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From academic concept to commercial reality: How to accelerate translational drug discovery

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Chapter 3: Just short of a decathlon: A day in the life of a BRIDGE Expert in Residence

In Chapters 1 and 2 of Evotec's White Paper series 'From academic concept to commercial reality: How to accelerate translational drug discovery', we examined from the respective perspectives of academic researchers and commercial investors the challenges of translating early-stage therapeutics projects into robust investment opportunities. We also discussed the solutions deployed currently by Evotec and others active in pre-seed drug discovery support. In the third and final Chapter of our series, we focus on a critical human component of Evotec's BRIDGE model: The Expert in Residence (EIR). We dissect why this role is so important for successful BRIDGE partnerships and provide real-life examples to give a flavor of what 'a day in the life of an EIR' looks like.

1. **The EIR as a 'Swiss Army Knife'**
   To date, Evotec has (co-) initiated eleven BRIDGEs on three continents (Figure 1), making BRIDGEs collectively one of the most comprehensive pre-seed accelerators globally.

   A unique aspect of our BRIDGEs is the inclusion of an EIR as part of the operational and governance structure. The EIR, who is typically embedded in close geographic proximity to the relevant BRIDGE-associated academic institutions, is an essential resource for all BRIDGE partners. EIRs are responsible for BRIDGE creation and day-to-day activities which include seeking new academic and corporate partners, identifying new drug discovery opportunities, creating workplans, managing operational and alliance issues for the program and navigating the launch of startups. Here, we describe in more detail the role of the EIR and highlight how this unique multi-tasking character gives Evotec's BRIDGEs a competitive advantage over other partnering structures.

Figure 1: BRIDGEs span the globe

As a central cog to any BRIDGE, an EIR needs to possess a veritable 'Swiss Army Knife' set of skills. EIRs must have a scientific background and proven experience in commercial drug discovery and development, usually across multiple disease areas and modalities. EIRs also need to embody experience spanning R&D leadership, intellectual property, legal transactions, product development, regulatory affairs, marketing and alliance management.

2. Building a contractual foundation for success

BRIDGE partnerships are each supported by a framework agreement between all parties that facilitates discussions regarding project opportunities, sets out the funding process and governance, and enables rapid, efficient progress from completed project to new company (NewCo) creation or licensing event, typically on pre-agreed terms. Once in place, the EIR is the alliance manager for these agreements (see below). However, before signature, the EIR also facilitates negotiations, using both their own experience and channeling that of Evotec's Academic Partnerships team to expediently identify compromises.

The terms of BRIDGE framework agreements must represent a compelling value proposition to the institution and its academic researchers, including appropriate financial terms and addressing unique academic needs such as publishing and retained rights. However, these terms must also incentivize the investment partner to develop the BRIDGE project outputs. With a local presence, the EIR is able to work closely both with funding partner(s) and academic institutions to negotiate equitable solutions.

When you have done many deals in your career, you can start to feel when you have reached a point in the negotiations where the only thing standing in the way of getting to signature is just the sheer will to pull everyone together, lock the doors and hammer out the last remaining details. Often it is the EIR that has their hand on the lock!

Michael Draper, EIR for LAB eN² in Cambridge, MA

3. Establishing durable relationships

All BRIDGEs have as a primary source of capital a partner who can be a venture capital group, a pharma company or a combination of both. The EIR plays an important role as a "bridge" between the academic partner and the financing partner and has the responsibility of understanding the investment partners' preferences for new projects including stage of technology, therapeutic area of focus, appetite for risk and preferred product profiles.

While the EIR is typically the first to be exposed to new discoveries by the academic partner(s), they must protect the confidential nature of this Intellectual Property (IP) and only disclose it to the investment partner(s) after weighing the value of the discovery. As such, the EIR serves as an important filter who can identify likely issues in advance of disclosure to

investment partner(s) in order to eliminate conflicts and potential IP contamination. This is especially important where the investment partner is a large pharma and may have internal R&D programs of its own or other relationships with biotech companies.

