Introduction to Lumanity

October 11, 2022

Lumanity

Biographies

Lumanity

Lumanity BioConsulting

Project Team

Jennifer McCann, PhD

Associate Consultant

Jennifer.mccann@lumanity.com

Jennifer is a life science strategy consultant who joined Lumanity BioConsulting following her Postdoctoral Research at Howard Hughes Medical Institute. She has a strong background in molecular biology, oncology, gene therapy and genome engineering technologies.

Prior to joining Lumanity BioConsulting, Jennifer served as a Research Associate for Howard Hughes Medical Institute where she led collaborations with national and international laboratories on mechanisms of mutational burden in various cancer types. Her research has resulted in numerous high-impact publications, awards and multi-million-dollar funding opportunities.

Jennifer earned her PhD in Microbiology, Immunology and Cancer Biology from the University of Minnesota, where she focused on protein regulation through proteomics research tactics in addition to patenting a novel approach to single-base editing genome engineering technology. While in graduate school, Jennifer also gained experience consulting by serving as a Project Manager for two Minneapolis-based companies. Prior to graduate school, Jennifer studied virology at UTSW Medical Center for several years post undergraduate (B.S. in Biology at the University of Utah).

At Lumanity BioConsulting, Jennifer focuses on leveraging her scientific background to both inform and support clientele regarding potential opportunities in the commercial space of biotechnology and healthcare.

Lumanity BioConsulting

Project Team

Jill Luttman, PhD

Associate Consultant

jillian.luttman@lumanity.com

Jill is an Associate Consultant at Lumanity BioConsulting with research experience in subject areas ranging from oncology, developmental biology, respiratory disease, and autoimmune & inflammatory disease. At LBC, she combines her scientific background and passion for drug development to help clients develop strategies to succeed.

Prior to joining LBC, Jill worked as a Precision Medicine scientist at xCures developing treatment options for a wide array of cancer patients through the identification of SOC, off-label, expanded access, or clinical trial options available for each disease type. Additionally, she conducted research on real-world patient data to identify emerging treatment paradigms improving patient outcomes.

Jill earned her PhD from the Department of Pharmacology and Cancer Biology at Duke University. Her research characterized tyrosine kinase signaling networks facilitating metabolic changes during metastatic disease progression in solid tumors. Her work resulted in the filing of 2 patents, the receival of an NSF Graduate Research Fellowship, presentation at conferences, and scientific publications. During graduate school, she interned at Altavant Sciences, a clinical-stage biopharmaceutical company specializing in severe respiratory diseases.

Before graduate school, Jill earned her BS in Biological Sciences from North Carolina State University where she spent two years working in a developmental biology lab studying gene regulatory networks involved in organogenesis.

Introduction to Lumanity

Lumanity

Incisive thinking, decisive action

We improve patient health by accelerating and optimizing access to medical advances

A foundation for growth

Lumanity was formed from companies with similar ambitions to cut through complex situations and deliver transformative outcomes

Lumanity

CELLO HEALTH	Business analytics, scientific and commercial advisory, and communications
BresMed™	Health economics and payer and HTA submissions
guidemark HEALTH	Marketing and medical education communications
CYANHEALTH ACCESS POTENTIAL	Payer strategy and payer marketing
ZIPHER MEDICAL AFFAIRS, LLC Translating Insights into Action	Medical affairs strategic consulting, and MSL optimization services

A global, diverse team of deeply experienced industry pioneers, subject matter experts, and proven problem-solvers

1200+
STAFF

WORK CONDUCTED IN
50+
COUNTRIES

North America
Washington D.C.
Marion, MA
Las Vegas, NV
Parsippany, NJ
Montclair, NJ
Yardley, PA

Europe
London
Edinburgh
Farnham
Manchester
Sheffield
Berlin
Utrecht

Team members in several other US cities and EU countries

Asia
New Delhi

Deep expertise across our uniquely blended teams…

200+
MARKET RESEARCHERS
Master practitioners, digital specialists, innovation leads, field, and compliance

350+
COMMS SPECIALISTS, SCIENTISTS & CREATIVES
Including client service, project managers, and medical writers

130+
CONSULTANTS
With a blend of industry experts and consulting specialists

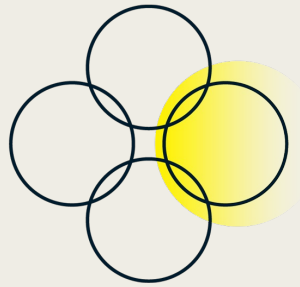
200+
HEOR SCIENTISTS & MARKET ACCESS STRATEGISTS
Offering HEOR and market access solutions

150+ CREDENTIALED SCIENTISTS | **PhDs, PharmDs and MDs providing a depth of understanding into cutting edge science**

… supporting a range of clients

PARTNERING WITH
24
of the top 25 global pharma companies

SUPPORTING
100+
small, start-ups, and emerging biotechs



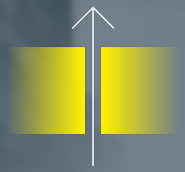
Lumanity

Our solutions

A differentiated set of connected capabilities to accelerate and optimize access to medical advances

Asset optimization & commercialization

Guiding robust pharmaceutical commercial decision making, uncovering real-world insights from innovation through development to commercialization and beyond

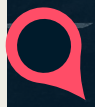


Value, access & outcomes

Uncovering the full potential of your products and demonstrating their value and effectiveness to stakeholders around the world

