Defined Health Overview

**Leading business development strategy**
consulting firm, assisting clients in the pharmaceutical, biotech and healthcare investment industries for more than 25 years

**Three core lines of business**, each focused on helping companies build and strengthen development-stage assets: compounds, portfolios and platforms
Defined Health is a Part of Cello Health
A worldwide team of more than 400 based in the US and UK

A UNIQUE FUSION OF EXPERTISE TO SOLVE PROBLEMS, REDUCE RISK AND UNLOCK THE FULL POTENTIAL OF ORGANIZATIONS, ASSETS AND BRANDS

INSIGHT & ANALYTICS

STRATEGY & COMMERCIAL

SCIENCE & EVIDENCE

Offices in London, Farnham, New York, San Francisco, Chicago, Philadelphia and Boston

200 Market Researchers, Master Practitioners, Digital Specialists, Innovation leads, Field and Compliance

140 Communication Specialists, Scientists & Creatives including Client Service, Project Managers and Medical Writers

70+ Consultants with a blend of industry experts and consulting specialists

60+ PhDs and MDs providing a depth of understanding into cutting edge science
Defined Health Areas of Expertise and Capabilities
Core Services

- Opportunity Assessments
- Opportunity Search & Evaluation
- Portfolio and Platform Strategy
**Defined Health 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
Defined Health
Deep Knowledge Across Therapeutic Areas

- Defined Health 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.
- Defined Health’s 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
Defined Health
Insight Across the Clinical Development Value Chain, with Particular Focus on Early-Stage Assets

Defined Health’s combination of scientific sophistication and strategic/commercial insight provides a competitive advantage for its core offerings across the clinical development value chain, with particular emphasis on assets in early phases of development.

Scientific Focus: Translation of mechanism to potential clinical value proposition
Clinical and Commercial Experience: Guidance on strategies for differentiation

Preclinical
Clinical
Launch

Opportunity Assessments, Indication Prioritization, and Strategy
Identify Value Inflection Points, Forecasting and Valuation
Opportunity Search and Evaluation
Payer Research, Pricing Analysis and Optimization
Insight from Key Stakeholders

- Defined Health has developed an extensive network of relationships with key stakeholders.

- Our consultants conduct in-depth collegial discussions with physicians and payers to understand their perspective on the value of development-stage assets as well as product portfolios and platforms.

- We also have the ability to do patient research to gain key insights into patient needs and willingness to pay for new products.
DH Brings Unique Perspective to Defining Value Proposition

Defined Health believes that the key to driving value inflection for early stage compounds is to go beyond mechanistic proof-of-concept to demonstrate clear potential for clinical differentiation and commercial value.

To capture this sentiment, DH has coined the phrase “proof-of-relevance.”

PoR = Proof of Relevance

To survive, biotech companies must embark on clinical programs that go beyond scientific proof-of-concept (demonstrating that the science is applicable to the disease) to prove that its approach provides a clinically and commercially relevant value proposition that makes the program attractive to all stakeholders.

- In its opportunity assessments, Defined Health provides unique perspective on clinical and commercial attributes that can (and must) be addressed in early stage clinical trials in order to demonstrate PoR.
Opportunity Assessments
Opportunity Assessments

Commercial assessments of development-stage assets are the nucleus of Defined Health’s continuously growing experience, insight and knowledge, across therapeutic areas.

- Methodology includes a combination of primary and secondary research whereby a target product profile is created, refined, and evaluated within the context of the product’s unique market and competitive environments.

