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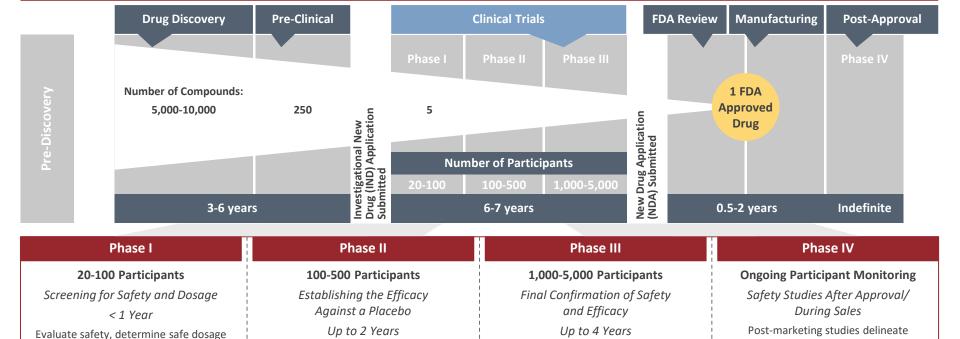
### **Clinical Trials Overview**

ranges, and begin to identify side effects

Discovering and developing safe and effective pharmaceuticals is a challenging undertaking that can take 10+ years and \$2+ billion.

- > Clinical trials are research studies to test potential treatments in volunteers for efficacy and safety ahead of receiving approval for wider use in the general population
  - >> Physician investigators initially enroll volunteers or patients into small pilot studies, and subsequently conduct progressively larger-scale comparative studies
- > Clinical trials are a key research step in the process of advancing medical knowledge and patient care, as they are a key step in discovering and testing new treatments or preventive measures for diseases with a drug, medical device, or biologic, such as a vaccine, blood product, or gene therapy

#### **ROLE OF CLINICAL TRIALS WITHIN THE DRUG DEVELOPMENT PROCESS**



Confirm drug's effectiveness, monitor side

effects, compare it to commonly used

treatments, and collect information that will allow it to be used safely

See if drug is effective and further evaluate

its safety

additional information, including the

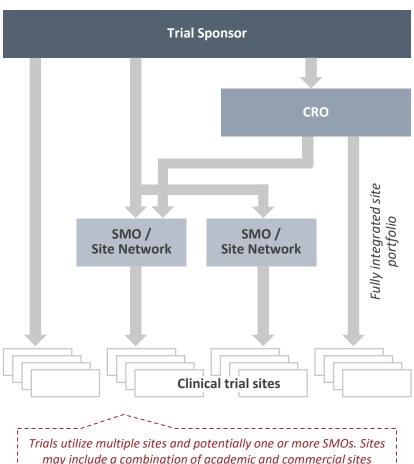
treatment's risks, benefits, and optimal

use, and are ongoing during the drug's use

### **Clinical Trial Sites Value Chain**

Site management activities may be performed by trial sponsors, CROs, or SMOs at multiple site locations.

#### POTENTIAL STAKEHOLDERS FOR SITE OPERATORS



may include a combination of academic and commercial sites

- **Site management** activities may be performed by the industry trial sponsors, contract research organizations (CROs), site management organizations (SMOs), or a combination of those stakeholders
  - > Outsourcing these services allows trial sponsors to operate with a lower cost base
  - Site management activities include:
    - Country / site selection
    - Regulatory submissions
    - Site initiation, monitoring, and coordination
    - Data management
- **Site-specific activities** are fully outsourced by trial sponsors and are undertaken by individual or networks of commercial or academic sites
  - These activities have always been fully outsourced in order to ensure trial sponsors have access to patients; high capital requirements and potential conflicts of interest are also a factor
  - Site-specific activities include:
    - > Patient recruitment, retention, and management
    - Trial administration
    - Data capture
- > Patient recruitment can be undertaken both at a site-specific level or centrally (the latter usually involving a PRO1.)
  - SMOs will also provide centralized coordination for all their sites involved in each trial

