

Acquiring and Partnering Assets: Insights Into BioPharma's Matchmaking

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This presentation is designed to introduce and review various strategies used to conduct asset searches and engage in the partnering process. The insights we share herein are based on completed projects for several of our biopharmaceuticals clients. The content is not intended to support or refute specific approaches or methodologies described by other industry professionals.



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Introduction and Background



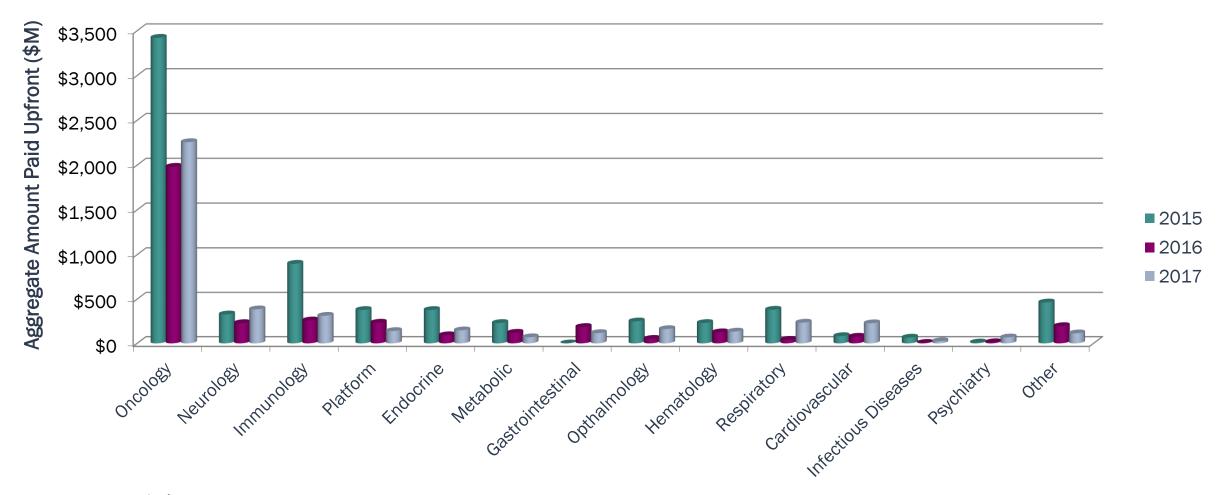
Introduction

- In the past decade the healthcare industry has experienced an unprecedented revolutionary shift in its ability to provide transformative treatments to patients.
 - Areas within cancer are progressively becoming chronic, manageable diseases for which there are an increasingly greater number of targeted and personalized treatment options available.
 - Gene therapy and cell therapy, with a handful of notable approvals, have not only earned their
 place as viable modalities among the traditional small molecules and biologics, but are now
 poised to provide a truly curative rather than symptom-management approach to treating rare
 diseases.
 - Digital health, in the form of wearables and the first approved "digital pill", will enable remote
 monitoring and streamlining of data exchange between physicians, payers and patients to
 improve non-adherence and, thereby, treatment outcomes and disease management, with
 the added hope of reducing the overall cost of treatments.
- The private investment community and public markets have clearly shown their enthusiasm for the
 healthcare industry by providing ample financial backing. This is exemplified by over 12 billion dollars
 invested by venture groups just last year alone and several notable Initial Public Offerings for
 companies whose assets have not even reached the clinical stage proof-of-concept.
- These trends, combined with reductions in internal R&D programs at pharma and continued interest in in-licensing or acquiring potential transformative product candidates, emphasizes the fact that searching for new therapeutic assets and finding partners for their development remains a viable value-creation option for companies with innovative science, a well-defined path from clinic to market and a creative reimbursement strategy.



Assets in development for oncological indications attract the most capital, a trend that has continued in the past three years and which has mostly been driven by therapeutic advances in immuno-oncology

Aggregate Amounts Paid Upfront By Disease (\$M) For Licensing Agreements Executed Between 2015 and 2017



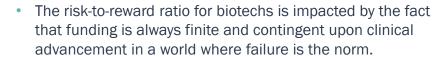


Innovative technologies that give rise to potential novel therapeutic assets are generally the remit of biotechnology companies; late-stage clinical development and commercialization often requires the expertise and market presence of big pharma

Biotech and Pharma – Differing Challenges



 With a few exceptions, most biotechnology companies (aka biotechs) are truly Research and Development (R&D) organizations that have been formed around a platform technology and which focus on asset-specific value construction.