- Output typically includes insight into the product’s market potential (in the form of high-level analysis or full revenue/NPV models) as well as recommendations for value optimization at various points in development.
Opportunity Assessments

Defined Health employs the following information resources when conducting opportunity assessments for clients:

**Secondary Research**

Provides the data to support the analysis and primary research

Sources include, but are not limited to:
- company pipelines
- prescription & pipeline databases
- analyst reports & SEC filings
- medical info sites
- scientific literature and conference proceedings
- industry publications
- information gathered from publicly available resources

**Telephone Interviews**

One-to-one in-depth telephone discussions with the following across the US & EU

- Key Opinion Leaders (KOLs)
- Front-line physicians
- Payers (Medical Directors, Pharmacy Directors, Hospital Pharmacists)

Prior to these in-depth discussions, DH drafts a discussion guide(s) and a target product profile which are refined with the client to meet the project objectives

**Web Surveys**

Web-based surveys with US and EU physicians

Provides insight from a larger sample (typical projects range from 50-200 respondents)

Survey questionnaire is drafted and viewed with the client before launch

Results from the surveys are analyzed and presented graphically along with key takeaways from the physician research
Primary and Secondary Research

Through the combination of primary and secondary research, Defined Health’s opportunity assessments evaluate four key areas:

1. **Unmet Need**
   - Epidemiology, patient segments, disease and treatment landscape – current and future
   - Level of clinical or patient need
   - Key remaining unmet needs

2. **Scientific**
   - Scientific basis/validation for the mechanism
   - Degree of differentiation and ability to address unmet needs
   - Potential limitations associated with the product’s profile

3. **Commercial**
   - Value proposition within current and future treatment algorithms
   - Pipeline quantity, quality, and novelty
   - Market access and pricing environment and challenges

4. **Development**
   - Clinical development path and critical endpoints for success
   - Expected regulatory challenges or roadblocks
   - Anticipated clinical development risk
## Additional Components of Opportunity Assessments

Opportunity assessments also frequently include the payer and financial components below. We view these as additional core competencies of our business.

### Cost-effectiveness Models

- Determine current cost of care and quality of life metrics
- Develop a value-based pricing model that takes into consideration a willingness to pay threshold, improvements to QoL and costs savings provided
- Identify relevant pricing analogs

### Payer Research

- Assess market access, reimbursement and pricing environment
- Determine potential coverage and formulary status/restrictions
- Evaluate what additional clinical/pharmacoeconomic data is needed
- Pressure-test price and establish pricing benchmarks

### Forecasting and Valuation

- Create dynamic and adaptive patient-based and prescription-based forecasts
- Benchmark valuations using comparable deal analysis
- Produce risk-adjusted NPV models of companies, products, and deals
- Perform sensitivity analysis of inputs to determine key value drivers
Cost-Effectiveness Models

• For price testing/optimization, Defined Health uses a comprehensive approach to arrive at a price that is derived from value-based pricing models, health economic/payer guidance, and relevant pricing analogs.

• DH develops dynamic value-based pricing models based on the NICE model. Our consultants then pressure-test the VBP during one-on-one discussions with key stakeholders in the market access space and triangulate it with pricing benchmarks of relevant analogs.

• We believe this multi-pronged approach ensures that the price attained is reasonable and justifiable.
Defined Health’s payer research evaluates key questions in the following six areas:

- **Value Inflection Points**
  - Desired improvements in outcomes
  - Key drug characteristics payers willing to pay for
  - Current unmet needs

- **Patient Segmentation**
  - Plan type by segment
  - Costs and unmet needs by segment
  - Reimbursement by segment

- **Trial Design & Data Required**
  - Coverage determinations based on pharmacy or medical benefit
  - Expected copays

- **Coverage & Formulary Status**
  - Current cost of care in the target patient segments
  - Target price point
  - Floor and ceiling price points

- **Restrictions on Use**
  - Restrictions of currently available drugs
  - Anticipated future restrictions
  - Pricing thresholds for stricter/looser restrictions

- **Pricing**
  - Endpoints to show value
  - Patient criteria to show the greatest value
  - Level of improvement to justify price
Forecasting and Valuation

- Financial forecast modeling is an essential component of Defined Health’s valuation capabilities. We build revenue forecasts (patient- or prescription-based) in a user-friendly Excel format to allow our clients to see in real-time how changes and sensitivities around distinct variables impact the forecast.