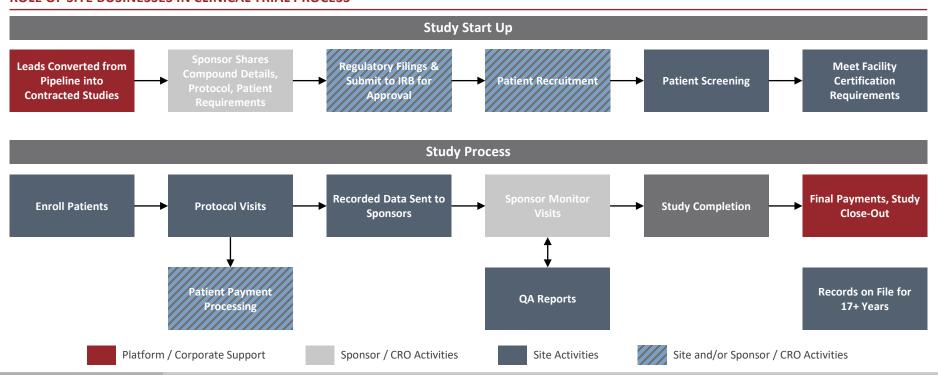


### Clinical Research Sites' Role in Clinical Trials

A typical sponsor/CRO will outsource clinical trial execution to multiple research sites to handle patient recruitment and retention, trial administration according to protocol, and data capture.

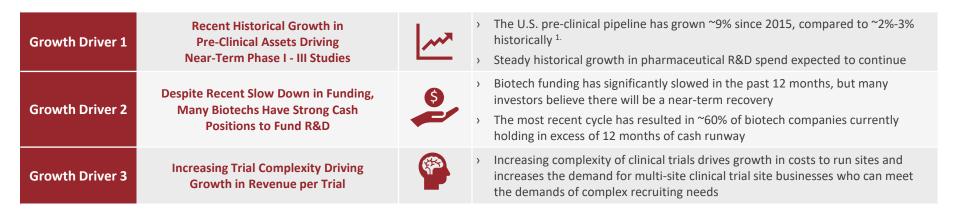
- > Clinical trials are complex processes, and outsourcing the execution of the trial promotes efficiencies throughout the process and enables sponsors to get their asset into the market faster
  - > Site-specific activities include patient recruitment, enrollment, retention and management, trial administration, and data capture
  - > Multi-site businesses, vs. single sites, offer expedited study start up and recruitment, de-risk project times due to integrated systems, offer a single point of contact for contracting, and have uniform SOPs that all increase the predictability of performance on trials
- > Sponsors and CROs focus on the design of protocols and the patient requirements needed, as well as performing monitor visits to ensure compliance and assess outcomes of the study

#### **ROLE OF SITE BUSINESSES IN CLINICAL TRIAL PROCESS**

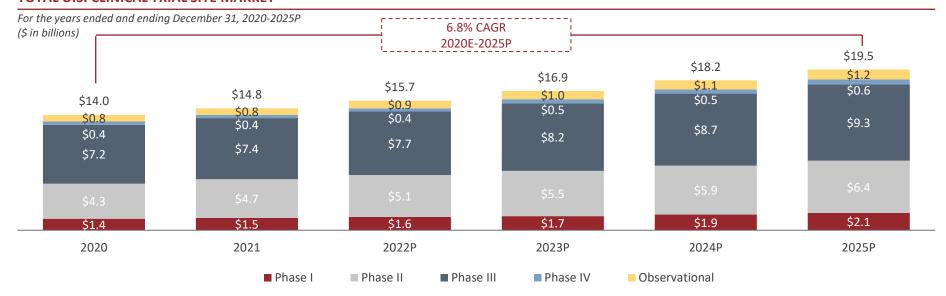


### Trends in Clinical Research Sites (3 Key Growth Drivers)

The clinical research site market is well-positioned for sustained growth, driven by several favorable trends and growth drivers.