- For a biotech company to become a commercial organization and shift its focus away from R&D/early clinical development to late-stage development and marketing operations constitutes a cultural evolution.
- Those who have made the strategic decision to become a fully integrated biopharma company often focus on commercializing assets in rare diseases, where building a sales force and establishing a relationship with patient advocacy groups can be achieved by a relatively small team.
- Asset partnering therefore continues to be an attractive growth strategy for many biotech companies, especially those with innovative platforms or multi-asset approaches.



- Pharmaceutical companies face several challenges as they consider pipeline expansion, including whether to invest in internal vs external innovation. A program that is brought in from the outside may effectively de-prioritize one that has been pursued internally. An increasing number of pharma organizations invest in their ownfunded external science innovation groups to bridge that gap.
- The majority of late stage assets in big pharma's pipelines are from biotech companies, a clear trend in R&D externalization.

 Additionally, in the past two decades in-licensed programs have delivered almost a two-fold higher rate of return in development versus in-house programs.^{1,2}
- The desire to acquire and develop a blockbuster, multi-billion dollar pharmaceutical is no longer realistic. The goal now is to become either "best in class", or "only in class" while meeting strategic corporate objectives and continuing to bring value to shareholders.
- In recent years it has become obvious that the healthcare system is moving towards a patient-centric, value-based approach with large commercial organizations, like big pharma, experiencing increasing pressure from regulators, payers, providers and patients.
- It is thus pertinent to select and then develop a product that has the biggest potential to address these challenges with the cleanest path to market.



Biotech usually consider three different options when licensing out their assets or platform technologies; options 1 and 2 are most likely, as is a hybrid approach that includes both 1 and 2

Typical Value Creation Business Development Models for Biotech Companies

	Scenarios	Pros	Cons	
1	 License out technology platform A biotech company licenses its platform technology to biopharma; the agreement may or may not include additional R&D services. Biopharma partner commits resources to identify, clinically develop and commercialize assets designed with that technology platform as future pharmaceutical products. 	 Low risk option when financial resources are limited Provides validation needed to raise additional funds Milestone payments and small future royalties on sales may still apply and provide much needed cash 	 Loss of control over the technology platform Selling before value of the platform is fully recognized 	
2	 License out preclinical through clinical proof of concept (POC) assets A biotech company uses its proprietary platform technology to develop assets (small molecules, proteins, antibodies and other modalities) Upon achieving a reasonable development milestone, or POC, the asset or a portfolio of assets is then exclusively licensed out to a biopharma company, who will develop it into a pharmaceutical product and take on the regulatory, commercial and marketing responsibilities. 	 Higher return on investment, as upfront payment alone may enable recovery of funds invested in development Should the asset become a successful product, additional commercial-stage milestones, payments and/or royalties will be due 	 Longer time horizon than technology licensing; exposure to a greater level of risk, which can be mitigated by a codevelopment or co-marketing arrangements Reasonable commercial efforts need to be enforced with the partner. Joint steering committee and alliance management become a necessity 	
3	 Develop and commercialize internally-developed or acquired assets A biotech company creates their own pharmaceutical assets and then subsequently becomes a fully-integrated biopharma company by developing and commercializing these assets. 	Attractive model when substantial investor backing exists, or when there is a well-established revenue stream from previously successful technology partnering or asset out-licensing	Financial burden and risk exposure is greater than for the other two options, but can be mitigated by co-development or co-marketing arrangements	



Selling Assets and Finding Partners

Most "buyers" (especially pharma) are flooded with incoming requests, reviewing several hundred opportunities annually. Prioritization thus becomes paramount.

For the "seller" (many biotech companies) it is important to understand the data and process requirements of a potential partner, how their existing pipeline can be complemented, and whether they are active in deal-making. It is also key to have the internal strategy defined for taking the asset out. Is straight out-license of rights for all territories and therapeutic applications desirable or would a co-development agreement make more sense perhaps because of internal expertise that resides within the seller organization?