- In addition, we provide benchmarking valuation of individual assets, platforms and company portfolios as well as risk-adjusted NPVs in Excel with sensitivity analysis surrounding the key inputs.

Patient Population & Treatment
- Epidemiology
- Key patient segments based on treatment practices
- Addressable patient segments

Competition
- Current and future competitive landscape
- Impact of new entrants/generics/biosimilars
- Impact of competition on peak revenue potential

Penetration
- Anticipated use based on product’s value proposition
- Potential adoption & uptake
- Appropriate analogs

Pricing
- Appropriate/acceptable price based on current & future market
- Impact of market access landscape on pricing potential
- Potential level of rebating/discounts
Opportunity Search & Evaluation
Search & Evaluation of Opportunities

- Defined Health assists clients by helping to define and execute on strategic goals to either establish a new presence or grow an existing presence in specific therapeutic and specialty areas.

- Defined Health has more than 25 years of experience that result in an incomparable ability to evaluate and prioritize markets and potential opportunities.
Search & Evaluation of Opportunities

• Defined Health has established a comprehensive & transparent process for identification and qualification of actionable partnering and in-licensing opportunities.

• We evaluate potential opportunities with our broad understanding of the current state of scientific, development and commercial environments within specific diseases.

• Defined Health provides valuable insights and assists in prioritizing of the most compelling assets available to meet the client’s objectives.
Search & Evaluation of Opportunities

We take a comprehensive, multi-pronged approach to evaluating potential licensing/acquisition candidates.

- Scientific Evaluation: understand the base mechanistic approach, and potential application to disease areas, as well as the current level of validation.

- Commercial Evaluation: provide an assessment of the market need and growth potential for the intended indication; compound’s ability to address unmet need, impact on the treatment paradigm, and competitive environment challenges.

- Clinical/Regulatory Evaluation: identify the clinical development risk for the product; likelihood of success in late-stage clinical trials and/or with FDA approval.
Portfolio and Platform Strategy
Portfolio and Platform Strategy

- Defined Health works with many emerging biotech companies to prioritize pipeline portfolios and define pathways to value inflection.

- Typically, these programs are at pre-clinical to early clinical development (Phase I-Phase 2a) so opportunity remains to shape the development program to maximize potential for clinical and commercial success.

- Output often includes a definition of therapeutic strategy and best transaction model going forward.

Portfolio Identification & Prioritization

- Path to value inflection is completely clear and facile
- Path to value inflection is moderately clear and facile
- Path to value inflection is uncertain and/or difficult

Potential to Overcome Risk & Challenges
Therapeutic Area Knowledge

Expertise & Experience
Selected Case Studies
ONCOLOGY

• **ONCOLOGY** is one of Defined Health’s leading areas of research. We have done hundreds of commercial assessments and forecasts of novel MOAs, as well as opportunity search projects, across all MOAs and tumors.

• The Oncology practice is led by Jeff Bockman, PhD, Senior Vice President and Mike Rice, MBA, Principal.

• Select examples of recently evaluated clinical development agents include:
  
  - Checkpoint inhibitors and costimulatory agonists, adoptive cell therapies (CART, TCR), cancer vaccines and oncolytic viruses, pro-apoptosis agents (including inhibitors of bcl2), angiogenesis inhibitors, agents targeting metastases including c-met and survivin, cell cycle targeting agents like cdk, key control pathways like PI3K and mTOR pathway inhibitors, epigenetic inhibitors (e.g., HDAC, HMT, LSD, and BRD), and classic oncogenes like p53 and myc.

• DH’s immuno-oncology experience goes back over a decade, long before IO became in vogue.

• In addition, Defined Health has looked extensively at next-generation cytotoxic agents, as well as reformulations, including drug delivery plays on taxanes, platinums, etc.
Oncology: Select Recent Case Studies

**Pharma Company:** Strategically identified licensing and acquisition targets in order to expand the company’s US presence in Immunotherapy/Immuno-Oncology; maintained ongoing arrangement to qualitatively evaluate specific opportunities the company was considering acting on, both from our recommendations and their own internal directives, M&A event transpired.

