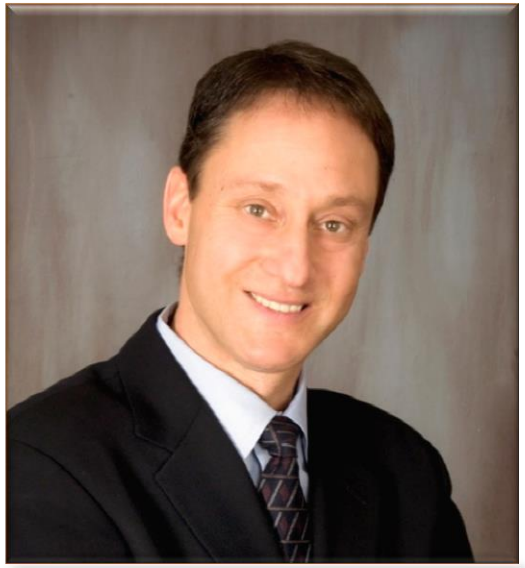
Outsourcing Relationships and their Evolving Impact on Clinical Trial Performance



Ken Getz, MBA

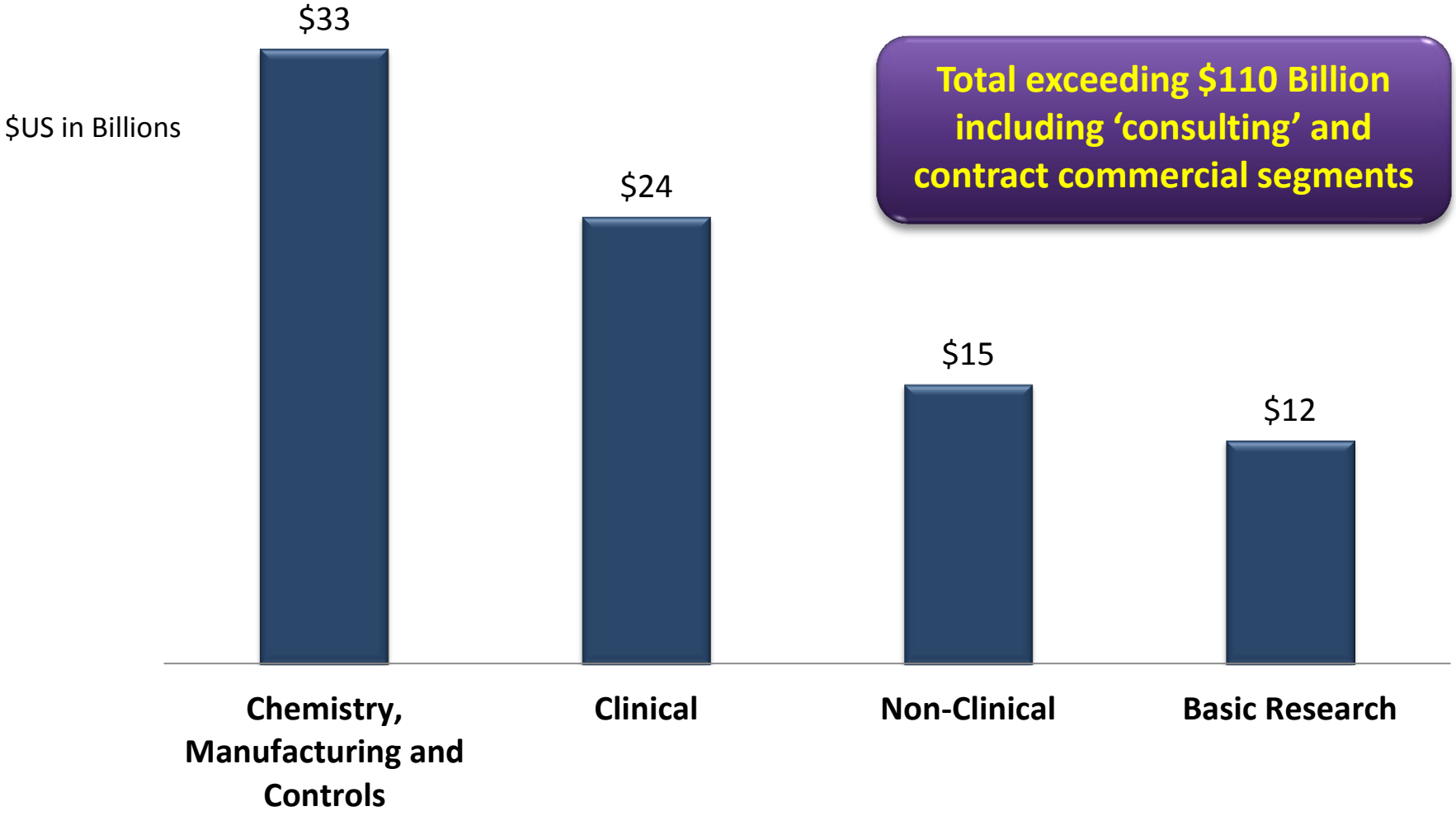
Director, Sponsored Research Program, Associate Professor