#### TOTAL U.S. CLINICAL TRIAL SITE MARKET 2.



<sup>1.</sup> Source: HealthAdvances



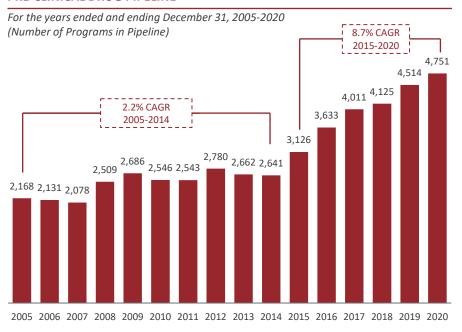
<sup>2.</sup> Ibid.

### **Growth Driver 1: Recent Historical Growth in Pre-clinical Assets**

Accelerating growth in pre-clinical assets over the past 5-6 years is fueling growth in clinical trial activity.

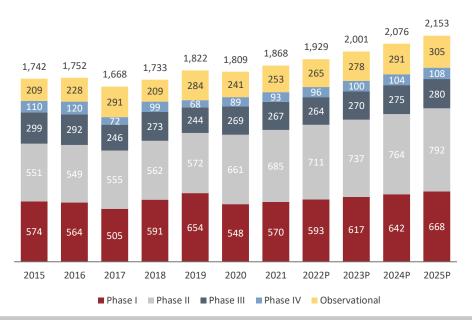
- > Growth in pre-clinical assets translates directly into the overall growth of the clinical trial market as products move into clinical trials after an average of ~3-4 years of pre-clinical development
  - > The recent cycle in biotech and pharma investment has resulted in supportive cash positions companies
  - > Innovations have driven clinical development in new drug delivery technologies
  - > The current bolus in pre-clinical investment is expected to translate to Phase III clinical trial growth in the next few years
- > U.S. clinical trials expected to grow at a CAGR of 3.5% through 2025 4.

#### PRE-CLINICAL DRUG PIPELINE 5.



#### TOTAL U.S. CLINICAL TRIALS 6.

For the years ended and ending December 31, 2015-2025P (Number of U.S. Clinical Trials)



<sup>4.</sup> Source: HealthAdvances

<sup>5.</sup> Ibid.

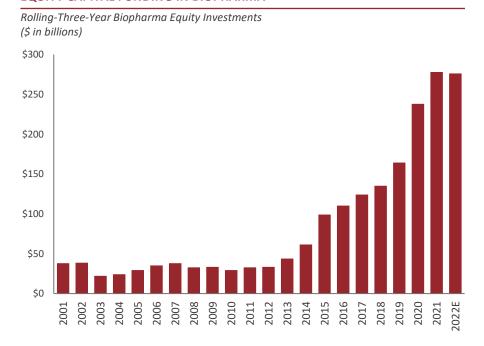
<sup>6.</sup> Ibid.

## **Growth Driver 2: Funding Cycle Has Bolstered Cash Position for Many Biotechs**

The current biotech funding cycle is approaching the longest observed downward trend; however, investor sentiment is cautiously optimistic, and outsourced spending is expected to remain elevated as companies seek to control costs.

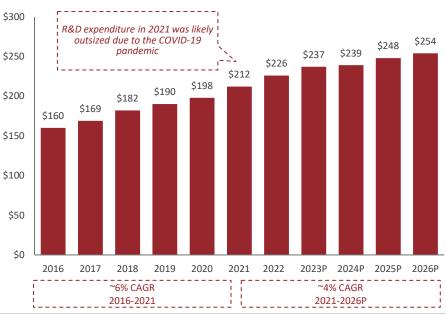
- > Continued clinical trial growth is being sustained by the healthy balance sheets of pharma and biotech companies, increases in pre-clinical development, and recent validation of new technologies (e.g., mRNA) that can move into the clinic
  - > The 2020-2021 IPO and follow-on public offering boom provided a robust (and cost-efficient) backdrop to raise funds and support ongoing development
  - > Though the current funding cycle is approaching the longest observed downtrend, many expect capital markets to move swiftly when funding thaws
- > Trials are becoming more complex, driving upticks in enrollment requirements, the number of sites needed to complete a trial, the number of protocols needed, and regulatory requirements for more diverse patient populations
  - > With rising R&D costs and the funding cycle trough, pharma sponsors look to leverage CROs and multi-site clinical research site platforms to manage larger and more complex trials