To attract potential buyers, the asset's information package has to meet certain threshold criteria in order to engage a partner in that first phone call or in-person meeting.

During the initial asset assessment stages, the key characteristics that a potential partner looks for are: compelling animal data in a model that closely recapitulates human disease state, human tissue or genetic, as well as transcription expression-related data that could drive biomarker selection strategy down the development road, and differentiation from the standard of care should a program move forward successfully in the clinic

It is expected that a licensor (seller) will be able to answer the following fundamental questions:

- Is my company offering disruptive technology or platform?
- Is the biology novel? What is the biological mechanism of action and rationale?
- What is the unmet medical need? What are the current treatment options and how satisfied is the target patient population with the current treatment?
- What benefits does the asset provide?
- ➤ How does it stack up against the competition (efficacy, safety, dosing, and cost)?
- What is the future potential target audience or customer for this product?
- Even if at early stage of development, can an insight be offered into clinical development, commercial strategy and payers' perspectives?

In our experience, the fastest way to derail any partnering discussions is to use poor animal models to demonstrate preclinical proof of principle, clinical endpoints that simply are not well thought out, patient populations that are poorly defined and selected for a trial, lack of intellectual property strategy or protection, or a lack of understanding of the competitive landscape and grandiose, unsupported claims of future market potential.



Checklist of Due Diligence Items





Seller Background & Biological Rationale

Key Information Category	List of Items
Company and Asset Background Bluestar BioAdvisors works with clients to craft their stories by creating and modifying slide presentations, teasers and a TPP	□ Corporate background (non-confidential and confidential presentations) □ Funds raised and their source(s) □ Management's experience and expertise □ Platform technology □ Candidate/Program □ When was program initiated? □ Where there any previous owners? □ Was the asset acquired or built organically? □ Developmental stage of the asset □ Target product profile (TPP)
Bluestar BioAdvisors, by interviewing various stakeholders, assesses the strength of preclinical/clinical (if applicable) data in the context of competitive landscape and future market potential	 □ Pedigree (lead asset and follow-on or back-up molecules) □ Mechanism of action and data supporting target engagement in a model of disease □ Physicochemical properties (solubility and stability) □ Bio-distribution and pharmacokinetics □ Toxicology (GLP and non-GLP) □ Unmet medical need □ Primary disease target □ Potential secondary disease target





Intellectual Property, Competitive Landscape & Market Data

Key Information Category	List of Items
Intellectual Property	 □ Patents and patent applications in key geographies (composition of matter, methods and use) □ Freedom to operate analysis □ Trademarks □ Copyrights and design rights □ Exclusivity/third party involvement (if any) □ Know-how; trade secrets
Market, Industry and Competitive Landscape Bluestar BioAdvisors analyzes competitive landscapes, conducts market assessment studies utilizing primary and secondary research to assist clients in addressing market potential for their assets, and provides insights into asset positioning with investors and partners	□ Competitive landscape □ Description of markets and estimated market size □ Market needs □ Comparison to Standard of Care □ Product form [e.g.: NCE, NBE, 505(b)2] □ Post-marketing requirements □ Life cycle management strategy





Clinical evidence & CMC

Key Information Category	List of Items	
Clinical Evidence, Development Plan Bluestar BioAdvisors, by interviewing various stakeholders, assesses the strength of clinical data in addressing the unmet medical need, potential to impact standard of care, as well as the future potential for reimbursement	□ Clinical trial design □ Primary and secondary endpoints □ Proposed differentiation from placebo or comparator □ Size of the population/trial □ Patient enrollment rate – length of the trial □ Clinical data □ Efficacy, safety □ Biomarkers, companion diagnostic, if relevant	
Chemistry, Manufacturing and Controls (CMC)	□ Data on synthesis, scalability and batch-to-batch consistency □ Analytical methods □ Manufacturing strategy and future plans □ Drug substance and Drug product suppliers □ Final product formulation	





