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Guiding principles of value creation through collaborative innovation in pharmaceutical research

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Open innovation has become the main trend in pharmaceutical research. Potential obstacles and pitfalls of collaborations often lead to missed opportunities and/or poorly executed partnerships. This paper aims to provide a framework that facilitates the execution of successful collaborations. We start by mapping out three checkpoints onto early-stage collaborative partnerships: inception, ignition and implementation. Different value types and value drivers are then laid out for each phase of the partnership. We proceed to propose a ratio-driven approach and a value-adjustment mechanism, enhancing the probability of successes in pharmaceutical research collaborations. These guiding principles combined should help the partners either reach agreement more quickly or move on to the next potential project.

Introduction

The biopharmaceutical industry continues to wrestle with the problem of R&D efficiency: R&D costs [1] are rising even as output [2,3] of new molecular entities has remained relatively flat [4,5]. As a consequence, the pharmaceutical community has continued to deepen its commitment to a more collaborative approach toward R&D, with open innovation [6] models ranging from true pre-competitive consortia [7,8] to more-structured arrangements [9,10] that can address intellectual property (IP) issues. In this paper, we address the latter group, focusing on the specific hurdles that can stand in the way of efficiently starting collaborations between willing parties. Many opportunities for productive collaborations are missed because potential partners often find it difficult to reach an agreement on the values of ideas, methods and prototypes in the drug discovery process. Sometimes, a lack of clarity on key short-to-mid-term metrics or key performance indicators [11] can exacerbate the problem. Finally, disagreement can arise regarding the status of potential therapeutic molecules – one company's hit is often another company's preclinical candidate. Herein, we seek to provide a framework to ease the launch of nascent collaborations, with the goal of reducing the number of missed opportunities for open innovation in pharmaceutical research.

Establishing an innovation-based collaboration is an inherently complex process owing to the dynamic nature, elusive valuation and intrinsic risk of early-stage pharmaceutical research. To illustrate our approach, we briefly describe a classic example that typifies the challenges and opportunities facing such collaborations.

- Company X specializes in antibody hit generation, whereas Company Y bases its business model on proprietary rapid screening technologies for hit identification and lead generation. The initial connection between the parties is made through an industry veteran, and a mutual respect quickly develops. Both teams recognize the crucial need for rapid generation of differentiated leads against novel biological targets and believe that they can create significant synergistic value by combining their proprietary technology platforms. They also recognize that they can more effectively provide services to third parties using the combined

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platforms. However, the discussion on how to collaborate lasts much longer than expected. Conversations become protracted as the partners debate how valuable their technology platform is and how value should be distributed, which party should take the lead in integrating the inputs and how many resources each should contribute. What once seemed like a straightforward partnership now appears like it might not be brought to fruition.

Unfortunately, situations like this hypothetical example occur constantly, whether it is between two small companies, a large pharmaceutical company and a biotechnology company or a university laboratory and a large pharmaceutical company. Our suggestions are designed to help potential partners pull themselves through this period of uncertainties by addressing key questions systematically:

- How can we structure the collaboration discussion?
- How should we recognize the various kinds of values that parties bring to the collaboration?
- How can we distribute values between two or more partners in an efficient manner?
- How do we avoid common pitfalls in the collaboration itself?

Based on our previous experience in the field of biopharmaceutical research, we point out the common mistakes and pitfalls that frequently hamper the execution of innovative collaborations. Quantitatively evaluating and attributing the values generated by partners in an innovative collaboration setting can be a complex process and often constitutes the biggest obstacle for such a collaboration to move forward. Although the respective collaborator's contributed values should ultimately be defined in quantitative terms, in the context of early-stage collaboration involving cutting-edge science or technology we recommend postponing the quantification of value contributions made by parties. This paper outlines guiding principles for value assessment and proposes a ratio-driven approach to circumvent the often-dragged-out discussions of value assignment among parties. We encourage partners to think in terms of ratios and only consider the final value – the exit value – when the collaboration is carried out successfully. The exit value at the point of implementation will be typically determined by more sophisticated capital market players than the initial scientific collaborators.