#### EQUITY CAPITAL FUNDING IN BIOPHARMA 7.



#### GLOBAL CLINICAL R&D SPEND FORECAST 8.

Global clinical R&D spend for the years ended and ending December 31, 2016-2026P (\$ in billions)



## **Growth Driver 3: Increasing Trial Complexity Driving Growth in Revenue** per Trial

Revenue per trial growth has accelerated in recent years as protocols become more complex, sponsors and CROs are managing more sites per trial, and sponsors seek diversity in difficult-to-access patient populations.

#### PROTOCOL COMPLEXITY

- The average number of endpoints per protocol has increased by 6% on average each year since 2003 9.
- Sites with the ability to successfully execute complex protocols will continue to be in high demand

#### **INCREASE IN SITES ENROLLED**

- Average sites per trial increased by ~4-5% every year between 2005 and 2019 <sup>10</sup>.
- More sites are needed in order to match increased patient enrollment and geographic diversity needs

### MODEST GAINS IN PATIENT ENROLLMENT

- Average patient enrollment fell from 2005 to 2010 but has made modest gains in the past 10 years
- There is also modest growth revenue per patient, projected at 2.5%+ CAGR through 2025, which will drive revenue per trial for site businesses <sup>11</sup>.

### DEMANDS FOR PATIENT DIVERSITY

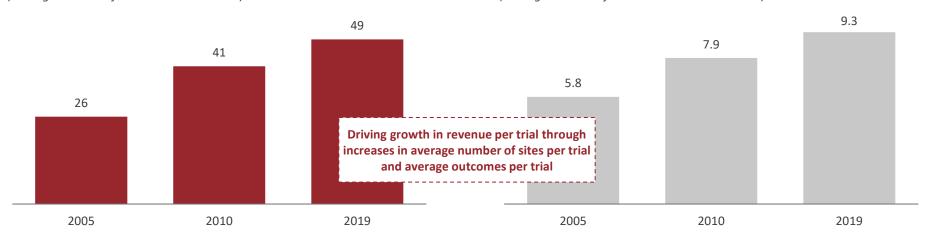
- In 2011, only 1% of trial participants were Hispanic, but by 2016, 18% of trial participants were Hispanic <sup>12</sup>.
- Clinical trials are increasingly utilizing diverse patient populations across multiple geographies to prepare to meet the future of regulatory requirements

#### INCREASE IN NUMBER OF AVERAGE SITES PER TRIAL 13.

For the years ended December 31, 2005-2019 (Average Number of Sites Per Phase III Trial)

#### INCREASE IN NUMBER OF AVERAGE OUTCOMES PER TRIAL 14.

For the years ended December 31, 2005-2019 (Average Number of Outcomes Per Phase III Trial)





Source: 9. Centerwatch

10. HealthAdvances

### The Rise of Virtual and Hybrid Clinical Trials

Industry experts expect few truly virtual trials and instead foresee most trials employing decentralized, hybrid virtual trial methods to supplement brick-and-mortar sites.

- > Virtual trials include any aspect of the trial process that is decentralized and can be completed from any location, which can drive improved access and patient recruiting for clinical trials
  - > Currently, clinical research providers are utilizing available virtual tools for interoperability efficiencies, such as eConsent, and in the near future, more aspects of trials will have virtual capabilities, including sophisticated data capture
- > Virtual components of clinical trials will serve as a growth driver and a competitive advantage for businesses with the ability to efficiently implement the infrastructure to execute on a hybrid trial site model
  - A hybrid trial site model of in-person and virtual solutions is expected to gain traction and grant patients flexibility when attending their protocol visits, ultimately driving their participation and increasing patient retention
  - > Over the next few years, integration of virtual clinical trial capabilities is likely to increase, and the industry is expected to start incorporating virtual / remote technologies into ~10%-15% of total clinical trials <sup>15.</sup>

#### **BUILDING A TOOLKIT OF DECENTRALIZED METHODS...**



eConsent

- > Video Visits
- > Home Health
- Remote Monitoring

- > Local Labs
- > Central Site
- Local Imaging
- Home Drug Supply

#### ...TO FACILITATE THE HYBRID VIRTUAL TRIAL EXPERIENCE

The COVID-19 pandemic catalyzed the adoption of virtual capabilities in clinical trials. While going fully virtual is highly unlikely, hybrid models are expected to gain traction.