Pricing, Reimbursement & Financial Analysis

Key Information Category	List of Items
Pricing and Reimbursement Bluestar BioAdvisors, by interviewing payers, hospital administrators and other relevant stakeholders, evaluates the future potential for pricing and reimbursement	 □ Correspondence with regulatory agencies □ Regulatory incentives, if any (e.g.: orphan designation, fast track, breakthrough designation, various vouchers, tax credits) □ Real World Evidence study requirements, if appropriate □ Risk Evaluation and Mitigation Strategy program, if appropriate □ Timing of Phase IV, if any □ Pricing/Profit Margin Royalty □ Health economics data
Financial Analysis Bluestar BioAdvisors conducts financial valuations (epidemiology - or prescription-based models), as well as comparable company, product, and transaction analyses	 □ Revenue projections or Sales forecast □ NPV or rNPV □ Investment to POC □ Investment to Market □ Third party support opportunities □ Alternatives to Partnering □ Cost of marketing post approval



Asset Search and Partnering Process



Searching for Assets

- Biopharma companies search for assets for a number of reasons, including:
 - To provide growth opportunities and pipeline de-risking
 - To complement current pipeline or product offering
 - To establish presence in an adjacency or to shift focus to a new product area
 - To gain a commercial footprint in a new geography
 - To ensure that they remain active in the marketplace and not miss out on an opportunity



- The process of in-licensing is often tedious and time consuming, thereby making it difficult for internal teams to run a comprehensive screen. Many business development executives take on a multi-faceted approach to maximize that process by increasing the chances of successfully identifying an asset to in-license and close on a transaction
 - Attend "Bio" conferences to meet with as many relevant asset holders as possible
 - Send inquiries to colleagues in the industry
 - Include internal departments (e.g., R&D teams) in the business development and licensing process
 - Update the BD/Partnering section of the website or send out fliers/marketing materials describing in-licensing business development strategy
 - Use select social media (e.g., LinkedIn)
 - Respond to in-coming queries and requests for evaluation
 - Work with consulting firms to systematically screen and analyze potential assets of interest



The systematic approach for finding and screening assets requires a multi-phased approach that allows for a customized, iterative search process

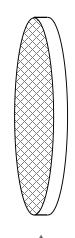
Search and Evaluation Process Flow

Identification and Characterization of Initial Candidates

- Refine selection criteria
- Screen various sources to uncover the universe of relevant assets
- Generate a unique and searchable "database" highlighting key product attributes in line with specific criteria

Prioritization Based on Assessment of Fit with Company

- Agree on prioritization metrics and process
- Conduct preliminary assessment of fit and prioritize assets
- Create brief profiles of high priority assets



Workshop to Select Assets for Further Analysis 3

Deeper Analysis of Prioritized Assets

- Conduct a deeper evaluation of commercial rationale and strategic fit of select assets
- Identify key risks and opportunities