Provision of rapid, actionable feedback to the technology transfer office (TTO) and investigator is another important component of the value added by the EIR. Often, investigators and TTOs are frustrated by the feedback they receive from external parties scouting for innovative ideas; usually along the lines of 'too early' or 'not aligned with our interest/strategy', and lacking substance. BRIDGE EIRs aim to give detailed reviews of the scientific and commercial opportunity with the goal to provide added value to the academic researcher and institute and to position the BRIDGE as one of the first places they turn to with their scientific or entrepreneurial plans.

Along with the opportunity to discover and nurture innovation, for me there is nothing better than to witness the appreciation of the academic partner, in many cases being exposed to drug discovery for the first time. To discuss and develop ideas together, to educate and learn from each other is the real value of these alliances.

Mark Slack, EIR for beLAB1407 in the UK

While doing so, the EIRs act as sounding boards, providing advice on how to best include experiments addressing questions critically relevant for the development of therapeutics, e.g. on the molecular mode of action or potential toxicity. Principle Investigators (PIs) are then invited to consider these suggestions and to continue discussions once addressed.

In one discussion we had an excellent team with a very interesting and advanced molecule. Due to the mode-of-action we expected potential toxicity specifically in one tissue. The team de-risked this successfully by running an assay the pharma investor suggested – and we proceeded to fund the project further.

Friedrich Reinhard, EIR for beLAb2122 in Heidelberg

4. **Think global, act local**
   BRIDGES are intentionally built in defined geographic ecosystems. This allows the EIR to have a local presence and work closely with TTOs and academic scientists on 'repeat encounters' and with ample opportunities to socialize the BRIDGE program and build awareness in the local community. It also allows for on-site meetings with investigators, which can be especially important in both the search and evaluation phase and when building workplans.

   The first thing I did after starting as the LAB282 EIR in early 2017 was to buy a new pair of hiking shoes. It turned out that much of the value seen from any PI's perspective was my offer to come to their office at a convenient time to explain to them the LAB2828 model and then to have an in-depth scientific discussion of their new concept and data.

   Thomas Hanke, EIR for LAB282 in Oxford

   Understanding that the most relevant (and competitive) new discoveries are typically not in the public domain and sometimes not even known to the TTOs (yet), it is our credo that the level of trust built between the EIR and the academic partners is critical for the initiation and sustainability of any new collaborative projects. Break-through discoveries are – by definition – the most fertile substrate for building new drug discovery programs and creating novel compositions of matter with strong intellectual property. Having built a trusted working relationship with the TTO, an EIR is positioned optimally to learn about developments before others.

   As EIR I witnessed how instrumental it is to proactively work with our partner TTOs to focus their search for new opportunities with the potential to be transformed into a discovery and development project. It is really rewarding to feel appreciated for the value brought to the collaboration with the TTOs and having selected projects that were ultimately approved by the Board.

   Antonio Felici, EIR for EXTEND in Italy

5. **Finding and evaluating the 'right' opportunities**
   How do EIR's identify opportunities that are a good fit for competitive drug discovery projects? The process of identifying a promising project generally starts with an initial discussion with a PI to explain the BRIDGE model and to discuss their area of research. This is often followed by rapid consultation involving the TTO to see if the initial idea proposed by the PI has any potential for bona fide drug discovery, i.e. whether it provides a basis to create a theoretical product profile that would fit both unmet medical needs and commercial necessities. This early review is mostly about science – but also about patient needs and populations, competitive positioning, market

trends for a particular therapeutic area, regulatory considerations and a clinical development pathway. BRIDGE EIRs are available to answer many of these difficult questions in the early triage process and make recommendations on the best projects to pursue, often supported by specialists within the wider Evotec organisation.

After an extensive career at Evotec, I thought I had witnessed all concepts and ideas. I was wrong. I realized quickly that a sound understanding of drug discovery alone is necessary but not sufficient. It was reassuring to have a strong pool of therapeutic experts and EIR colleagues backing me up.