#### **Hybrid Trial Site Model**



- > Patient still travels to sites for some in-person services
- > Sites employ virtual solutions to limit burden on patients (e.g., reduced visits)

# Brick-and-Mortar Clinical Trial Sites Remain Essential Despite the Rise of Hybrid and Virtual Trials

Importantly, clinical trial sites own the patient relationship and will play an integral role in working with vendors to employ and accommodate virtual methods and new technologies.



#### TRADITIONAL CLINICAL TRIALS

- Traditional clinical trials may be conducted at dedicated (e.g., independent sites, SMOs) and non-dedicated trial sites (e.g., AMCs, physicians' offices)
- Site-specific activities include patient recruitment, retention and management, trial administration, and data capture



## TECH-ENABLED CLINICAL TRIALS

- SMO partners and other clinical trial participants are beginning to weave in additional tech capabilities to address the rising complexity of clinical trials
  - Integrated and streamlined trial activities (e.g., endpoint collection, administration)
  - Digitized and automated workflows (e.g., patient recruitment, monitoring)



### DECENTRALIZED / HYBRID CLINICAL TRIALS

- Decentralized clinical trials (DCT) may feature:
  - Tech to support patients who are remotely monitored
  - Remote data collection through technology (e.g., virtual interface, remote monitoring/wearables) or via mobile clinicians
- However, very few trials are fully decentralized; trials in this space typically feature components of DCT for a hybrid approach

Clinical trial sites ultimately own the patient relationship and therefore remain crucial to the success of clinical trial types

### **Levels of Site Integration across Trial Sites**

Multi-site, dedicated clinical trial operators feature highest inter-site integration.

Level of integration between sites Low High Single, independent clinical trial site Investigative site networks (ISN) Scaled site operators Fully focused on running clinical trials Sites pay to join a network for All sites under the same ownership marketing purposes Lack of scale limits resources and Standardized SOPs standard operating procedure (SOPs) May have some shared business **Dedicated** Full-time dedicated training staff functions and standard SOPs clinical Offer consulting, trial management, trial centers Contracts may come to sites via site management, and advanced network or independently add-on services **Independent provider sites** (e.g., AMCs, physicians' offices) Clinical trial site enablers Limited SOPs and potentially no Provide a network and services to Some scaled operators have developed dedicated trained staff better equip providers to run capabilities beyond traditional site clinical trials management to manage the full Sites not Contracts awarded directly to site spectrum of the clinical trial process, fully Often include technology to help inclusive of CRO activities dedicated to facilitate trial recruitment clinical trials Some scaled operators may also include physicians' offices within their broader network

### **Strategic Models of Scaled Operators:**

### Therapeutic Area Specialists & Operational Executors

Traditionally, scaled operators focused on operational excellence or therapeutic area specialization; additional capabilities differentiate market participants.

### **Operational executors**

- Focus on sites that can run trials across a broad range of diseases, especially ones with high trial / patient volume and less complex trial protocols
- > Continuously expand TA coverage to ensure that the broadest range of trials is addressable
- Emphasize operational excellence, availability of many sites able to serve each trial, and superior service and capabilities as key points of differentiation

#### Therapeutic area (TA) specialists

- TA specialized sites sell an established track record of trial success, a high-science understanding of indication nuances, and access to specialized patient populations
- Position the narrower site group as a more efficient option
   vs. academic medical centers or physicians' private practices
- After establishing reputation in a TA, pursue opportunity to expand into adjacent indications for growth opportunities

Low

Specific therapeutic area focus

High

#### Specialized site-based capabilities

- Select a niche capability required in certain trial protocols and acquire sites with similar features (e.g., surgical suites, Phase I inpatient facility, complex imaging, sleep equipment, telemetry, EEGs)
- Develop a best-in-class supporting organization to position the sites as the go-to option for trials requiring those specific capabilities