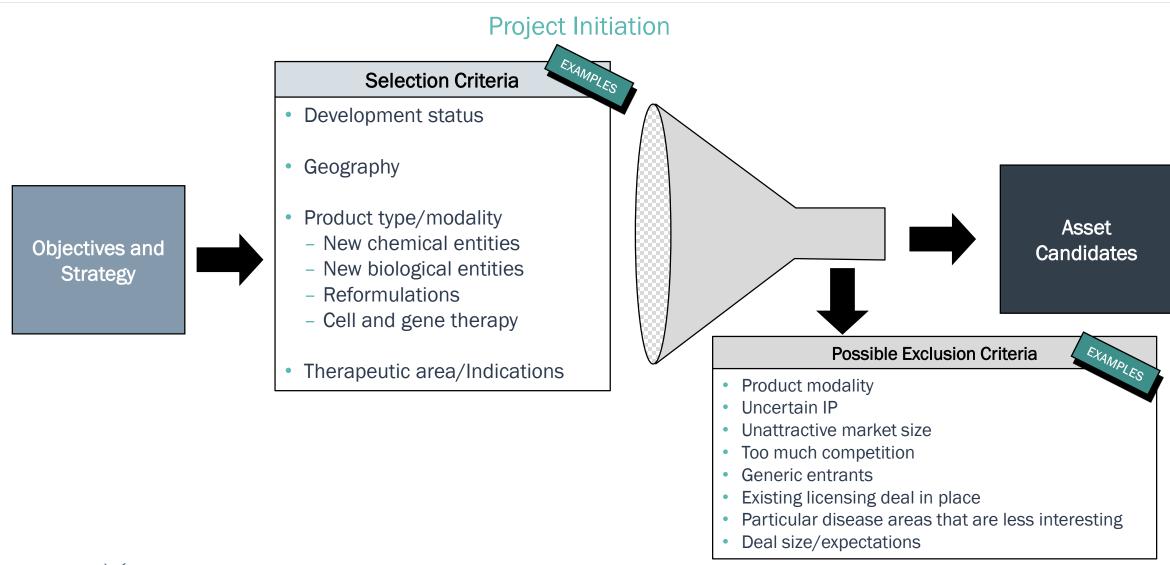


Early-Stage Business
Development

 Contact asset holders to gauge their level of interest in preliminary business development discussions



There are several key strategic issues that influence the search and define specific asset selection criteria





The output from the searches is used to develop a comprehensive list of assets that highlights their key attributes

Asset Database

Sources:

- External and proprietary databases
- Market and industry reports
- Company presentations
- Conference attendance

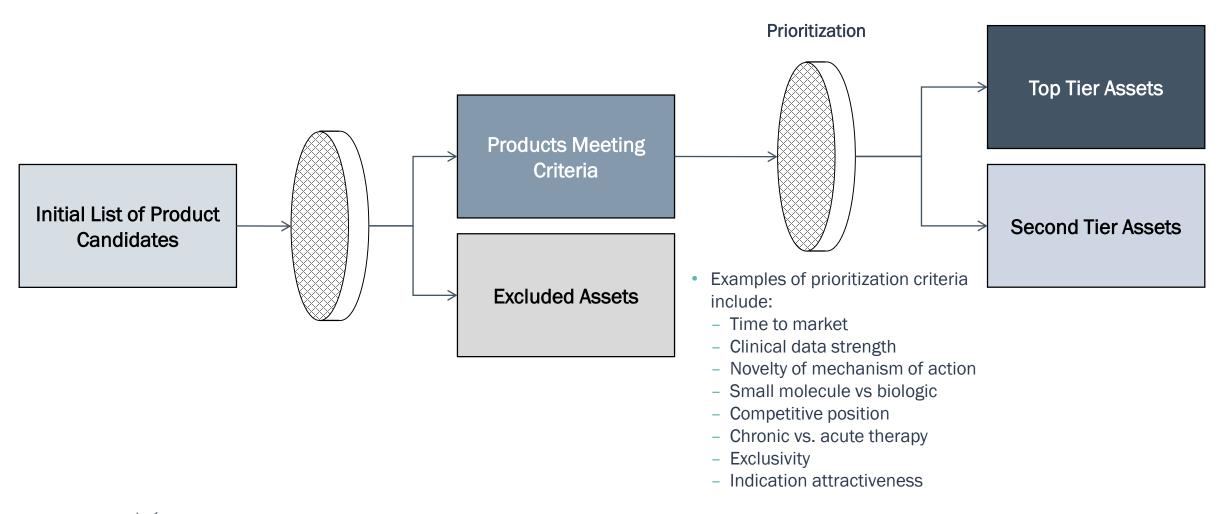


Product Name	Indication	Company Name	Dev. Status	Mechanism of Action	Route of Admin.	Clinical Data Highlights	Licensing/ Transaction History	Comments



From the asset list, we apply a set of prioritization criteria, agreed upon with our clients, to identify high priority assets