Four principles to guide collaborative innovation

Principle 1: frame the collaboration in three phases

To provide a clear framework for innovation collaboration, we suggest that the potential collaboration partners frame the collaboration in three phases, each of which is completed with a checkpoint (Fig. 1). Each checkpoint can be viewed as a milestone during the collaboration process, normally accompanied by detailed discussions between the parties, including the construction of workplans to ensure the successful progression of a collaboration. By inserting these key checkpoints into the otherwise complex process, one can lower the threshold for starting the collaboration and map out a clearer path for value generation. Below is the detailed characterization of each phase and checkpoint.

- Phase 1 → inception. The early part of Phase 1 is often marked by a scouting period, during which the two parties meet as part of a random encounter or as the result of a focused search. The potential collaborators come to recognize that they have a project of mutual interest in drug discovery and development. A positive tone often characterizes these early conversations, because the scientists begin to realize that a collaboration could augment the value of their ideas, methods or prototypes, and perhaps even accelerate their R&D. After a confidentiality disclosure agreement (CDA) is put in place, the discussions at inception should focus on material transfer agreements (MTA), pilot experiments and other assessments that might be necessary to increase confidence or provide preliminary proof-of-concept. Some collaborations fail to reach the point

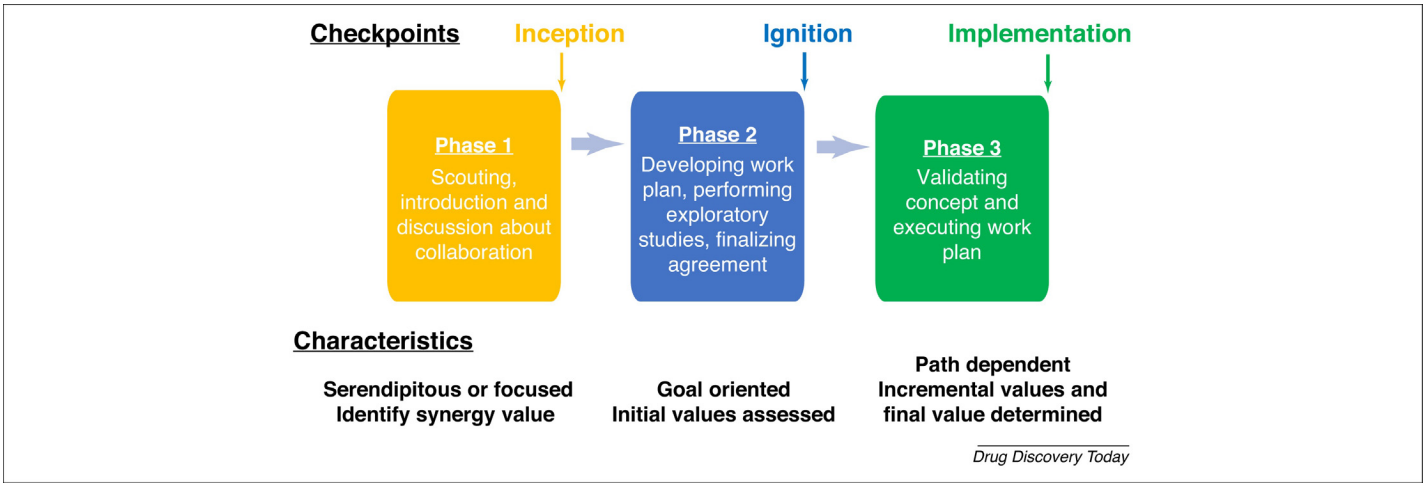

FIGURE 1

Frame the collaboration in three phases with distinct characteristics and three checkpoints. Phase 1: inception. This phase is often marked by a scouting period, during which potential collaborative parties meet as part of a random encounter or as the result of a focused search. The involved parties focus their energies on assessing potential synergies and on the design of crucial experiments. Phase 2: ignition. The main scientific goal for collaborators is to conduct whatever exploratory studies are necessary to properly develop a joint research plan. In parallel, the discussion of value distribution among parties will reach an initial agreement. At the end of Phase 2, the collaboration should have reached the point of 'ignition', at which time a research plan is in place, a collaboration agreement is executed and the parties are ready to launch into a full collaboration. Phase 3: implementation. The primary objective is to implement the research plan and accomplish the collaborative research objectives. Depending on the path and the outcome of the collaboration at this phase, parties can reassess and readjust value distribution to better reflect the initial and incremental contributions made.