#### **Recruiting enablers**

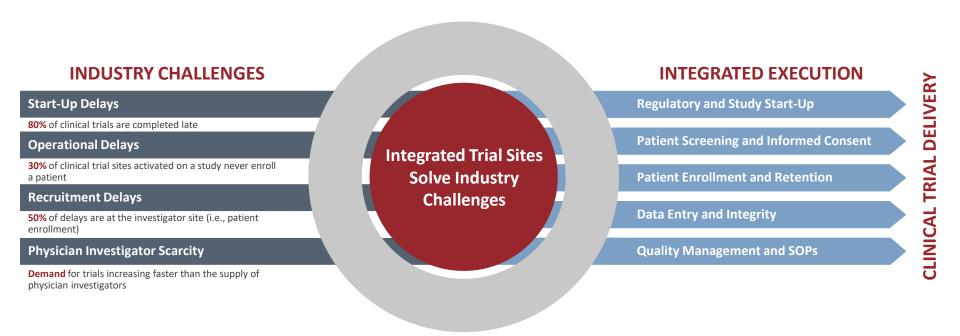
- > Focus on acquiring sites that have large databases for recruitment access to EMRs and deploy centralized recruitment and pre-screening
- > Incorporate sites that can reach specialized populations (e.g., demographic groups)
- Establish best-in-class processes and partnerships to facilitate recruitment and retention and emphasize successful track record

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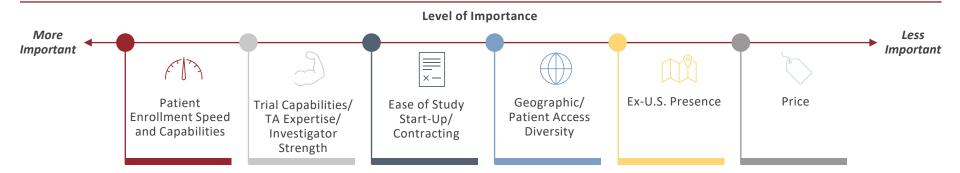
### **Clinical Trial Site Business:**

### Industry Challenges and Critical Success Factors

Clinical trial sites with integrated operations have demonstrated the ability to overcome industry challenges and execute high-quality clinical trials.



#### **CRITICAL SUCCESS FACTORS:**

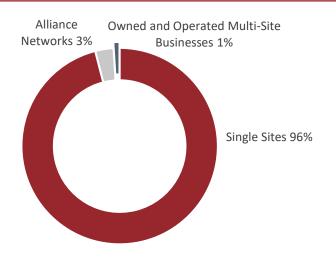


### Opportunities Exist in a Highly Fragmented Market

The overall market for clinical trial site businesses is highly fragmented and poised for continued consolidation, with multi-site platforms or alliance networks accounting for only ~4% of total trial sites.

- > There are ~20,500 clinical trial sites in the U.S., with ~96% being single sites, which typically do not have the same access to patients as organized multi-site trial sites <sup>16</sup>.
  - > A clinical trial site provider possessing multiple sites generally has improved recruitment capabilities as well as centralized support functions
- > Consolidation of the sector is in early innings, and is expected to accelerate in the coming years
  - > The market will continue to consolidate as pharmaceutical sponsors and CROs are increasingly looking to contract with fully owned, integrated models that provide a level of service, breadth of sites, and depth of therapeutic expertise that single sites or smaller networks cannot replicate
  - > Individual sites are increasingly unable to meet recruitment goals as studies continue to get more complex, giving providers of scale a significant competitive advantage
  - > Having a greater number of sites drives more effective patient recruitment, enrollment, and retention; this competitive advantage will accelerate the consolidation trend

#### CLINICAL RESEARCH SITE FRAGMENTATION



~59,000 unique clinical trial sites utilized in the U.S. between 2015 and 2020

~20,500 unique trial sites in the U.S. annually on average

**533** clinical trial sites associated with Alliance Networks

**177** owned and operated by multi-site clinical trial businesses

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### Scorecard for Realizing a Premium Valuation

There are several key valuation drivers to focus on for achieving a premium value for a clinical trial site business.