Mark Slack, EIR for beLAB1407 in the UK

If the initial idea is deemed promising by the EIR, and there are no encumbrances identified by the TTO, then they will work with the PI to develop a proposal that goes to the BRIDGE steering committee (or other relevant governance structure, e.g. the Board of a Startup Studio) to approve funding. In some BRIDGEs, this takes the form of an initial pre-proposal to confirm fit with the interests of the joint steering committee (JSC), followed by a full-scale application including a detailed and highly collaborative workplan and budget that takes into consideration the respective capabilities and strengths of the academic institutions and Evotec.

Successful positioning of novel opportunities for support can sometimes be achieved by thinking beyond the initial proposed application and working with the PI to make the project more appealing. In EXTEND we received an application about an innovative editing platform applied to rare disease in the CNS space. I discussed with the PI the opportunity of a wider applicability of the platform and a new experimental strategy to treat metabolic diseases, with the promise of a potentially higher return-of-investment.

Antonio Felici, EIR for EXTEND in Italy

Selected projects are generally funded to reach key preclinical value-inflection points with Go/No-go decision criteria built into the project plan. After reaching milestones, projects are typically eligible to be granted additional funding with the aim to prime the opportunity for biotech company formation or partnering.

To date, more than 120 BRIDGE projects have been funded covering numerous therapeutic modalities including small molecules, antibodies, peptides, antisense oligonucleotides (ASOs) and gene therapies. Work packages include target validation (although it is preferred that much of this important gate-keeping knowledge has already been accomplished by the PI and/or is in the public domain), screening and hit identification, medicinal chemistry, antibody development, RNA or cell therapy development, structural biology and/or *in vivo* or *in vitro* validation.

The EIRs must deploy their experience with different therapeutic indications, areas of biology, and drug modalities on a day-by-day basis. However, they are not alone as they are embedded in an extensive network of Evotec experts, and it is the responsibility of the EIR to best leverage this network to optimally build and execute on agreed workplans.

On a recent Tuesday my day included discussions on eight different therapeutic areas including oncology, diabetes (type 1 and 2), obesity, heart failure, kidney disease, two different rare diseases and a delivery platform technology. It involved multiple different modalities including antibodies, small molecules, siRNA, gene therapy, and peptides. Thankfully I was supported in many of these discussions by Evotec experts who I am grateful for every day for providing me and our BRIDGE partners with their advice.

Michael Draper, EIR for LAB eN² in Cambridge, MA

6. Keep the engine running smoothy – EIRs as alliance managers

Finding great science is critical, but equally important is the management of the alliance, where consistent effort is needed to navigate the inevitable ups and downs of stakeholder relationships. BRIDGES by their nature involve multiple parties, including Evotec, the funding parties and usually multiple universities. Each partner – of course – has different needs and points of views on (almost) any scientific, governance or commercial topic.

As discussed already in Chapter 1, EIRs must translate the message between academic scientists and industry experts, who often do not speak the same language and who usually approach problems differently. Being a 'translator' requires understanding the needs and interests of both parties, creatively finding compromise solutions beyond the smallest common denominator, being able to expertly manage relationships with a wide range of personality types and adapting the communication style accordingly. All of this is essential to form one project team working collaboratively towards a successful outcome.

While the governance structure established in a BRIDGE agreement provides a framework for managing some of the arising issues on scope, purpose, operational and governance topics, the contractual framework can only be a starting point. Different views on the type of projects to fund, the interpretation of data, decisions on further funding allocation as well as the regular day-to-day issues of identifying dates and venues for governance meetings are all challenges the EIR faces – and overcomes – routinely.

EIRs also support branding and communications for BRIDGEs and often find themselves responsible for creating both form and content of websites, LinkedIn/social media profiles and press releases. In essence, an EIR needs to be both a 'jack of all trades' and a master of several!

In project and portfolio management, there is an adage that projects are not just about science, but also about people. In other words, projects are far more likely to succeed when they are supported by strong teamwork based on mutual trust and genuine support. This is something that EIRs strive for by working closely with the PI, supporting them during scientific discussions with Evotec therapeutic area experts, helping them during the preparation of materials for JSC presentations and providing transparent and candid feedback at all stages of the process.

As an EIR I am in the great position to be able start projects quickly after they have been approved. I can typically inform the PI about the decision to fund within a couple of days of the JSC, potentially modifying the project based on feedback from this meeting.