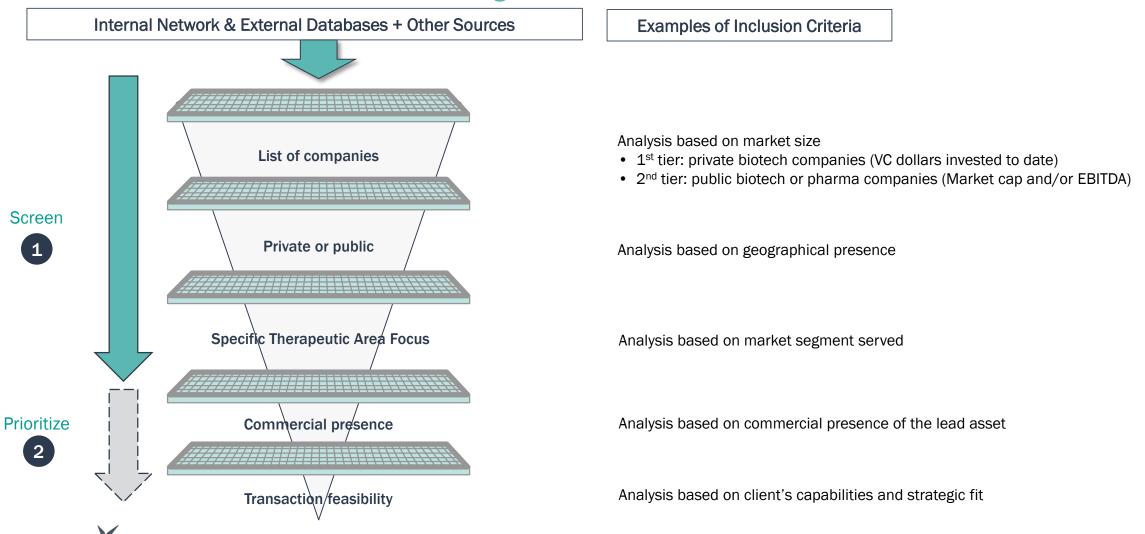
Key Activities





A similar approach used to search for assets can be applied to identify and screen for companies, as M&A or investment targets

Screening and Inclusion Criteria



If assets are identified for further analysis, we can conduct additional research to develop a deeper understanding of the opportunities and risks

Profile for Deeper Dive Candidates

Opportunity	 Size of the relevant patient population Disease severity and magnitude of unmet need Ability to address the unmet need Relevant stakeholders/likely prescribers Competitive intensity 	Rationale for Attractiveness
Risks	 Validity of the mechanism of action Stage of development Size and length of trials Modality of the asset (e.g., biologic, small molecule, stem cells, gene therapy, etc.) Likelihood of availability for licensing 	of the Opportunity

Depending on the number of assets being researched, we seek perspective of experts to gauge potential of the assets to satisfy unmet needs among the relevant patient population and to further assess commercial attractiveness



The final phases of asset or company search analyses may include creation of in-depth profiles and outreach to target companies to gauge their interest in preliminary business development discussions

Detailed Company Profile Objectives

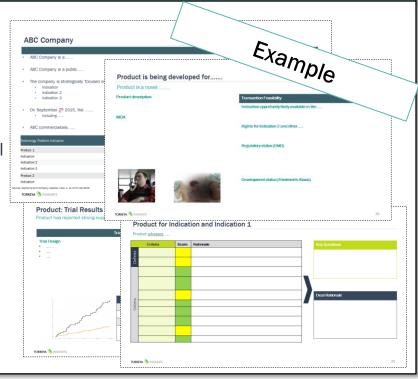
- The expanded profiles capture detailed information about the targeted companies and further evaluate the current state of their operations.
- The intent is to determine whether the candidate company is an attractive partner and constitutes a logical fit for client based on the prioritization criteria and commercial portfolio.

Key Items

- Executive management
- Board of directors
- Financial summary (as available):
 - Current price
 - Market cap
 - Cash
 - Debt
 - Enterprise value
- Company pipeline
- Clinical development highlights
- Clinical trial plans
- Regulatory interaction
- Indication epidemiology
- Commercial portfolio overview
- Product descriptions
- Competitors