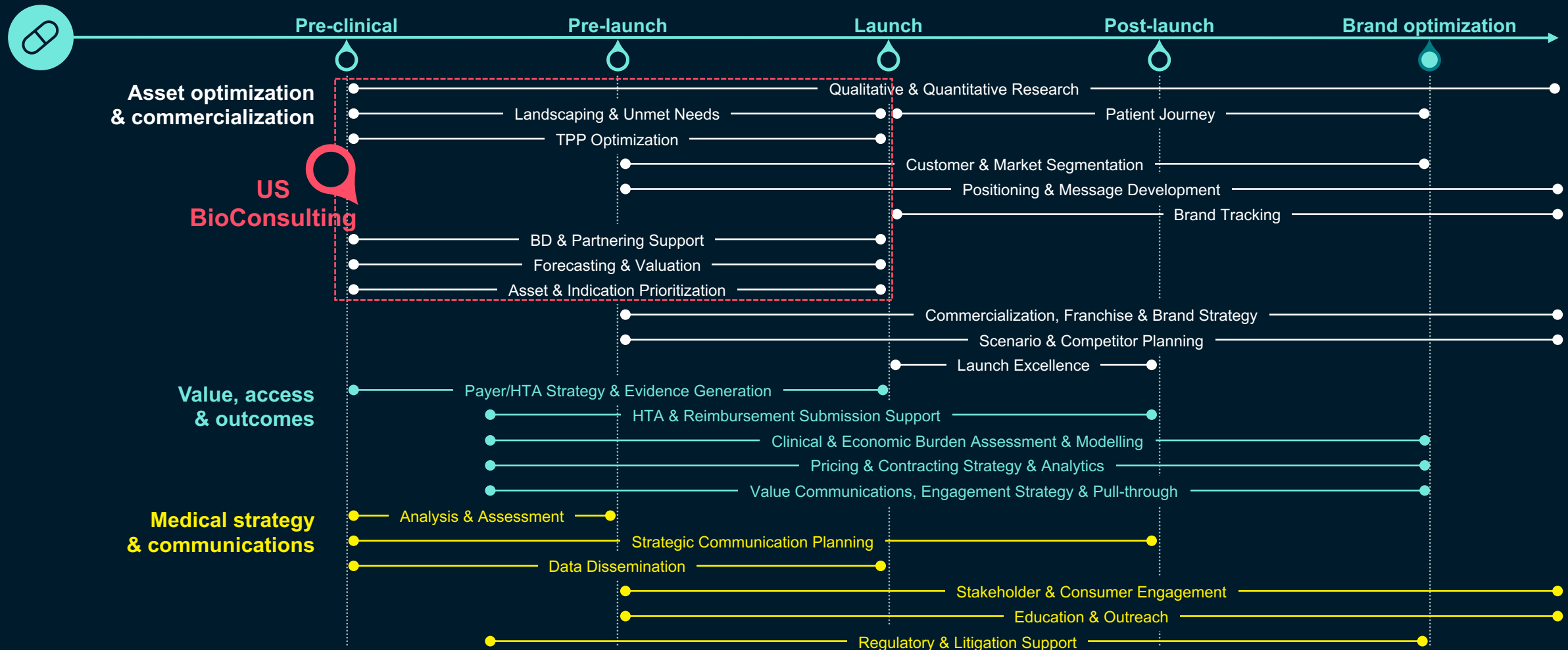
Medical strategy & communications

Effectively articulating your scientific breakthrough to enable healthcare providers, regulators, payers, and patients to understand and unlock the value of your product



This is where US BioConsulting falls in the Lumanity capabilities!

Capabilities across the product lifecycle



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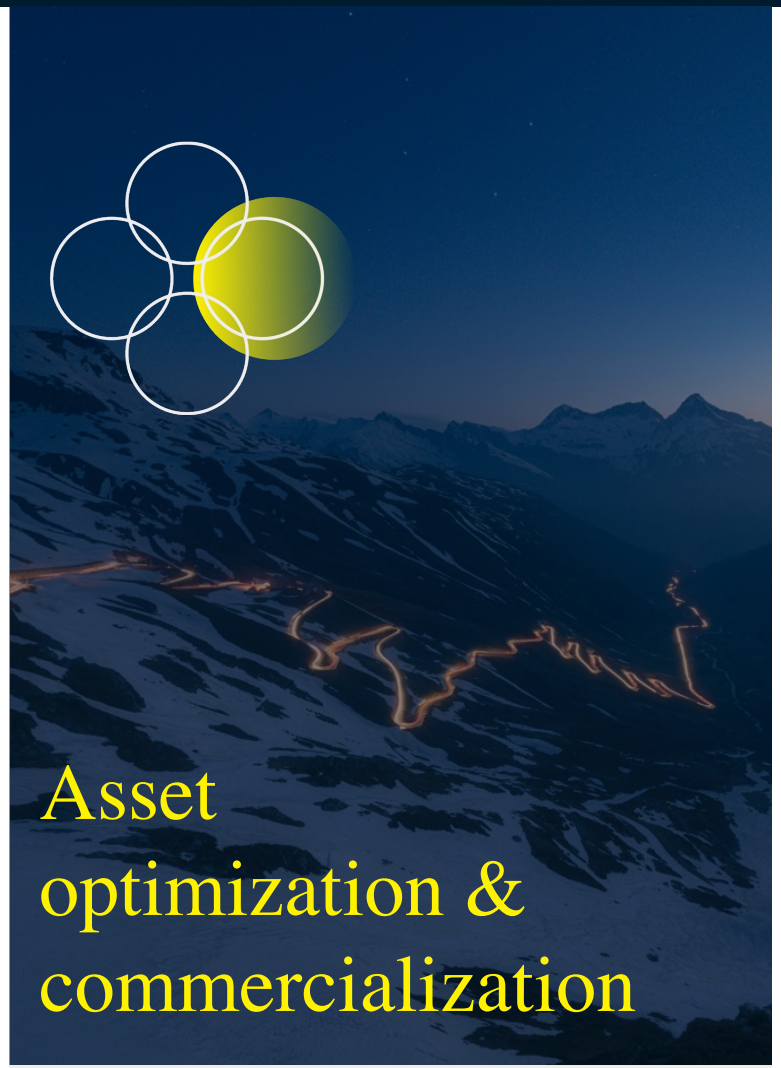

Asset optimization & commercialization

Guide confident and robust commercial decision-making

Assess the Scientific and Commercial Landscape

Pulling on our extensive understanding of the **scientific and commercial landscape,** underpinned by robust data analysis, we ground your decision making in the most appropriate future context and help craft your **acquisition and commercial development strategies**

Understand Key Stakeholder Needs, Drivers, and Behaviors

We help ensure the voice of patients, caregivers, HCPs, and payers is at the heart of your strategy. Conducting unmet needs assessments, patient pathways, social media listening, and more, we use behavioral science techniques to help you **understand what drives behaviors** and how to **change them towards better outcomes**

Develop and Implement a Winning Commercial Strategy

By providing **insight-driven strategy** we help you make choices that maximize opportunities, mitigate risk and drive innovation, differentiation, and value. In addition to positioning your product for market success through indication prioritization, forecasting, and corporate and commercialization strategies, we have **innovative launch technologies** and **expert support globally** to bring you across the finish line

Lumanity US BioConsulting Core Services

- **Opportunity Assessments**
- **Opportunity Search & Evaluation**
- **Portfolio and Platform Strategy**
- **Corporate and Partnering Strategy**

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Lumanity US BioConsulting Core Services

Opportunity Assessments

- Assess commercial value in markets of interest
- Evaluate mechanistic approach and scientific rationale
- Position and differentiation from evolving SoC
- Define target patient populations, clinical endpoints and target product profiles
- Determine payer perspective

Opportunity Search & Evaluation

- Establish criteria for identifying programs that fit with strategy
- Identify assets and/or companies that best match criteria
- Work with our client to prioritize opportunities
- Provide deeper analysis of priority targets
- Identify value inflection points to optimize partnering strategy

Portfolio and Platform Strategy

- Analyze and prioritize pipeline portfolio
- Identify and assess novel indications for development
- Prioritize and sequence potential indications
- Define value inflection strategy for clinical candidates
- Advise on optimal time and stage of development for partnering

