

Equity deal terms

Perhaps the most striking difference between the United States and United Kingdom is seen with equity deal terms. In the United Kingdom, a typical licensing deal is a rarely negotiable 50:50 split between the university and the academic bioentrepreneur, whereas US interviewees often reported universities taking a 5–10% negotiable equity share.

To expand upon our survey data from entrepreneurs, we researched the IP policies from 100 US and UK universities and found guidelines for about half (Tables 1 and 2). University equity claims were not specified in the policy documents of many world-leading universities in the life sciences (and ergo top recipients of taxpayer-funded grants), including Harvard (Cambridge, MA, USA), Oxford and University College London (Supplementary Tables 1 and 2).

Many universities claimed at least a 50% equity share (including Oxford, Imperial College London, the University of Massachusetts and the University of Texas system), but US institutions are clearly more willing to take a lower proportion of equity than UK institutions. The Massachusetts Institute of Technology and Washington University in St. Louis state they take at most 5% equity in spinouts, Carnegie Mellon University claims a maximum of 6%, and Stanford University and the University of California system claim a maximum of 10%. It should be noted that although the University of Wisconsin-Madison has not historically claimed ownership over any IP generated through research conducted by their staff and students, their policy states that ownership of all IP generated through externally funded research, which would account for the vast majority of their IP, is transferred to a designated patent management organization, the Wisconsin Alumni Research Foundation⁵. The policies and deal structures of WARF were not publicly discoverable at the time of publication.

UK schools aimed for much higher portions. At the lowest end, the University of Cambridge, University of Dundee and Brunel University all sought 20% slices, fourfold higher than that of their lowest American counterparts.

Negotiating licensing deals

Our interviews with TTOs and bioentrepreneurs suggest that there are important differences in negotiating deals in the United States and the United Kingdom.

Factors to consider in US licensing deals. US founders often do not realize that some deal terms are negotiable, including upfront fees, option payments, equity, royalty payments, milestone payments, territories covered, field

University	Guideline university share of equity	Guideline type	
University of Cambridge (RG)	20 ^b	Negotiable ^b	
Brunel University	20	Non-negotiable	
University of Dundee	20	Min.	
Heriot-Watt University	24	Negotiable	
University of York (RG)	25	Negotiable	
Newcastle University (RG)	25		
University of Exeter (RG)	25	Max.c	
University of Manchester (RG)	30	Negotiable	
University of Leeds (RG)	30	Non-negotiable	
King's College London (RG)	50	Max.	
University of Glasgow (RG)	50	Non-negotiable	
Aston University	50	Max.	
City University London	50	Negotiable	
Northumbria University	50	Negotiable	
University of Reading	50	Negotiable	
University of the West of England, Bristol	50	Negotiable	
Imperial College London (RG)	50 ^d	Negotiable ^d	
University of Edinburgh (RG)	50 ^d	Negotiable ^d	
University of Oxford (RG)	50 ^b	Negotiable (rarely)	
University of Warwick (RG)	50 ^b	Non-negotiable ^b	
University of Leicester	51	Min.	
Queen Mary, University of London (RG)	60	Negotiable	
Swansea University	60 ^d	Negotiable ^d	
University of Cardiff (RG)	60 ^d	Negotiable ^d	
University of Liverpool (RG)	60	Non-negotiable	
University of Nottingham (RG)	60	Negotiable	
University of Sussex	60	Max.	
University of Sheffield (RG)	60 ^d	Negotiable ^d	
University of Birmingham (RG)	60		
University of Bath (RG)	67	Non-negotiable	
University College London (RG)	Not specified in policy		
University of Bristol (RG)	Did not respond to inquiry		
University of Durham (RG)	No official published guidelines	No official published guidelines	
University of Southampton (RG)	Not specified in policy	Not specified in policy	
University of St Andrews	Not specified in policy	Not specified in policy	

^a64% (24 of 37) UK universities researched specified a guideline percentage for the university's share of equity in a spinout company using university IP in a publicly accessible policy statement or a third-party website (°). Anonymous survey respondents from three more UK universities reported the standard share of equity taken by their university from their personal experiences (^b). Full table with references are provided in **Supplementary Table 2**. The authors have made their best efforts to find the most up-to-date, publicly discoverable, online policy documents. RG, Russell Group. ^bReported in anonymous survey. ^cFigure kindly provided by TTO, specifying that such guidelines are only available to University of Exeter staff. ^dSpecified on third-party website and not part of a publicly available official policy statement.

of use and exclusivity versus nonexclusivity. They also do not always appreciate that agreements can be renegotiated after they are signed. Check your university policy; your university might offer a lower upfront payment in exchange for higher royalty rates or vice versa. In our survey, several bioentrepreneurs mentioned that they were able to negotiate payments and duration for options before fully licensing the technology. In some cases, the upfront payment option had been deferred altogether. Remember to be flexible—several US-based TTOs explained that a company without funds could get an option or license agreement by accepting highly structured mile-

stones in lieu of payments.