**Small Biotech Company:** Assessed value of several development-stage opportunities to supplement the client’s existing portfolio, which included a P3 immunotherapy asset, and provided guidance on the strategic issues of making such moves; considered complexity of moving into new MOAs outside their comfort zone which led to re-thinking of near-term strategic objectives.

**Small Antibody Platform Biotech Company:** Helped develop forward-looking Immunotherapy/Immuno-Oncology strategy for prioritizing clinical development programs for their internally identified novel targets directed antibodies for combination with extent checkpoint inhibitors or other IO modalities such as costimulatory agonists.

**Large Biotech Company:** Prepared strategic analysis of the evolving Immunotherapy/Immuno-Oncology landscape towards identifying next wave approaches, platforms and targets. Client enacted various subsequent IO deals.

**Financial Firm:** Evaluated marketed, blockbuster-potential product to gauge its further growth in the initial indication, and additional upside in clinical development stage indications; provided a detail, multiple indication and multiple scenario, US and EU 10 year forecast model.

**Leading Oncology Company:** Identified early stage licensing opportunities through a systematic scientific, clinical & commercial screen of all Phase I compounds worldwide. Various deals ensued.

**Major Pharma Company:** Developed qualitative and quantitative rationale regarding life cycle management of company’s late stage asset, including identifying key new tumor types and niche market opportunities in this highly competitive space; product has since launched.

**Pharma Company:** Evaluated a novel, but long-studied MOA/target for a non-oncology-focused company looking to enter the space; suggested key tumors and development path, performed competitive analyses, developed top-line forecast model, and identified challenges.
Central Nervous System: Experience & Expertise

**CENTRAL NERVOUS SYSTEM**

- **CENTRAL NERVOUS SYSTEM (CNS)** disorders is one of Defined Health’s most active business practices with projects considering neurological, psychiatric and pain indications.
- The CNS practice is led by Ginger Johnson, PhD, CEO, and Joel Sandler, PhD, Associate Principal.
- As CNS mechanisms have potential across various neurological, psychological and even pain indications, we are often asked to assess CNS opportunities at the earliest clinical stages. We have worked with multiple companies to define a clinical development / opportunity sequencing strategies to maximize the value of a CNS asset. CNS specialty markets (e.g., neurologists, psychiatrists, pain specialists) are an area of focus for many of our clients and, are therefore, spaces in which we actively identify and recommend partnering opportunities.
- Specific CNS diseases in which Defined Health has amassed a substantial knowledge base include, but are not limited to:
  - Alzheimer’s Disease
  - Parkinson’s Disease
  - Multiple Sclerosis
  - Epilepsy
  - Addiction Disorders
  - ADHD
  - Depression
  - Anxiety
  - Schizophrenia
  - Insomnia/Sleep Disorders
  - Migraine
  - Inflammatory/Nociceptive Pain
  - Neuropathic Pain
  - CNS Orphan Diseases (e.g., ALS, Huntington’s)
Central Nervous System: Select Recent Case Studies

- **Pharma Company**: Assessed early-stage, novel mechanism agents to complement their neurology pipeline, specifically focused on neurodegenerative disorders including Alzheimer’s disease, Parkinson’s disease and multiple sclerosis, as well as orphan indications; worked with the company’s scientific and business development team to prioritize and further evaluate attractive opportunities and several of the identified opportunities are being considered for partnering.

- **Specialty Pharma Company**: Valued and prioritized a defined group of potential in-licensing candidates all focused on the treatment of acute pain, including migraine and post-operative pain.

- **European Pharma Company**: Developed clinical development strategy for a novel mechanism across various neuropathic pain types; evaluated the potential of the agent to address the needs of specific patient subsets, clinical/regulatory risk and commercial positioning and value compared to future standard of care.

- **Pharma Company**: Evaluated the future market potential for an early-stage, repurposed agent targeting multiple subsets of anxiety and depression disorders as either a monotherapy or adjunct to standard of care.