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of inception because the parties involved cannot agree on the value distribution of the hypothetical collaborative project in Phase 1. We recommend that the parties instead focus their energies on assessing potential synergies and on the design of crucial experiments. The discussion about value distribution is better suited for Phase 2.

- Phase 2 → ignition. In Phase 2 the main scientific goal for collaborators is to conduct whatever exploratory studies are necessary to properly develop a joint research plan. In parallel, the discussion of value distribution among parties will inevitably take place. Often the discussions about the financial arrangements are cumbersome; in the worst case, they can become contentious. We refer to Principles 2 and 3 (see below) for our perspectives on how to simplify this process and achieve the productive outcome necessary to move the project forward. At the end of Phase 2, the collaboration should have reached the point of 'ignition', at which time a research plan is in place, a contract is signed and the parties are ready to launch into a full collaboration.
- Phase 3 → implementation. The primary objective of Phase 3 is to implement the research plan and accomplish the collaborative research objectives. Depending on the outcome of the collaboration at this phase (Principle 4), it might prove necessary to reassess aspects of the financial or funding arrangements. If the research objectives have been achieved and the initial concept validated, the collaborators will reach the point of implementation. Afterwards, the project should be ready to be implemented in a full industrial setting. Often, only one of the parties takes the leading role after this stage, and it could even be a different party than the one that was leading the collaboration itself.

By dissecting the collaboration efforts into three distinct phases, the discussion is streamlined and can focus the individual participants on the most relevant topics. Importantly, this framework emphasizes getting into a collaborative mode very early on (inception), rather than working through every last detail of the research plan or the commercial terms too early. In our hypothetical example with two biotech startups, the parties went back and forth on the collaboration model and value distribution, thus slowing down negotiations and diminishing the chances of a successful outcome of the collaboration. By breaking the collaboration down into three phases, the discussion will become more productive, because it would be clear what the focus and expectations should be in the next phase (Fig. 1).

Finally, we note that the simplicity of the framework is meant to be enabling and not limiting. For instance, many complicated projects might involve multiple research phases, conducted either before implementation or even in parallel with it (e.g., as an extension of the original work while the lead project is advancing). Even for these more involved projects, the overall framework should still be useful in avoiding missed opportunities. In fact, the need for a streamlined approach based on a clear model with explicit milestones is particularly pronounced in dealing with highly complex partnerships. In such situations, the negotiations can be disentangled and clarified by invoking the current stages and corresponding checkpoint as a reference point.

Principle 2: separate initial contributions from incremental contributions

Once the proposed collaboration is mapped onto three phases and a research plan is at a draft stage, it becomes possible to more readily separate initial contributions from incremental contributions. Figure 2 outlines a hypothetical collaboration between two parties: X and Y. As parties prepare to move the collaboration from inception to ignition, they can characterize the value (V_X and V_Y) that each of them has brought to the project in the form of technical knowhow, IP, novel processes or some drug related assets and resources in any format for further exploration. It might even be possible to define an initial synergistic value (ΔV_{S1}) that arises by virtue of bringing this collection of assets together in a collaborative project [12]. With this evaluation completed, a research plan should be finalized before ignition, one purpose of which is to define what incremental value (ΔV_X and ΔV_Y) each party intends to contribute during the collaboration. The incremental value generated here can be novel IP, scientific and technical knowledge generated from the research plans or the progression of the projects ensuring value enhancement, among other things. Again, if the parties are well-matched, it would be possible to define a shared synergistic value (ΔV_{S2}) generated by working together under the research plans.

In the hypothetical example, one of the initial obstacles is that partners are unable to separate the initial contributions from potential incremental contributions. Indeed, this kind of problem is common, because parties often seek to undertake the task of value distribution too early. If the two parties: X and Y, agree upon the initial value each brings to the table and can project the incremental values that they can contribute going forward, the focus would be generating joint research plans instead of engaging in the lengthy discussion of how quantitative values should be distributed in the end. The shift of focus at the early collaborative stage would ensure greater chances of moving the collaboration forward as well as saving precious time to speed up the real research work, which is often the name of the game in the dynamic pharmaceutical research world. The successful collaboration between Amgen and Kirin on EPO is a revealing example of this. Gordon Binder elaborated on this deal and its underlying philosophy in his book *Science Lessons* (Page 126). According to Binder, the contract specified that 'The division of the cost of the advertising program will be negotiated later', an approach that is a great validation to Principle 2 here.