Corporate & Partnering Strategy

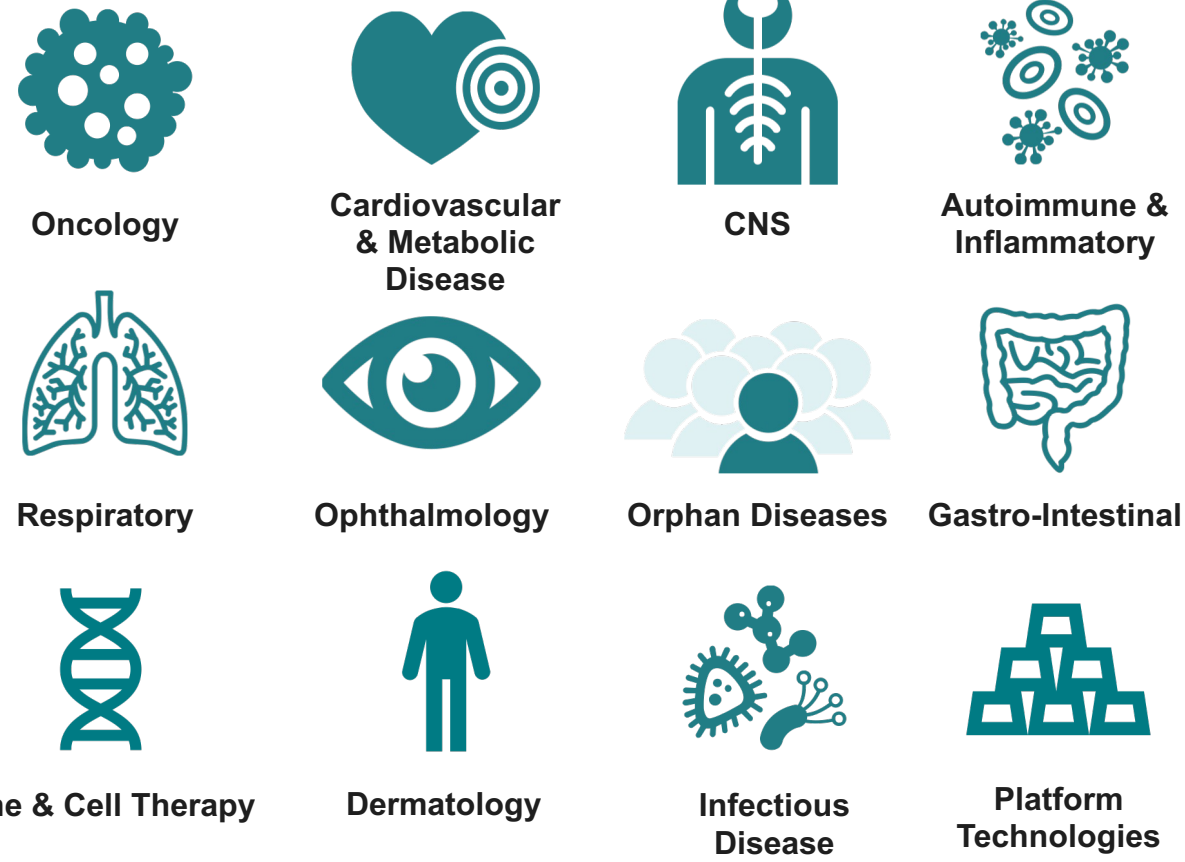
- Facilitate C-suite strategic “workshopping” to develop corporate and partnering strategy for value optimization
- Deal benchmarking and valuation
- Pitch deck refinement and messaging
- ID and facilitate discussions with target partners
- Advise on deal structure and value to support negotiation

An early-stage biotech with a novel drug discovery platform would like our assistance on initial drug targets, what would you recommend?

A later-stage biotech with a marketed mAb wants to expand into other indications, what would you recommend?

Lumanity – Deep Knowledge Across Therapeutic Areas

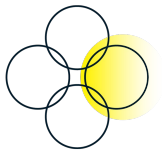
- **Lumanity's US BioConsulting arm has a deep knowledge base within and across all therapeutic categories.**
- **The focus of our work closely mirrors the therapeutic area focus of today's biopharmaceutical pipeline.**
- **Our research is conducted by its trained consultants, all of whom have PhD or MS degrees and/or significant relevant experience in pharma and the targeted scientific areas.**
- **Our consultants possess a combination of commercial, scientific, and clinical knowledge that enable comprehensive analyses and actionable recommendations.**



And other emerging areas of interest such as NASH & fibrosis

Asset optimization & commercialization

Guide robust commercial decision making and uncovering real-world insights



Assess the scientific and commercial landscape

1

- Market and landscape assessment
- Horizon scanning
- Competitive analysis
- KOL research
- Analogue intelligence
- Scenario planning
- Opportunity assessment
- Search and evaluation
- Early access commercial strategy

Understand key stakeholder needs, drivers, and behaviors

2

- Patient's unmet needs assessments
- Input to clinical trial design, including patient related outcomes
- Understanding the patient journey and treatment pathways
- Social media listening as a tool for understanding your stakeholders
- Qualitative research to assess drivers and barriers of behavior
- Qualitative and quantitative approaches to patient HCP and patient HCP segmentation
- Awareness and usage research

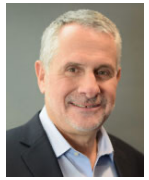
Develop a winning commercial strategy

3

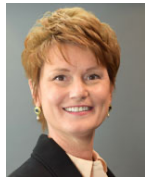
- Indication prioritization
- Forecasting
- Search and evaluation
- Corporate and partnering strategy
- Platform, asset, and brand strategy
- Portfolio and therapeutic area strategy
- Product profile optimization
- Competitor planning and response
- Positioning platform development and testing
- Communication platform optimization
- Omnichannel strategy
- Go-to-market strategy
- Pharma launch excellence technology
- Commercialization and launch planning
- Effectiveness and brand performance tracking

Lumanity US BioConsulting Leadership Team

Senior Management

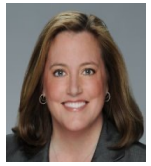


Ed Saltzman
Executive Chairman



Ginger S. Johnson, PhD
Chief Executive Officer

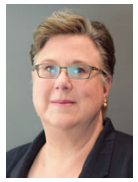
Jeffrey M. Bockman, PhD
EVP, Oncology Practice Head



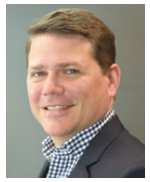
Beth Fordham-Meier, BS, CLP
Vice President, Business Development