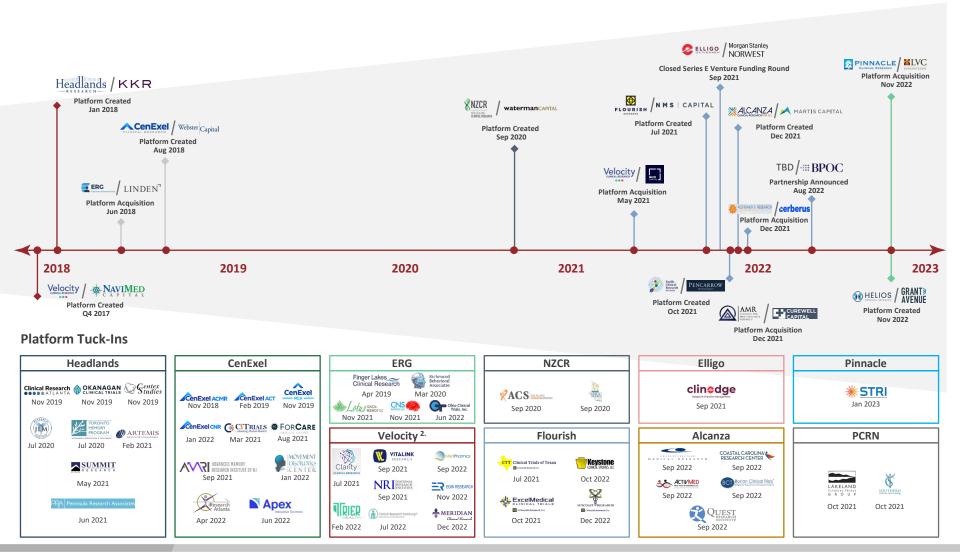
Valuation Driver	Valuation Impact	Key Question	Winning the Value Point
Backlog and Pipeline Visibility	Low High	What does current backlog/pipeline predict in terms of forward earnings based on historical record?	<ul> <li>Trial-by-trial backlog and pipeline conversion analysis over time, and coverage analysis on forward looking profitability</li> </ul>
Margin Sustainability	Low High	Did COVID-19 vaccine work increase margins in a way that is unsustainable long-term?	<ul> <li>Analysis of historical and projected margins, gross margins by trial during budgeting vs actual site-level margin</li> </ul>
Therapeutic Area Concentration Risk	Low High	How has the platform weathered changes in demand and is the portfolio diverse enough?	<ul> <li>Historical revenue and projected backlog/pipeline analysis by TA, including rev. per patient per visit and volume per trial</li> </ul>
Principal Investigator "Key Person" Risk	Low High	Is there concentration risk in the PI base that could adversely impact the business?	<ul> <li>PI database and loop covering historical retention, compensation model, ownership (if any), and age/planned retirements</li> </ul>
Business Development Capabilities	Low High	Is there an opportunity to increase sites per study through cross-selling/strategic account management?	<ul> <li>Historical and projected sites per study analysis, contract negotiation analysis</li> </ul>
Acquisition Story	Low High	What is the track record and current outlook to acquire and grow additional sites?	<ul> <li>Pre- and post-acquisition performance analysis, purchase price multiple analysis, M&amp;A pipeline</li> </ul>
Patient Enrollment Capabilities	Low High	Has the platform built a better mousetrap to offer value to sponsors by over-enrolling studies?	<ul> <li>Patient funnel, actual versus targeted enrollment (internal and sponsor/CRO targets)</li> </ul>
De Novo Story	Low High	Are there predictable investment economics and returns on new sites?	De novo ramp and maturity analysis
Decentralized Trials	Low High	Will revenue per patient be impacted by future DCT methods being increasingly adopted?	<ul> <li>Excerpts from industry conversations and an overview deck of management's view to build/buy/partner for each DCT method</li> </ul>

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### Flurry of Activity in Clinical Trial Sites

There has been significant private equity activity in the clinical trial site space in recent years, with ten notable platforms acquired or created since January 2021, and consolidation is expected to continue.