By separating initial contributions from incremental contributions, we believe that parties will be able to proceed efficiently to assign the value distribution. The early use of an MTA at the end of Phase 1 can help the parties better assess initial value contributions and potential synergistic value before having to commit to a contract (Principle 1); likewise, this practice of 'pre-collaborative experimentation' (Phase 2 in Fig. 1) can also help the parties define how they will each generate incremental value in the collaboration itself.

Principle 3: assign value to the parties using ratios

With the value contribution framework in place, it is possible to define each party's share using simple ratios of initial value and incremental value (Fig. 2). Ratios can be extremely powerful at this stage of partnerships, because the final value V_A will most probably only emerge at the point of implementation, when more-efficient capital market players start to be involved. We recommend that collaborators start the value distribution by applying an even 50:50 split at the start and adjusting in coarse increments. There are three key ratios that need to be considered:

- Ratio of initial value contributions (V_X vs V_Y).
- Ratio of incremental contributions by each party (ΔV_X vs ΔV_Y).
- Ratio of initial value ($V_X + V_Y + \Delta V_{S1}$) to incremental value ($\Delta V_X + \Delta V_Y + \Delta V_{S2}$).

To the extent that these ratios are approximately 1, the 50:50 split will provide an efficient

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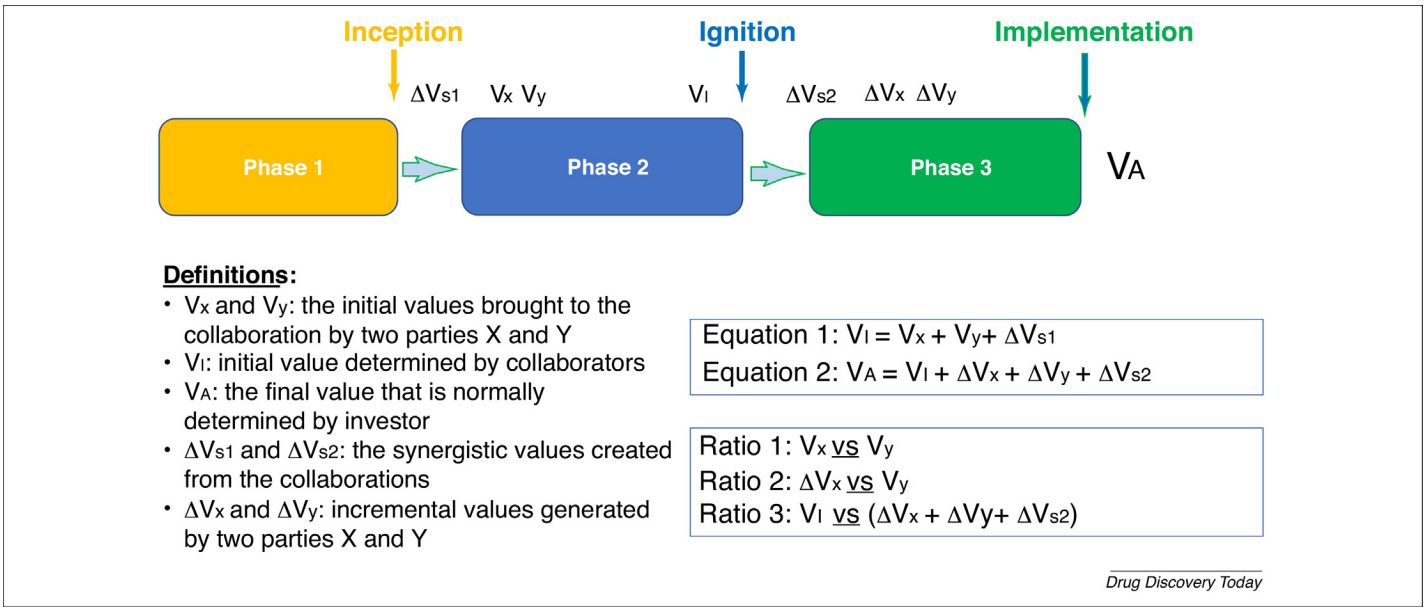