- **Major Pharma Company**: Evaluated and prioritized indications for an early CNS-acting compound across multiple indications including Alzheimer’s disease/mild cognitive impairment, schizophrenia-related cognitive disorder and Parkinson’s related cognitive disorder.

- **Financial Firm**: Strategically assessed the potential growth of a marketed product within the neuropathic pain and fibromyalgia markets, taking into particular consideration the impact of current pipeline agents.

- **European Pharma Company**: Worked with management team to prioritize options for execution on the company’s strategic plan to establish a commercial presence in the US market, ranging from acquisition of a company with existing commercial infrastructure to acquisition of a marketed product and organic build of sales force.

- **Drug Delivery Company**: Assessed and prioritized potential opportunities for delivery of various CNS therapeutics utilizing the company’s proprietary technology.
CARDIOVASCULAR & METABOLIC

• CARDIOVASCULAR DISEASE has historically been one of Defined Health’s largest areas of business.
• The CV & Metabolic franchise is led by Michael Rice, MS/MBA, Principal and Ed Saltzman, Executive Chairman.
• Defined Health has provided independent assessments and strategic advice for hundreds of development-stage cardioprevention, acute care and regenerative therapies, as well as interventional devices.
• Specific CV diseases in which Defined Health has amassed a substantial knowledge base include:
  - Dyslipidemia
  - Atherosclerosis / CAD
  - Genetically defined lipid disorders
  - Regenerative Medicine
  - Heart Failure
  - Dyshrhythmia/A-Fib
  - ACS / Myocardial Infarction
  - Hypertension
  - Peripheral Vascular Disease
  - Thrombosis and Restenosis
  - Reperfusion Injury
  - CV related Metabolic Disorders

• METABOLIC DISEASES is likewise one of Defined Health’s large practice areas. We have performed hundreds of opportunity assessments of products for diabetes, dyslipidemia, metabolic syndrome and obesity, as well as providing high-level strategic advice to companies wishing to navigate the increasingly challenging regulatory & commercial environment associated with these large markets. Specific metabolic targets in which Defined Health has amassed substantial knowledge include: GLP-1 mimetics, SGLT2 inhibitors, DPPIV inhibitors, PCSK9 antibodies, HDL mimetics, and others.
Cardiovascular & Metabolic Disease: Select Recent Case Studies

- Franchise Strategy: Cardiovascular landscape assessment and strategy for Big Pharmacos considering re-entering the CV space
- Evaluation, market positioning and valuation of a novel HDL raising therapy in high risk patient segments
- Landscape and therapeutic approaches for genetically defined CV disorders such as: HoFH/HeFH, ABCA1/Tangiers, LCAT, ACAT and ApoA1 deficiency, Cardiomyopathy
- Strategic advice for potential expansion of a pharmaceutical grade omega-3 fatty acid to other indications and therapeutic areas.
- In-licensing opportunity assessment of an oral anti-arrhythmic for the maintenance of normal sinus rhythm in patients with chronic atrial fibrillation. Epidemiology, segmentation, treatment algorithm among primary care and cardiology specialists and competitive assessment
- Therapeutic overview of acute cardioversion and antiarrhythmic use in atrial fibrillation for a client evaluating opportunities in this non-core business space
- EU clinical plan and commercial launch strategy for an acute antihypertensive used in perioperative and emergent hypertensive crisis
- In-licensing opportunity assessment of an IV thrombolytic agent in stroke, PAOD and early use in acute STEMI pts
- AMI overview and out-licensing opportunity assessment of novel biodegradable polymer delivered via intracoronary injection. Aided client in commercial positioning and exploring partnering options
- Strategically prioritization of potential indications for a dual acting receptor antagonist in PAH, diabetic nephropathy, CHF and resistant hypertension
- Developed a vision for a unique emergent / urgent care franchise to drive an acute care franchise strategy
- Ex-US specialty company evaluating US market entry for an extended release agent in direct competition by a large pharma in the process of market development
Defined Health Principals

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