Michael C. Rice, MS, MBA
Vice President

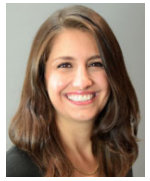
Principals



Janet F. Czachura
Principal



David J. Lomb, PhD
Principal



Danielle M. Marra, MS, MBA
Principal

Joel S. Sandler, PhD
Principal

Managing / Senior Consultants

Steven Smith, PhD
Managing Consultant

Andrew Y. Ng, PhD
Managing Consultant

Kristin N. Abramo, PhD
Senior Consultant

Case Study

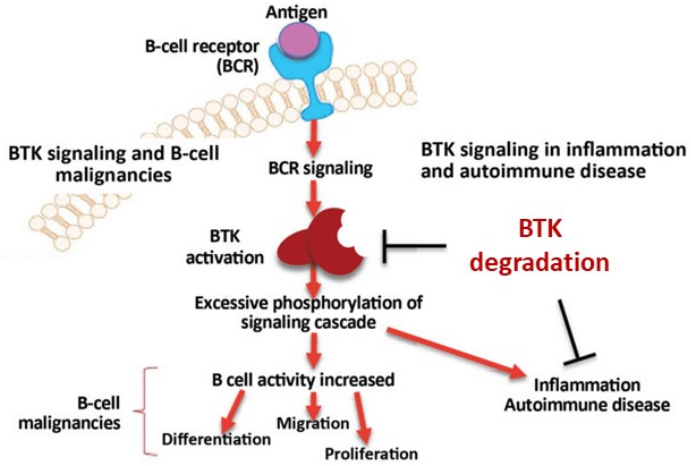
Lumanity

Project Methodology

Background

Company X is a biotechnology company focused on discovering and developing novel, first-in-class, small molecule drugs in order to modulate protein levels to treat a broad range of diseases (e.g., B-cell malignancies, GvHD, autoimmune and inflammatory diseases (AIIDs)).

- Company X is developing an orally delivered BTK degrader for the treatment of B-cell malignancies and potentially autoimmune disease.
  - BTK is a non-receptor tyrosine kinase that plays a key role in the survival and function of most white bloods (excluding T cells and plasma cells) which has been implicated in pathogenesis of certain B-cell malignancies and AIIDs.
  - BTK inhibition promotes B-cell apoptosis but also results in rapid anti-inflammatory effects, neutralization of pathogenic autoantibodies, and blocks the production of new autoantibodies.
  - BTK inhibitors are approved for B-cell malignancies (e.g., Imbruvica/ibrutinib, Calquence/acalabrutinib) but the adverse event profiles associated with these first-generation, irreversible BTK inhibitors makes them unsuitable for chronic treatment of most AIIDs.
- Company X's first Investigation New Drug (IND) application is anticipated to be for an orally available BTK degrader for B-cell malignancies.



Situation Analysis and Project Objectives

- As inhibition of BTK could have positive effects on a wide variety of autoimmune and inflammatory diseases, Company X needs to determine which diseases make the most clinical and commercial sense to pursue as lead indications for its BTK degrader program.
- ***To this end, Company X has asked Lumanity BioConsulting (LBC) to submit a proposal for a project that will help the company to identify, evaluate and score all autoimmune and inflammatory diseases in which BTK inhibition would be expected to have a positive therapeutic effect and could be an attractive commercial opportunity.***
  - The autoimmune and inflammatory disease space consists of at least **150 unique diseases** which can be roughly grouped into several different categories (e.g., autoimmune diseases, autoinflammatory diseases, allergic diseases, organ transplant rejection/GvHD, and diseases where inflammation plays a predominant role).
  - A subset of these diseases represents well-established markets with entrenched standard of care (e.g., rheumatoid arthritis, psoriasis, IBD, etc.) while the remainder include a wide variety of more rare diseases (e.g., inclusion body myositis, necrotizing myopathy, systemic sclerosis, cryopyrin-associated periodic syndrome (CAPS), etc.).
- The following proposal outlines the key criteria and methodology LBC proposes to use to identify and evaluate autoimmune and inflammatory diseases for Company X's BTK degrader program.

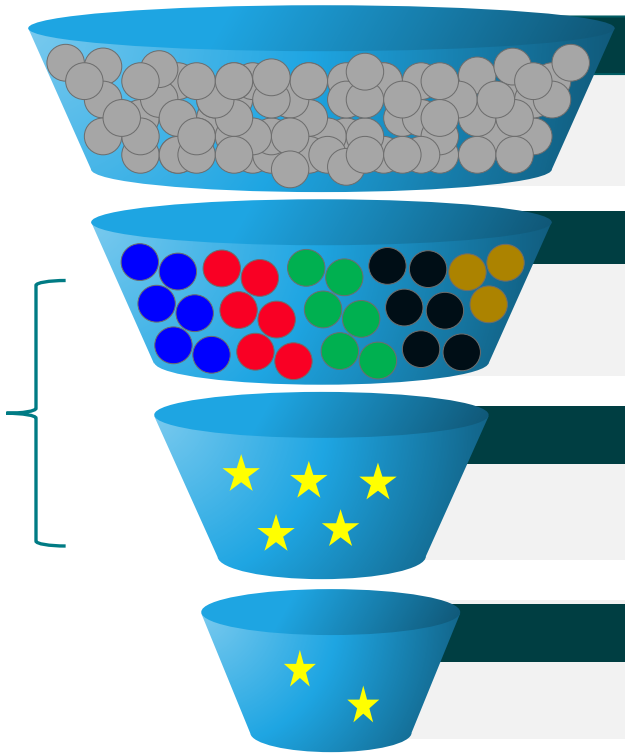
Methodology

Project Overview

LBC proposes the following process for the evaluation and prioritization of autoimmune and inflammatory disease (AIID) indications for Company X's BTK degrader program. This process is divided into multiple stages, as outlined below.

We believe that a collaborative process will provide the best outcome for this assessment and will engage the Company X team with regular status updates throughout the project and will solicit input/feedback where appropriate.

Can you think of any relevant criteria you would use for Stage 2 triage?



Stage 1

Indication Triage

LBC will review a starting list of 150+ AIID indications to identify all those that meet triage criteria (i.e., B cells implicated in pathogenesis of disease, data demonstrating a positive therapeutic benefit of B cell targeted therapies, additional criteria to be determined, etc.)

Stage 2

Indication Evaluation and Scoring

Triaged indications will be evaluated based on an assessment framework developed in collaboration with Company X. At conclusion of the evaluation process, indications will be prioritized based on rating score and LBC's qualitative assessment of the opportunity/fit of the indication for Company X.

Workshop to discuss prioritized list of indications

Workshop to discuss prioritization results (via 1-page summaries of the top 10 indications) with the Company X team and support indication selection for optional deep dive analyses.