CSDD, Tufts University Medical School

Agenda

- Overview of the current outsourcing landscape
- Relationship improvement opportunities
- Anticipating the impact of new directions in outsourcing

Global Spending on Contract R&D Services *(2012)*



Source: Tufts CSDD

Tufts Center for the Study of Drug Development
TUFTS UNIVERSITY

Demand for Contract Clinical Services

(Billions USD)	2003	2005	2007	2009	2011	2013e	Annualized Growth
Total Global Development Spending	$33.6	$41.5	$49.6	$54.8	$63.2	$69.7	7.6%
Total Spending on Contract Clinical Services*	$4.9	$6.4	$8.5	$10.1	$12.9	$13.7	14.1%

*Note: Represents 'NET' CRO revenue -- Does not include pass-through clinical services (e.g., central lab fees, investigator grants)

Source: TCSDD

Impact of Transactional Outsourcing on 'Development Speed'

Tufts CSDD Analysis of sponsor data on 83 NDAs and BLAs (2005)

- 'High' CRO usage projects were submitted more than 30 days closer to the projected submission date;
- 'High' usage projects offered a development speed advantage across all measures, most notably during the close-out phase;

	Impact of CRO Usage
Protocol Ready to FPFV*	20% Faster
Protocol Ready to Study Drug Availability	15% Faster
Protocol Ready to LPLV	5% Faster
LPLV to Data Lock*	25% Faster

*Source: TCSDD Study: * indicates significance at P<.01*

Impact of Transactional Outsourcing on Performance 'Quality'

Tufts CSDD Analysis of sponsor data on 83 NDAs and BLAs (2005)

- **No statistically significant differences on measures of performance quality with one exception.**
- **At the conclusion of a project, databases tend to be unlocked more times on projects involving 'high' usage.**
  - **Median time to final database lock, however, remains significantly faster than for projects in which the majority of work is performed in-house.**
- **No evidence to suggest differences in investigative site compliance with GCP**

From Transactional Relationships to Alliances

Transactional Relationships

Ad-Hoc
Capacity-based
Reactive, project task outsourcing
Shadow headcount, sponsor SOPs
Mid-management governance committee
Lowest-bid/Many Providers
High out-of-scope costs/ Fee for service