FIGURE 2

The definition of various values and distribution ratio considerations. The relationship of values and ratios can be best illustrated by a hypothetical collaboration between two parties: X and Y. V_X and V_Y are individual values that have each been brought to the project in the form of technical knowhow, intellectual property (IP), novel processes or some drug-related assets and resources in any format for further exploration. An initial synergistic value (ΔV_{S1}) is generated by virtue of bringing this collection of assets together in a collaborative context. Incremental values (ΔV_X and ΔV_Y) are values from new contributions of each party, which could arise from novel IP, scientific and technical knowledge generated from the research plans and the progression of the projects to ensure value enhancement, etc., during the collaboration process. A second synergistic value (ΔV_{S2}) will also be generated during the collaboration phase. The final value V_A will most probably only emerge at the point of implementation, when more-sophisticated capital market players start to be involved. Parties involved should just focus on three key ratios: 1. ratio of initial value contributions (V_X vs V_Y); 2. ratio of incremental contributions by each party (ΔV_X vs ΔV_Y); 3. ratio of initial value ($V_X + V_Y + \Delta V_{S1}$) to incremental value ($\Delta V_X + \Delta V_Y + \Delta V_{S2}$). The ratio-driven valuation approach, as we recommend in this paper, can be extremely powerful for partners to reach agreement fair and quickly.

solution and eliminate months of negotiation. In case the ratios deviate substantially from 1, then coarse adjustments can be introduced if the differences between the contributions from both parties are clear. A similar logic can be applied to the division of terms around control, such as licensing of IP, manufacturing responsibilities and marketing obligations [12]. The final adjustment of value distribution will take place at the implementation stage where the capital market players are involved and incremental values and synergies are better defined.

In our hypothetical example, the potential collaborators would have benefitted from taking a simpler approach to capturing value by, for instance, splitting the potential service income obtained from their combined platforms. Likewise, to the extent that drug candidates are discovered in their own use of the platform, they could agree to split the value of the milestones and potential sales royalties from any licensing deal. Most parties involved in collaboration discussions think of value in dollar terms. However, in any early-stage collaboration, contributions are made in various forms. Some are tangible and some are intangible. Some are easily quantifiable, whereas others are not. For instance, market prices for running a standard, well validated assay are typically tangible value contributions that parties involved can easily discover and agree on. However, the cost of developing a proprietary assay is not that easily quantifiable. It is even more challenging to put price tags on IP and domain knowledge involved in the collaboration, without going through major undertakings involving legal, IP and financial professionals. Forcing the quantification of each type of contributions at an early stage kills many promising collaborations. Our proposed ratio-driven approach will significantly improve the chance of moving the collaboration along to fruition. The authors know of two startup companies that recently adopted this approach. They agreed to a 50:50 split at the completion of lead optimization, with contributions from both sides being roughly equal. Then, one party chaperoned the molecule and completed an investigational new drug (IND) filing package with assistance from the other party. The two parties also agreed that at the IND filing stage that the value split would be adjusted to 70:30.

Principle 4: optimize multifaceted endeavors for improved value creation

Many collaborative innovations involve promising but exploratory science and technologies. Consequently, there is no guarantee that the parties will arrive at the implementation checkpoint with a viable path forward. To maximize the chances for a successful outcome, it is essential that collaborators recognize that all research is path dependent, and opportunities that present themselves during the collaboration can be unique and might need to be seized in that moment. We provide some practical recommendations regarding how to maximize the opportunities for strong value realization.

- In Phases 1 and 2 of the relationship, it is important to make sure that the parties are clear on their own strategies and on how the proposed research collaboration (Phase 3) will help them meet their goals [13]. Thinking about synergistic value is one way to reach that clarity.
- The initial stage of Phase 3 can have a disproportionate impact on the project's success. It is essential to make progress early