Stage 3

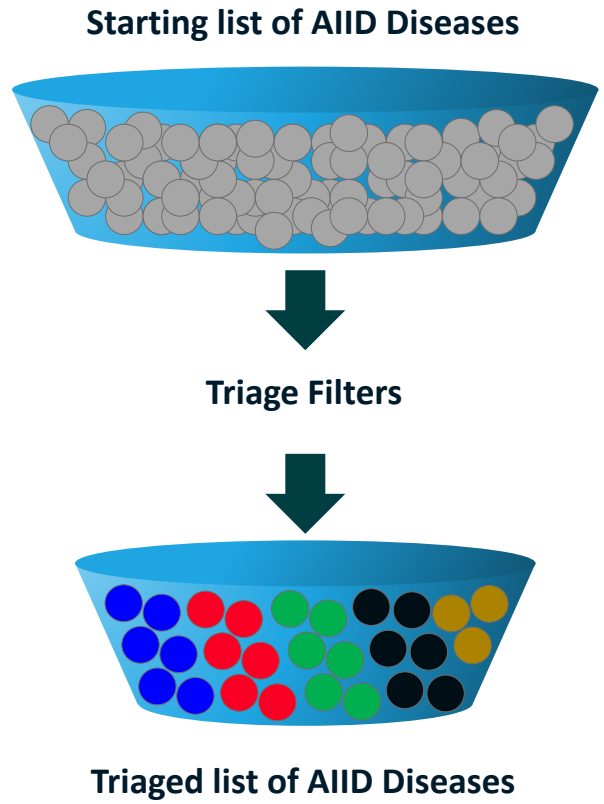
In-depth assessments of prioritized indications

Deep dive assessments of selected prioritized indication(s) and final indication ranking.

Methodology

Stage 1 – Indication Triage

- LBC has generated and maintains a curated database of 153 autoimmune and inflammatory disease indications across all therapeutic areas and this will be the indication prioritization starting list.
- For each of these indications, LBC will utilize a set of filters to determine whether a given indication should be considered for further evaluation as a potential development path for Company X's BTK degrader program.
- Suggested filters are listed below but will be finalized via additional discussions with the Company X team.
  - **Filter #1** – data demonstrating that B cells play a key role in the pathophysiology of the disease.
  - **Filter #2** – data demonstrating a positive therapeutic benefit of treatment with a B-cell targeted therapy (e.g., rituximab, ocrelizumab, obinutuzumab, belimumab).
  - **Additional Filters** – additional triage filters may be added after discussion with Company X.
- ***Only diseases that meet the requirements of at least one triage filter will be subjected to evaluation and scoring in Stage 2 of this project.***



Methodology

Stage 2 – Indication Evaluation and Prioritization

- Stage 2 will begin with a teleconference discuss the rating framework to be used for the indication evaluation and scoring process.
- LBC will compose a draft rating framework which will be shared with the Company X team before the teleconference to ensure that the factors most important to the Company are included (e.g., including scientific rationale/preclinical validation, commercial, regulatory, and clinical attractiveness, probability of success, applicability of available routes of administration, etc.).
  - These criteria will be discussed in depth and will be tailored to meet Company X's specific needs. Considerations on weighting and risk tolerance will also be discussed to inform the framework. A maximum of 12 rating categories will be used for to evaluate and score each indication that met all of the filtering requirements in Stage 1.
- Once the final rating matrix is agreed upon, LBC will evaluate and rate a "test batch" of indications. The ratings and rationale supporting the scoring will be captured in an Excel spreadsheet and will be shared with the Company X team to provide an opportunity to consider the output and confirm that the LBC and Company X teams are aligned. Following this, the LBC team will proceed with evaluating and rating the remaining indications.

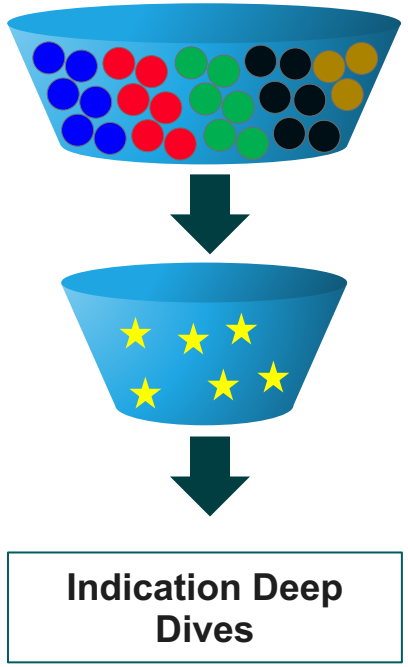
		High (5)	Medium (3)	Low (1)
Scientific	**Applicability/Translatability of Animal Models**	Existence of established and validated animal mode(s) (e.g., highly representative of human disease, precedent exist for successful translation)	Animal model(s) exist but are either not well validated or not entirely representative of disease state	No well-established or validated animal model(s) available
Commercial	**Level of Unmet Need**	Significant impact on morbidity and/or mortality and/or SOC not established or has limited efficacy (i.e., significant unmet need)	Meaningful impact on morbidity, limited impact on mortality and/or SOC is effective but has tolerability/AE issues (i.e., moderate unmet need)	Limited impact on morbidity and no impact on mortality and/or SOC is highly effective with limited tolerability/AE issues (i.e., limited unmet need)
	Competitive Intensity – Marketed Products	No approved competitive products on the market	Limited number of approved competitive products on the market (<3)	Multiple approved competitive products on the market (≥3)
	Competitive Products – Pipeline	Few competitive products in the pipeline (<5), future competitive threat low	Limited number of competitive products in pipeline (10-20), future competitive threat moderate	Significant number of pipeline products in the pipeline (>40), future competitive threat moderate/high
	Estimated Market Opportunity	Distinction of H/M/L will be made at conclusion of ratings once the size of all addressable patient populations across indications are determined		
Clinical and Regulatory	**Regulatory Risk**	Clinical endpoints and trial design established and validated (i.e., ≥1 approved product)	Clinical endpoints and trial design established and validated but no FDA approved products	Clinical endpoints and trial design not well-established or validated
	Feasibility of Clinical Trials	No difficulty expected in clinical trial recruitment AND/OR homogeneous patient population	Some difficulty expected in clinical trial recruitment AND/OR heterogeneous patient population	Difficulty expected in clinical trial recruitment AND/OR highly heterogeneous patient population
	Size of Clinical Trials	Average number of patients required for trial Distinction of H/M/L will be made at conclusion of ratings once the size of all clinical trials across indications is determined		
	Length of Clinical Trials	Average length of time measured by the primary endpoint Distinction of H/M/L will be made at conclusion of ratings once the length of all clinical trials across indications is determined		
	Probability of Clinical Success	History of successful clinical trials (>3) in the indication for a similar patient population	History of at least one successful clinical trial in the indication for a similar patient population	No history of successful clinical trials in the indication for a similar patient population

Lumanity

Methodology

Stage 2 – Indication Evaluation and Prioritization

- **Once each indication is evaluated and rated, total scores will be calculated.** Different weighting criteria can be applied to the individual criteria and output can be evaluated based on a dynamic evaluation of different weighting scenarios.
- **LBC will then assign A (high potential), B (moderate potential), and C (low potential) ratings to each indication.** These A/B/C ratings consider both the total score for the indication as well as our qualitative assessment of the disease based on our deep experience in the space.
- Single slide overviews of the top 10 scoring indications will then be created in PowerPoint. The purpose of these 1-page overviews is to provide the key takeaways from our assessment in an executive-summary style format for review, comparison, and discussion.
- **In the last step of the prioritization process, LBC will have a workshop with the Company X team to review A-list and potentially some B-list indications.** This workshop is designed to provide discussion, dialogue, and support for our ratings and answer and questions from the Company X team.
- Following the workshop, Company X will internally review the prioritized indications and may select indications to be evaluated in deep dive assessments.
  - The deep dive assessments, described more fully beginning on slide 12, will be priced per deep dive to allow for flexibility in selecting the number of indications.
- **At the conclusion of the deep dive assessments, LBC will provide a final ranking of the indications (if multiple indications selected).** This ranking will be based on a collective review and comparison of the selected indications from the in-depth evaluations.