### **Competitive Landscape**



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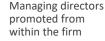


Transportation & Logistics



Revenue from





history









Healthcare & Life Sciences



Industrials



Technology

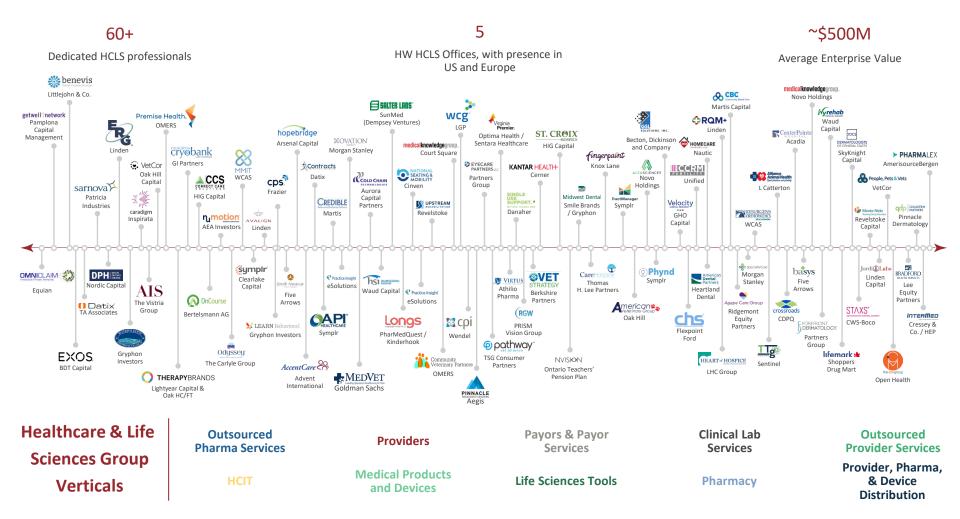




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HW's recent deal experience provides additional insight into key investors' playbooks and hot buttons while reinforcing our thought leadership with practical experience

#### 2019 – 2023 Pharma Services Deals

STAXS°

a portfolio company of

OSilverfleet

has been acquired by

**H**/NIEL

a portfolio company of

has been acquired by

holdings





KNOX-LANE

has made a strategic

fingerpaint













WCg COPERNICUS

a portfolio company of

ARSENAL

has been recapitalized by

LGP LEONARD GREEN



medicalknowledgegroup.

a portfolio company of

WINDROSE

has been recapitalized by



#### **Thought Leadership in Pharma Services**

Return on Innovation, Part 1:
Commercialization Services

ARTICLE - OCTOBER 1, 2018

ARTICLE - MAY 31, 2019

Return on Innovation, Part 2: Contract Research Organizations

Return on Innovation, Part 3: Pharmaceutical Safety and Risk Management

Return on Innovation, Part 4: Contract Development and Manufacturing Organizations (CDMOs)

Return on Innovation, Part 5: Real-World Evidence

Return on Innovation, Part 6: Clinical Trial Sites

Return on Innovation, Part 7: Outsourced
Pharma Services: Differentiation Via Data

HarrisWilliams.com

#### **Select Buyers Engaged on Recent Deals**



Jordi Labs

has been acquired by

♣RQM+

a portfolio company of

LINDEN

KANTAR HEALTH

a portfolio company of

BainCapital

has been acquired by

**Cerner** 

AmerisourceBergen











































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**Paul Hepper Managing Director** Healthcare & Life Sciences Group

+1 804.887.6026 phepper@harriswilliams.com



**Cheairs Porter Managing Director** Healthcare & Life Sciences Group +1 804.536.3426

cporter@harriswilliams.com

**Geoffrey Smith Jr. Managing Director** Healthcare & Life Sciences Group

+1 804.647.5926

gsmith@harriswilliams.com



**Lucas Scholl** 

Vice President

Healthcare & Life Sciences Group

+1 415.416.0766

lscholl@harriswilliams.com

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