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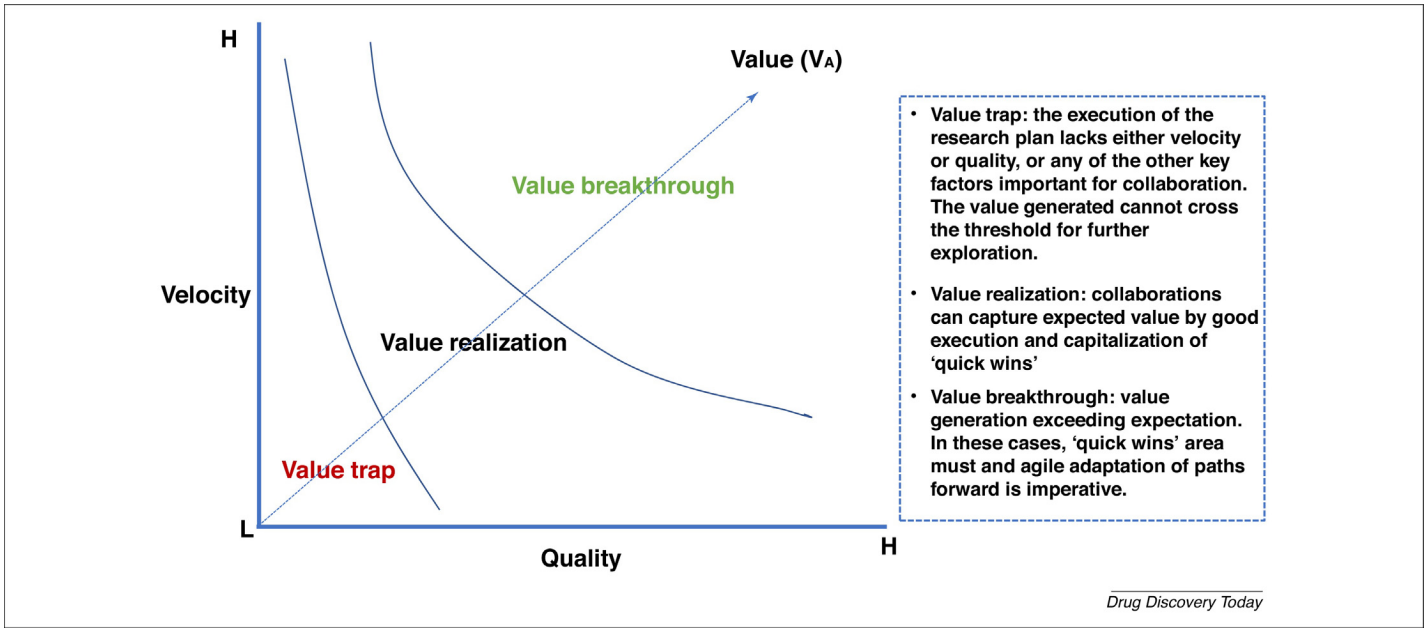

FIGURE 3

Path-dependent value realization and different outcomes. The optimal path in an R&D project is one that maximizes speed and quality. If the project is severely deficient in either of these parameters, the collaboration will end up in a value trap, which means suboptimal value realization. By contrast, if the collaborators fully commit, achieve some 'quick wins' early, perform high-quality research and capitalize on the synergies in their approaches, they will probably be able to breakthrough value realization. The outcome between those two situations is considered normal value realization.

and achieve some validation – the often-cited 'quick wins' – to build trust in the relationship and confidence in the ideas.

- A high-quality research plan can enable faster execution in the collaboration stage (Phase 3). Furthermore, by considering the contingencies in advance, the parties can be better prepared to take advantage of chance observations.
- Even though key scientific decisions will probably be made jointly in Phase 3, most collaborations are likely to benefit if one party is clearly the driver. This party can be compensated with incentives that are either tangible (e.g., financial) or intangible (e.g., first presentation of the work).

Ultimately, the optimal path in an R&D project is one that maximizes speed [14] and quality [15]. If the project is severely deficient in either of these parameters the collaboration will probably achieve only suboptimal value realization, which results in a value trap despite the potential for value realization (Fig. 3). By contrast, if the collaborators execute well, achieve some 'quick wins', perform high-quality research and fully capitalize on the synergies in their approaches, they can achieve disproportionately high-value realization, which can lead to value breakthrough where the collaboration will be viewed as exceptionally successful (Fig. 3).

Concluding remarks

The four principles to guide value generation and distribution in collaborative innovations can be utilized by all participants involved in the initial stages of open innovation drug discovery. Our approach aims to break down some early barriers and facilitate the start of a productive research collaboration. By framing a complex process into three distinct phases with well-defined checkpoints, one can focus on the most important tasks at each stage and ensure that proper milestones are achieved. By mapping out different value components to overall value generation and by establishing some rules of thumb for the valuation mechanism, the collaborating partners can simplify what is often one of the more contentious parts of the process and think about assigning value from a position of mutual understanding. Finally, by considering the path dependency of the collaboration, the parties can avoid common pitfalls and take specific actions that will increase their chances of success.

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