Key Output

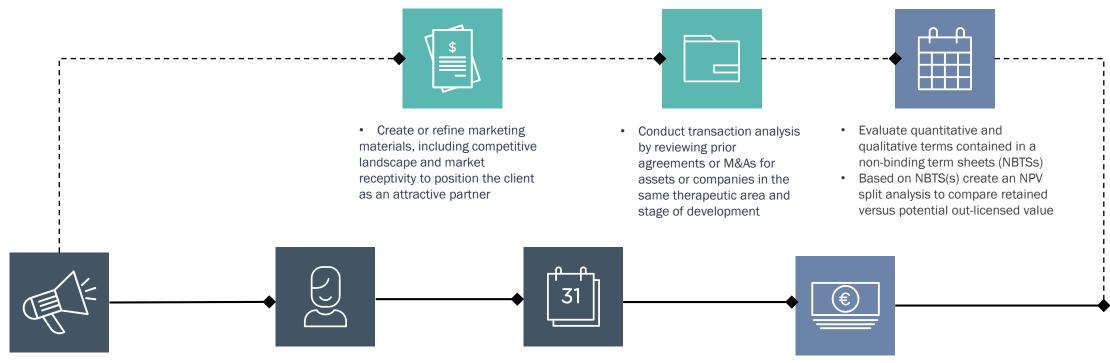
- Detailed company overview and strategy
- Financial overview and measure of transaction feasibility
- Stock price volatility based on experienced events and inflection points (for public companies)
- Clinical development highlights and planned clinical trial structure
- Evaluation of the commercial portfolio with sales and prescription data
- Market and epidemiology outlook in targeted indications
- Analysis of relevant competitors
- Scoring scale to measure how well the opportunity fits Client's prioritization criteria





We can serve as a catalyst in preliminary business development discussions

Partnering Outreach Workflow



- Review any prior interactions and contact key stakeholders (usually BD executives, chairmen or CEOs), initially in a double-blinded fashion
- Create a "live" tracking database of all contacts and outcome of interactions with prospective parties
- Assist in the execution of CDAs and manage meetings with client organization either in person or telephonically
- Manage the process and advise the client on the best strategy to undertake in these early stages of business development discussions
- Should a client require assistance with deal execution, the Bluestar team may transition the project to a business partner who will negotiate and close a transaction on client's behalf
- We may continue to serve as a partner and provide additional analyses, as needed



4

Based on discussions and reviews, we monitor our client's feedback and record prioritization decisions throughout the search process

Reason for Rejection

Company	Asset	Portfolio Fit	Territory/ Infrastructure	Not for Sale	Comment
A	1		✓	✓	Not for sale, too big, no added infrastructure
В	2				Previously reviewed and rejected
С	3		✓		More of a CMO than Pharma marketing company
D	4		✓		Previously reviewed, no presence in key geographies
Е	5	✓			No interest, not in therapeutic area
F	6		✓		Previously reviewed, declined (noted growing French and German footprint. Potentially one to review)
G	7	✓			Failed due diligence

The database lists all potential opportunities in a concise manner, allowing the client to review at any time during the process and in future discussions, both internally and externally.



Case Studies



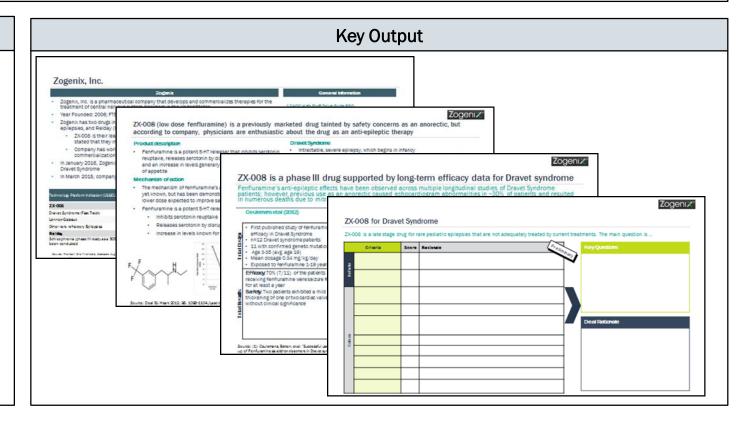
Case Study 1: Conducted an asset search for business development opportunities for a company seeking to expand its rare disease portfolio

Project Background and Objectives

- U.S.-based pharmaceutical company anticipating the launch of a new rare disease product was seeking to add to its portfolio through licensing or acquisition opportunities
- Bluestar team was hired to apply criteria to a search for compelling opportunities, profile attractive assets, and determine which assets were worthy of further analysis