Indications for review and rating

Prioritized list of indications (Tier A/B/C)

Selection of prioritized indications for in-depth assessments

Methodology

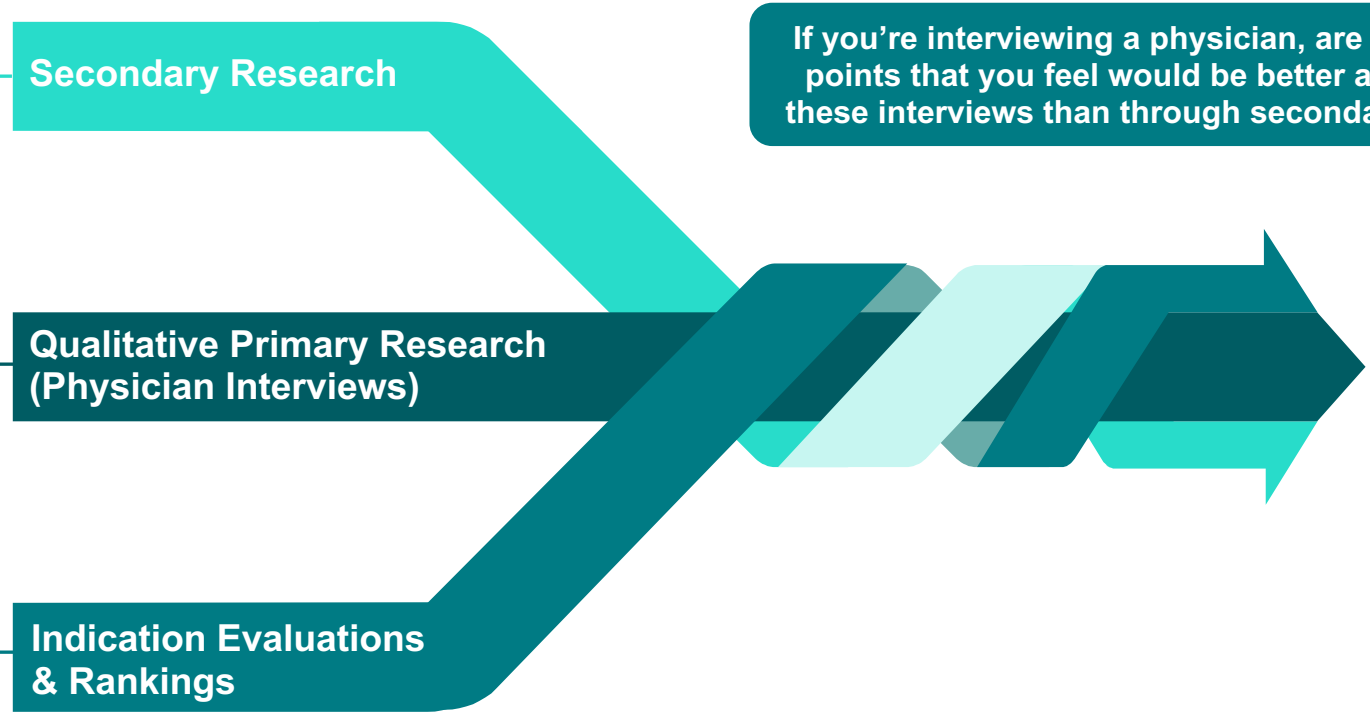
Stage 3 – Indication Deep Dives

The deep dive assessments would provide a more robust and nuanced understanding of each indication as well as the potential for success of the BTK degrader program in each selected indication. LBC will use a combination of primary and secondary research along with LBC's insights to provide Company X with an in-depth overview of each selected indication.

Will be used to provide Company X with the most current thinking on epidemiology, diagnosis, staging, segmentation, and current and future treatment of each indication, and will prepare LBC for qualitative primary research with physicians

Will be used to investigate experts' perceptions regarding patient journey, patient segmentation, current treatment, unmet needs, pipeline products and clinical benchmarks (i.e., development of target product profiles), as well as to collect feedback on the anticipated positioning of a BTK inhibitor in each indication

A collective review and comparison of the selected indications will be used to provide a final prioritized ranking based on scientific, clinical, regulatory, and commercial criteria and potential for success



If you're interviewing a physician, are there certain points that you feel would be better addressed in these interviews than through secondary research?

Findings from primary and secondary research will be synthesized to provide Company X with a strategy for indication selection and sequencing for the BTK degrader program

Methodology

Stage 3 – Indication Deep Dives

Key questions for KOLs in the primary research include:

Current Management

- How are patients with indication X currently being diagnosed in clinical practice?
- What is the patient journey to diagnosis? How easy is it to diagnose the patients and how are they segmented for treatment?
- What is the current standard of care approach to treating patients with indication X? Does it vary by patient segment?
- Are there any expected changes to the size of the patient population in the future?

Unmet Needs and Competition

- What are the key unmet needs remaining to be addressed?
- What targets, MOAs and specific products in the pipeline are considered most promising and why?
- How is treatment expected to change in the future with the introduction of new products?
- Are there any approaches with paradigm-shifting potential? Will they impact the entire treatment population or just a segment?

Potential for BTK inhibitor

- What do experts perceive to be the overall value proposition of BTK inhibitor for indication X?
- Which patients, and under what circumstances, would benefit from treatment with a BTK inhibitor and why?
- What proportion of patients with indication X does this represent?
- What are the biggest challenges expected for a new treatment for indication X?