However, although there are variations around the basic structure of deals, and negotiations might tilt toward the academic entrepreneurs or the university prolonged negotiations often revert to the mean in the United States. One US-based attorney suggested that variance in deal terms are mainly due to the inexperience of one of the parties involved. So know your averages, but don't be timid about asking for what you need.

Factors to consider in UK licensing deals. In the UK, licensing deal equity terms are often perceived as being non-negotiable, though this is not always the case. In fact, many institute policies explicitly state that equity terms are negotiable (**Table 2**), and several of our survey respondents have reported that they were able to discuss terms. One UK-based TTO explained the apparent lack of flexibility this way: "If other TTOs say that they don't negotiate, I think that is because they are scared. They are trying to preserve their position in the negotiations. They don't want to be on public record saying that they are willing to negotiate."

Several UK entrepreneurs we spoke to felt that the non-negotiable, 50:50 split they were offered overestimated the contribution of the university to the venture. Still, this fixed rate does greatly simplify, and thus shorten, the initial negotiation time, the length of which is a major complaint of bioentrepreneurs in the United States. One UK TTO representative stated that "[we want to] actually build a business instead of spending a lot of time upfront negotiating something that isn't actually worth anything." Though one can argue the deal would move even swifter if the TTO took a less aggressive stand (for instance, asking for 5% instead of 50%), which would allow the bioentrepreneur and investor to start the real work of building the company over the coming years, and rewarding them accordingly. Furthermore, a few UK-based bioentrepreneurs highlighted the nonequity-based benefits of their deals, such as increased research funding from the school.

Concluding remarks

In today's economy, where early-stage ventures grow by matching technology with the unfulfilled needs of markets, university-based bioentrepreneurs have much to contribute. Although many factors are involved in starting a company and bringing a product to market, academic innovators require not just technical expertise, but an understanding of the mechanics, politics, and logistics of TTOs and of the technology licensing process. As we have noted, successful spinouts must clear several challenging hurdles, including finding comparable deal terms for reference, satisfying demanding university conflict of interest policies and presenting a credible business plan to sophisticated investors, busy TTO officials and experienced industry professionals. As one bioentrepreneur who weathered this process cautioned, "It will take ten times longer and cost ten times more than you think."

From our study it is also clear that there are differences in the behaviours of US and UK TTOs. It is difficult to understand the justification of UK TTOs, such as Oxford's Isis Innovation, taking 50% of a company's equity at formation—which after investment can leave

the academic entrepreneur with an extremely low stake from the get-go, for what was likely years of work, and will require many years and millions more to develop. Notably, the regions attracting the most life science investment and with the most successful life science spinouts (San Francisco Bay Area, Boston, and Cambridge UK) had four TTOs (Stanford OTL, UCSF ITA, MIT TLO, and Cambridge Enterprise) that rewarded the academics and investors the most. The data would suggest that TTOs taking less upfront and leaving more to the academic and investors who will actually carry the idea forward pays off in the long term. Simply put: holding a smaller piece of something is still more valuable than a large piece of nothing.

It is also worth noting that while a discussion on royalties was outside the scope of this study, it was clear from our research that many university TTOs "double dip" and take significant equity and royalty. Several bioentrepreneurs in the UK mentioned that the TTO also sought as much as two-thirds of the royalty stream.

Perhaps more disquieting than the out-sized equity and royalty stakes that universities are claiming is the lack of transparency from many universities on this critical issue. Even private institutions (such as Harvard or Northwestern) are recipients of vast sums of government grants and under a government mandate to commercialize research produced from that money. The government has done this with the public's interest in mind, and surely it is also in the public's rightful interest to know how these assets (funded by the taxpayer) are being allocated. Indeed, even for the universities for whom we have data regarding equity policies, it was often hidden deep within a jumble of legalese. To that end we encourage universities and research institutes receiving public monies to be fully transparent in their equity and royalty policies, and not use these information asymmetries as a bargaining advantage against fledgling bioentrepreneurs.

Moreover, while we did not assess Canadian, other EU (non-UK), or Asian TTOs, these information asymmetries exist regardless of geography. As such, the tools and insight presented here are just as applicable outside of the US and UK.

It is clear that becoming familiar with the technology transfer process is an important part of the technology commercialization process for researchers. In the words of one academic bioentrepreneur, "The only thing I regret is that I didn't get prepared for this process earlier."

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- 1. Gavetti, G. Organ. Sci. 23, 267-285 (2012).
- Teece, D.J. Strateg. Manag. J. 28, 1319-1350 (2007).
- Decter, M., Bennett, D. & Leseure, M. Technovation 27, 145-155 (2007).
- Jain, S., George, G. & Maltarich, M. Res. Policy 38, 922-935 (2009).
- 5. University of Wisconsin system. Patent Policy (UW, 1985). https://www.wisconsin.edu/financial-administration/ financial-administrative-policies-procedures/gappnumeric-index/g34-patent-policy/
- Huggett, B. Nat. Biotechnol. 32, 1085 (2014).
- Williams, E. Too Few University Spin-out Companies? (University of Warwick, 2005). http://www2.warwick. ac.uk/services/ventures/spin-outs.pdf>

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