Key Activities

- Bluestar supported the client's business development team for 6 months and conducted bi-weekly calls presenting new ideas to the team
- Asset profiles included company overviews, disease and patient population background, product highlights (e.g., mechanism of action, clinical data, points of differentiation), and fit with the client's criteria
- At project completion, the client team provided feedback that Bluestar was able to provide new ideas that they themselves had yet to find, offered new ways to consider opportunities that the client might have previously disregarded, and provided updates for assets that the client was monitoring





Case Study 2: Engaged in business development support for a biopharma company developing an asset in Inflammatory Bowel Disease

Project Background and Objectives

- Assisted a small biopharmaceutical company, developing an NCE with a novel mechanism of action for the treatment of Inflammatory Bowel
 Disease, through an out-licensing transaction process
- The licensing process began with preparation of the marketing materials, identification of interested parties, and partnering outreach

Key Activities

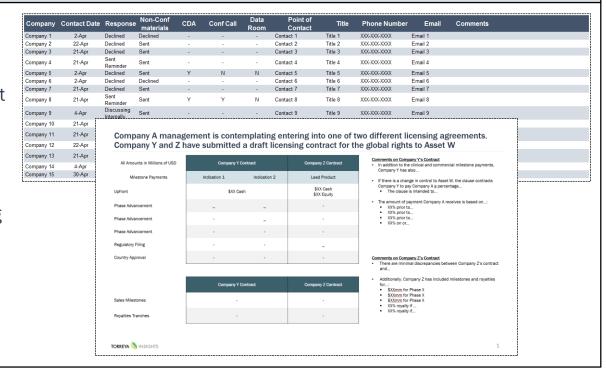
- Preparation of Partnership Materials
 - Created non-confidential and confidential information memorandum
 - Identified potential strategic partners with an existing therapeutic portfolio
- Partnership Outreach
 - Supported the outreach to target organizations
 - Tracked communications among all parties
- Transaction Negotiation
 - Evaluated quantitative and qualitative terms and provided support in negotiations

Non-confidential and confidential information

memoranda

- Organized tracking sheet of each team members communication with interested parties
- Analysis of each competing bid, including "NPV split" analysis based on a DCF

Key Output





About Bluestar BioAdvisors



About Bluestar BioAdvisors



- We assist clients in answering key strategic questions about asset value, positioning, and future market potential.
- We also serve as an independent, objective advisor, guiding our clients through the critical decision-making points of portfolio planning and business development activities.
- Our clients range from startups to major multinationals. They may be seeking to:
 - Better understand how to optimally develop and position products to meet the needs of the market
 - Gain an independent perspective on how to prioritize investments or develop product/therapeutic area strategies
 - Obtain assistance with identifying and characterizing new licensing or acquisition opportunities
- Our services focus on market and product assessments, commercial diligence, forecasting/NPV analysis, product positioning, competitive landscape analysis, asset search and evaluation, and therapeutic area/indication prioritization and strategy.



Bluestar BioAdvisors frequently supports companies through the process of identifying and assessing potential asset acquisitions or in-licensing opportunities



Asset Search and Evaluation

- Develop set of search inclusion/exclusion criteria
- Identify and characterize relevant assets that fit clients' criteria
- Generate searchable database of asset opportunities highlighting key attributes
- Collaborate with clients to define prioritization criteria
- Prioritize assets and develop profiles outlining opportunities and risks of high-interest targets



Market Assessments

- Evaluate the commercial market potential of asset(s)
- Conduct extensive secondary research to assess the treatment dynamics, competitive landscape, including development stage assets
- Perform qualitative and/or quantitative research with key stakeholders to evaluate market dynamics that will impact adoption and to test a target product profile
- Assessments are utilized to make go/no-go decisions or serve as the foundation for detailed analyses within a diligence process



Forecasting

- Create revenue forecasts with detailed assumptions, including, but not limited to:
 - Addressable patient population(s)
 - Market share and speed of adoption
 - Duration and frequency of treatment
 - Pricing and reimbursement
 - Competition
- Conduct NPV analyses, including sensitivity analyses
- Analyze non-binding terms sheets to provide insight into negotiation strategy and tactics



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