Deliverables

Deliverables

Stage 1 – Indication Triage

- The deliverable for the indication triage step of this project will consist of an Excel spreadsheet with all data for the indications captured in detail including disease prevalence in the US, category of autoimmune and inflammatory disease (e.g., autoimmune, autoinflammatory, allergic, organ transplant rejection/GvHD, inflammatory disease), the type of immune response (e.g., T cell, B cell, innate, mixed, etc.), etc.
- ***The key output of Stage 1 will be a list of all indications that meet triage criteria (e.g., B cells implicated in pathogenesis of disease, data demonstrating a positive therapeutic benefit of B cell targeted therapies, additional criteria to be determined, etc.).***

Consultant	Drop (Yes/No)	Rationale for Exclusion	Disease Name	Synonyms	Disease description	Therapeutic Area	Therapeutic Area	Primary Organ(s) Affected	AIID Category
DJL	Yes	AAG is a very rare	Autoimmune autonomic		Autoimmune	Neurology	Multisystem	Heart, Bladder,	Autoimmune
DJL	Yes	Blau syndrome is an	Blau's Syndrome		Blau syndrome	Dermatology	Rheumatology	Skin, Eyes,	Autoinflammator
DJL	Yes	Cogan's Syndrome is an	Cogan's syndrome		Cogan syndrome	Sensory		Eye, Ear	Autoimmune
DJL	Yes	Majeed syndrome is an	Majeed Syndrome	Chronic recurrent	Majeed syndrome	Dermatology	Multisystem	Skin, Bones,	Autoinflammator

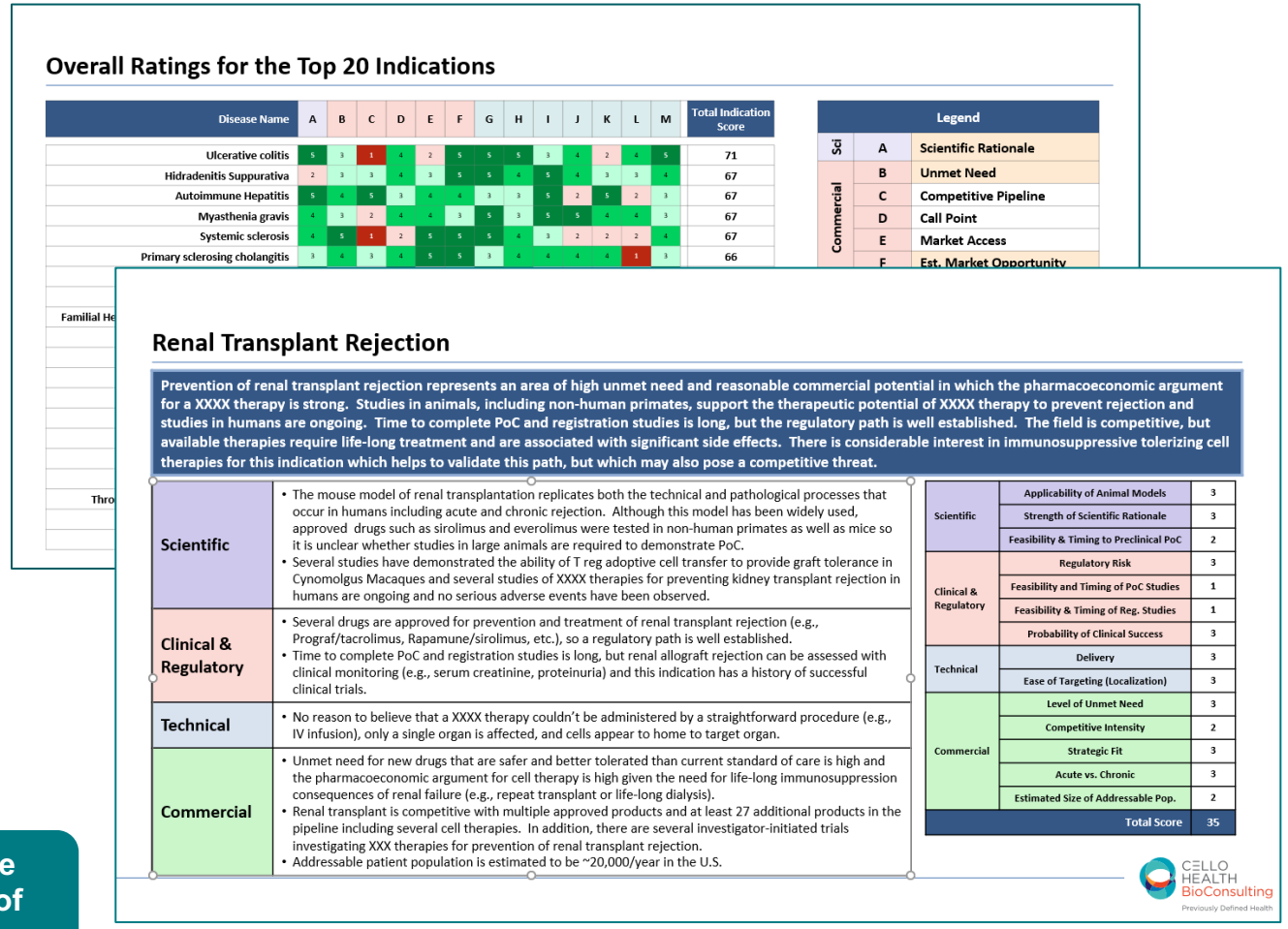
Deliverables

Stage 2 – Indication Evaluation and Prioritization

The deliverable for the indication evaluation and prioritization will include both the Excel spreadsheet with all data for the indications captured in detail as well as a PowerPoint presentation as described below:

- The assessment and ratings of all criteria in the evaluation framework will be captured in an Excel spreadsheets and will include ratings, detailed rationale, and rolled-up scoring and categorization of the prioritized indications into A-, B-, and C- ratings.
- An executive summary, which will highlight LBC's recommendations and rationale for the top indications of interest for Company X.
- One-page indication overviews for the top 10 scoring indications which will provide a high-level description of the disease and top-line takeaways for each of the rating categories which support the ratings and overall prioritization score.

Can you think of how these categories can be weighted differently depending on the stage of development the asset is in?



Overall Ratings for the Top 20 Indications

Disease Name	A	B	C	D	E	F	G	H	I	J	K	L	M	Total Indication Score
Ulcerative colitis	5	3	1	4	2	5	5	5	3	4	2	4	5	71
Hidradenitis Suppurativa	2	3	3	4	3	5	5	4	5	4	3	3	4	67
Autoimmune Hepatitis	5	4	5	3	4	4	3	3	5	2	5	2	3	67
Myasthenia gravis	4	3	2	4	4	3	5	3	5	5	4	4	3	67
Systemic sclerosis	4	5	1	2	5	5	5	4	3	2	2	2	4	67
Primary sclerosing cholangitis	3	4	3	4	5	5	3	4	4	4	4	1	3	66
Familial He														
Thro														

Legend		
Sci	A	Scientific Rationale
Commercial	B	Unmet Need
	C	Competitive Pipeline
	D	Call Point
	E	Market Access
	F	Est. Market Opportunity

Renal Transplant Rejection

Prevention of renal transplant rejection represents an area of high unmet need and reasonable commercial potential in which the pharmacoeconomic argument for a XXXX therapy is strong. Studies in animals, including non-human primates, support the therapeutic potential of XXXX therapy to prevent rejection and studies in humans are ongoing. Time to complete PoC and registration studies is long, but the regulatory path is well established. The field is competitive, but available therapies require life-long treatment and are associated with significant side effects. There is considerable interest in immunosuppressive tolerizing cell therapies for this indication which helps to validate this path, but which may also pose a competitive threat.