Friedrich Reinhard, EIR for beLAB2122 in Heidelberg

7. And then there is 'IP'

Generation and evaluation of IP plays an essential role in each BRIDGE project. This includes IP created by universities and research institutions, third-party IP that they use in their work, and foreground IP created as the result of funded projects. Some of the work at academic institutions is protected by patent applications or granted patents, but other work is no more than laboratory-scale concepts which require further maturation before it can be protected. In many cases EIRs can – together with TTO representatives – help PIs to identify and understand what background IP may be valuable and relevant, especially where this takes the form of know-how, data or other unpatented/non-patentable IP. No matter what form such background IP takes: identifying, reviewing, and securing access to it is of great importance to BRIDGE projects.

Appropriate access to background IP ensures that if an investment is made in a BRIDGE project, there will be freedom to operate (FTO) in the future for the investor, NewCo or pharma partner developing the project further. Defining such background IP is also critical in developing a vision for the IP foundations on which a downstream NewCo will be built, and which will provide a defensible proprietary position.

I find that an important part of my role is helping the PIs and TTO colleagues understand how crucial it is for the investors to be certain that the required background IP is defined in the application and the required rights can flow directly into a NewCo at project end. This can be unfamiliar to PIs who may have more experience in other licensing scenarios.

Stephen Hess, EIR for 65LAB in Singapore

In addition to evaluating background IP, EIRs must manage any new (foreground) IP that is generated as a result of the BRIDGE project work. The EIR thus works closely with the person or department responsible for the protection and management of IP at the academic institution to ensure access to background IP and manage new IP that is developed.

Management of new IP can be a complicated process. Academic investigators need to publish to survive. This is often at odds with the need to protect newly generated IP. Managing both starts from the design of the project with an attempt to ensure that elements of the project deliverables can be published and continues throughout the life of the project and beyond. Once again, the EIR is at the center of all this, working on the early project design and identifying courses of action that meet both academic and investment partner needs.

As an EIR I was working on a project that was in the later stages of investment and involved investigators at two different institutions. The two institutions had worked out the management and ownership details related to background IP. However, shortly before the funding committee meeting, I learned that the two institutions had not established an agreement defining the ownership of new foreground IP. Thankfully, I had a strong working

relationship with both licensing officers at each institution, and we were quickly able to work out a solution to allow the project to move forward.

Michael Draper, EIR for LAB eN² in Cambridge, MA

8. **How do EIRs work with similar functions at partner organizations?**
While the majority of Evotec's BRIDGEs involve an embedded EIR having primary responsibility for sourcing candidate projects from partner institutions, some comprise a separate legal entity with their own management team and individuals responsible for identifying new projects. While these Startup Studios undertake a large part of the typical EIR role in-house, Evotec still assigns EIRs from its Academic Partnerships team as primary liaisons to fulfil other aspects of the role.

   For instance, the EIR/liaison will remain the front door to the wider Evotec organization, enabling the startup studio to benefit from a suite of therapeutic area and modality experts. The EIR will also marshal such experts to support the generation of experimental plans, maximizing the probability of the outputs, aligning with investor expectations, and generally fulfilling the role of Alliance Manager. In short, Evotec's EIRs aim to complement scouting/search-and-evaluation functions at our partners which typically works very smoothly as long as the roles and responsibilities are clearly defined.

   Danube Labs is a BRIDGE partnership between Evotec, Austria-based CEBINA and CEBINA Bridge Capital Ltd. Focused on Central and Eastern Europe, an area that currently has limited academia-derived spinouts, CEBINA sources highly innovative academic projects and works collaboratively and seamlessly with Evotec's EIR and cross-functional teams to develop individualized and state-of-the art workplans designed to translate the early academic projects into drug development opportunities.

   Eszter Nagy, CEO CEBINA

9. **How does an EIR contribute to building a NewCo from a BRIDGE project?**
Let's look into a 'fast-forward-scenario' and assume that a new BRIDGE has started with a competitive and differentiated project, which subsequently has been successfully completed (by managing all sensitivities with everyone at all times) and which is now ready to be advanced towards a business plan and NewCo creation. How will the EIR be involved?