Scientific	• The mouse model of renal transplantation replicates both the technical and pathological processes that occur in humans including acute and chronic rejection. Although this model has been widely used, approved drugs such as sirolimus and everolimus were tested in non-human primates as well as mice so it is unclear whether studies in large animals are required to demonstrate PoC. • Several studies have demonstrated the ability of T reg adoptive cell transfer to provide graft tolerance in Cynomolgus Macaques and several studies of XXXX therapies for preventing kidney transplant rejection in humans are ongoing and no serious adverse events have been observed.
Clinical & Regulatory	• Several drugs are approved for prevention and treatment of renal transplant rejection (e.g., Prograf/tacrolimus, Rapamune/sirolimus, etc.), so a regulatory path is well established. • Time to complete PoC and registration studies is long, but renal allograft rejection can be assessed with clinical monitoring (e.g., serum creatinine, proteinuria) and this indication has a history of successful clinical trials.
Technical	• No reason to believe that a XXXX therapy couldn't be administered by a straightforward procedure (e.g., IV infusion), only a single organ is affected, and cells appear to home to target organ.
Commercial	• Unmet need for new drugs that are safer and better tolerated than current standard of care is high and the pharmacoeconomic argument for cell therapy is high given the need for life-long immunosuppression consequences of renal failure (e.g., repeat transplant or life-long dialysis). • Renal transplant is competitive with multiple approved products and at least 27 additional products in the pipeline including several cell therapies. In addition, there are several investigator-initiated trials investigating XXX therapies for prevention of renal transplant rejection. • Addressable patient population is estimated to be ~20,000/year in the U.S.

Scientific	Applicability of Animal Models	3
	Strength of Scientific Rationale	3
	Feasibility & Timing to Preclinical PoC	2
Clinical & Regulatory	Regulatory Risk	3
	Feasibility and Timing of PoC Studies	1
	Feasibility & Timing of Reg. Studies	1
	Probability of Clinical Success	3
Technical	Delivery	3
	Ease of Targeting (Localization)	3
Commercial	Level of Unmet Need	3
	Competitive Intensity	2
	Strategic Fit	3
	Acute vs. Chronic	3
	Estimated Size of Addressable Pop.	2
	Total Score	35

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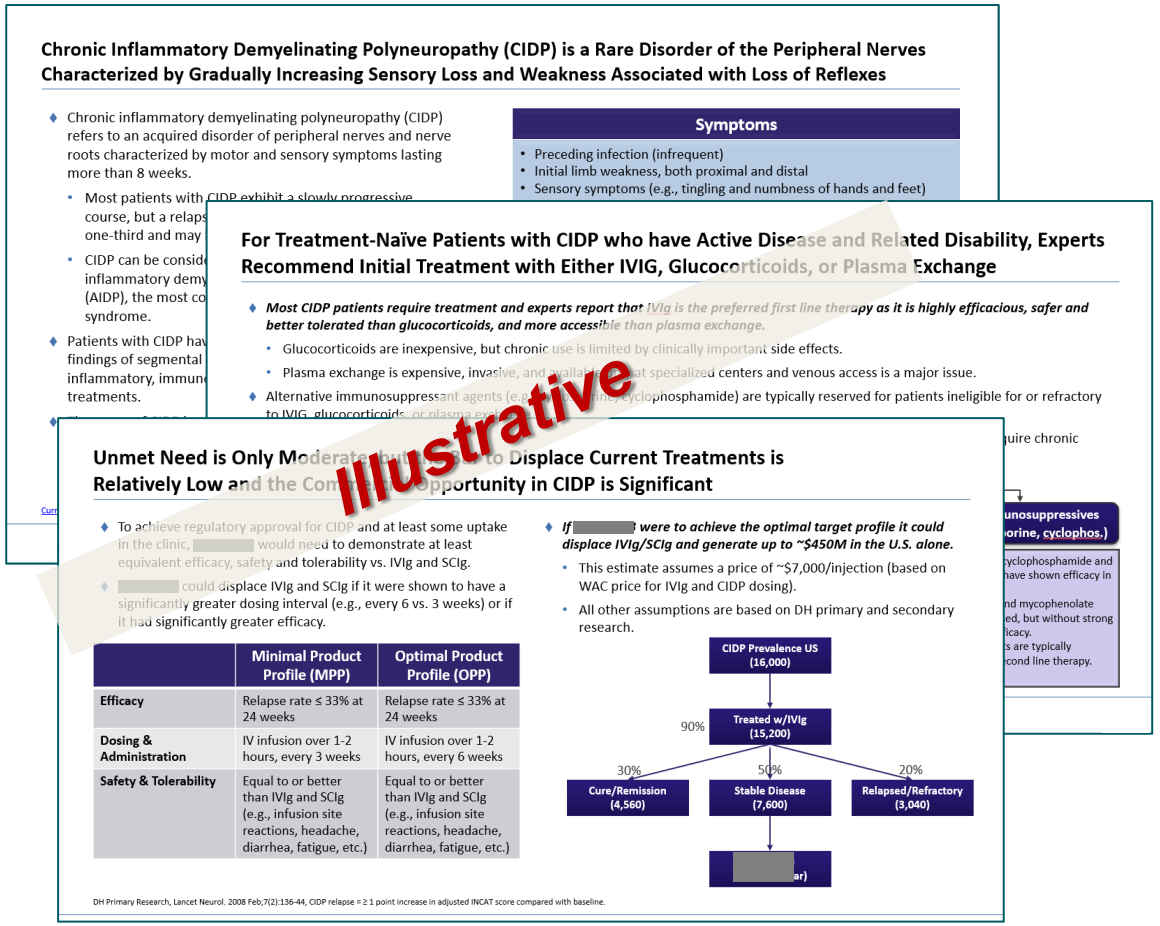
Deliverables

Stage 3 – Indication Deep Dives

The deliverable for the deep dives will consist of a detailed PowerPoint presentation addressing the following for each indication:

- Epidemiology and addressable patient segments
- Scientific rationale for an immunoproteasome inhibitor
- Unmet needs by patient segment
- Value proposition for BTK degrader program
- Target product profile based on target patient population, endpoints, safety, route of administration and magnitude of benefit required to drive prescribing and payment in each indication
- Identification of key points of value inflection
- Clinical development recommendations, with high-level assessment of associated cost, time, and risk
- Development feasibility (i.e. likelihood of attaining regulatory approval) – history of approvals for the indication, and opinion of KOLs
- Top-line, peak-year US estimate of addressable patient population



Thank you

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