With their detailed knowledge of all project-related scientific, IP and commercial aspects, EIRs will not only be one of the critical sources of information for due diligence for any incoming investor, but – as an Evotec representative – may be on the 'investor side' as well. A prominent example of Evotec having increased their initial stake in a NewCo is the first Oxford University/LAB282 spin-out, a precision oncology company named Dark Blue Therapeutics (darkbluetx.com) which has evolved from a start-up concept into a bona fide biotech company over the last four years with Evotec as an anchor investor. In this example, the former Evotec EIR took on a Board role in the company. For other BRIDGEs, an EIR may well take a senior or C-level position in associated spinouts.

Evotec as a co-founder provided industry standard validation of the science that had been developed within academia. This was critical to attract an experienced drug discovery/development team to the company. The relationships fostered by Thomas Hanke (Evotec's EIR) and the Oxford academics enabled a smooth transition from LAB282. This has evolved into a unique way to work with the academics in the commercial setting, embedding them in the Dark Blue project teams. A 'win-win' for the academics and Dark Blue. Evotec as a shareholder and, critically, as an investor creates alignment with other company stakeholders to drive the company forward focused on value creating milestones.

Alastair McKinnon, CEO Dark Blue Therapeutics

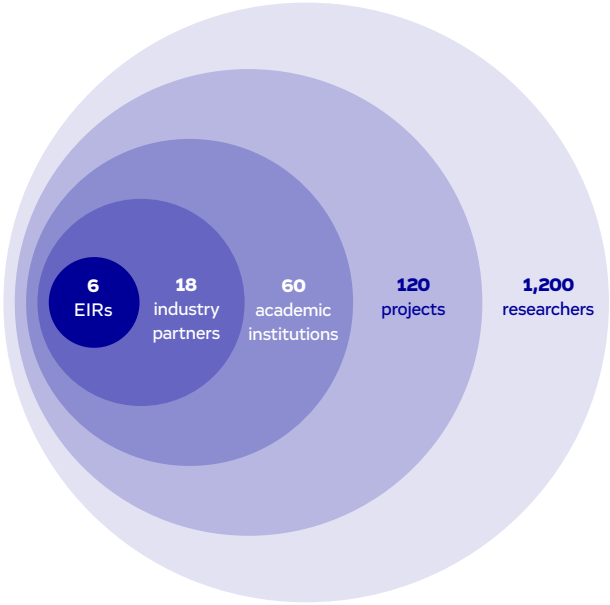

Figure 2: EIRs at the heart of BRIDGEs as a globally leading accelerator initiative

Conclusions: Is it all worth it?
Pre-seed advancement of academic projects is a complex task and EIRs are routinely shouldering their fair amount of weight for this endeavour. While the overall contribution of BRIDGEs to the accelerated creation of sustainable biotech companies at the global level is yet difficult to be quantified, a mid-term resume can already be drawn at this point in time.

Perhaps the simplest way of analyzing the impact of BRIDGEs is looking at the number of partners and advanced projects: In mid-2024, BRIDGE EIRs have worked with over 60 top-tier academic institutions (7 of which are ranked among the top 25 universities globally) and 18 industry partners to advance over 120 first-in-class therapeutic ideas from very early drug discovery projects to stop-go decision points along the drug development value chain. More than 1,200 academic researchers have been engaged (Figure 2). The first spin-out company is close to nominating a clinical candidate.

While a first patient is yet to be treated with a drug candidate from a BRIDGE-supported project, at Evotec we strongly believe that BRIDGEs are enriching the drug discovery ecosystem and helping to bridge the ever-present 'valley of death'.

In October 2022, LAB150 celebrated the addition of Amgen as a pharma partner. A community networking event was kindly hosted by JLABS on top of the University Avenue West Tower in Toronto. Just prior to my presentation, I was approached by a Canadian colleague who candidly commented: 'What you are doing here is heavy lifting'. He was spot-on – but Evotec EIRs are the translational equivalent of Olympic athletes and able to take the strain!

Thomas Hanke, Evotec Head of Academic Partnerships