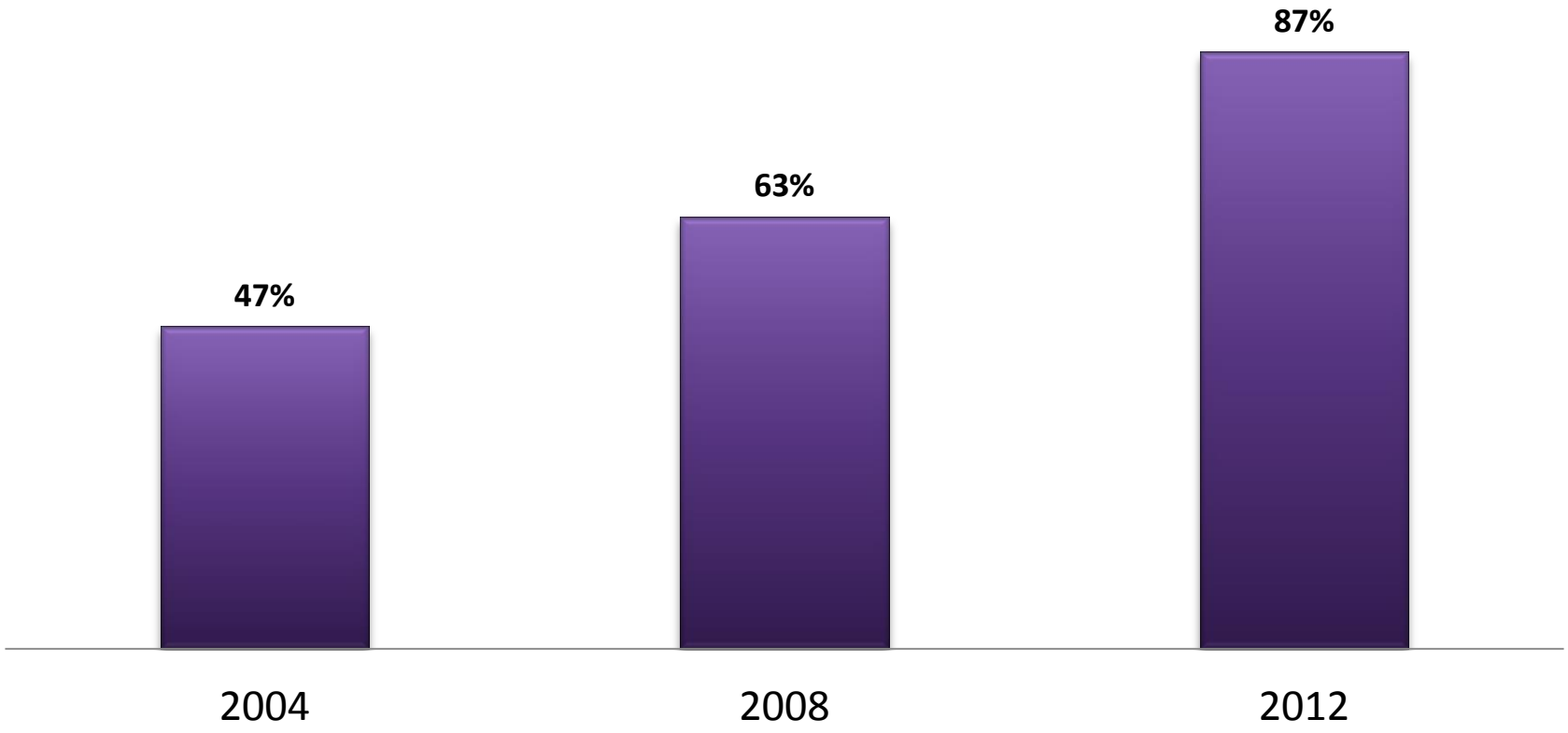
Integrated Clinical Research Alliances

Formalized
Virtual/Competency-based
Planned, portfolio outsourcing
Lean operation, integrated/coordinated
Multi-level shared governance & SOPs
Few Partner-Providers
Shared operating risk/Fixed pricing

Lower transaction costs
More transparency
Greater risk sharing
More motivated staff
Faster start-up
More senior level commitment

Tracking the Transition

Proportion of Top 30 Pharma Companies in at least One FSP/Multi-FSP/Integrated Alliance



Source: CenterWatch, 2013

Tufts Center for the Study of Drug Development
TUFTS UNIVERSITY

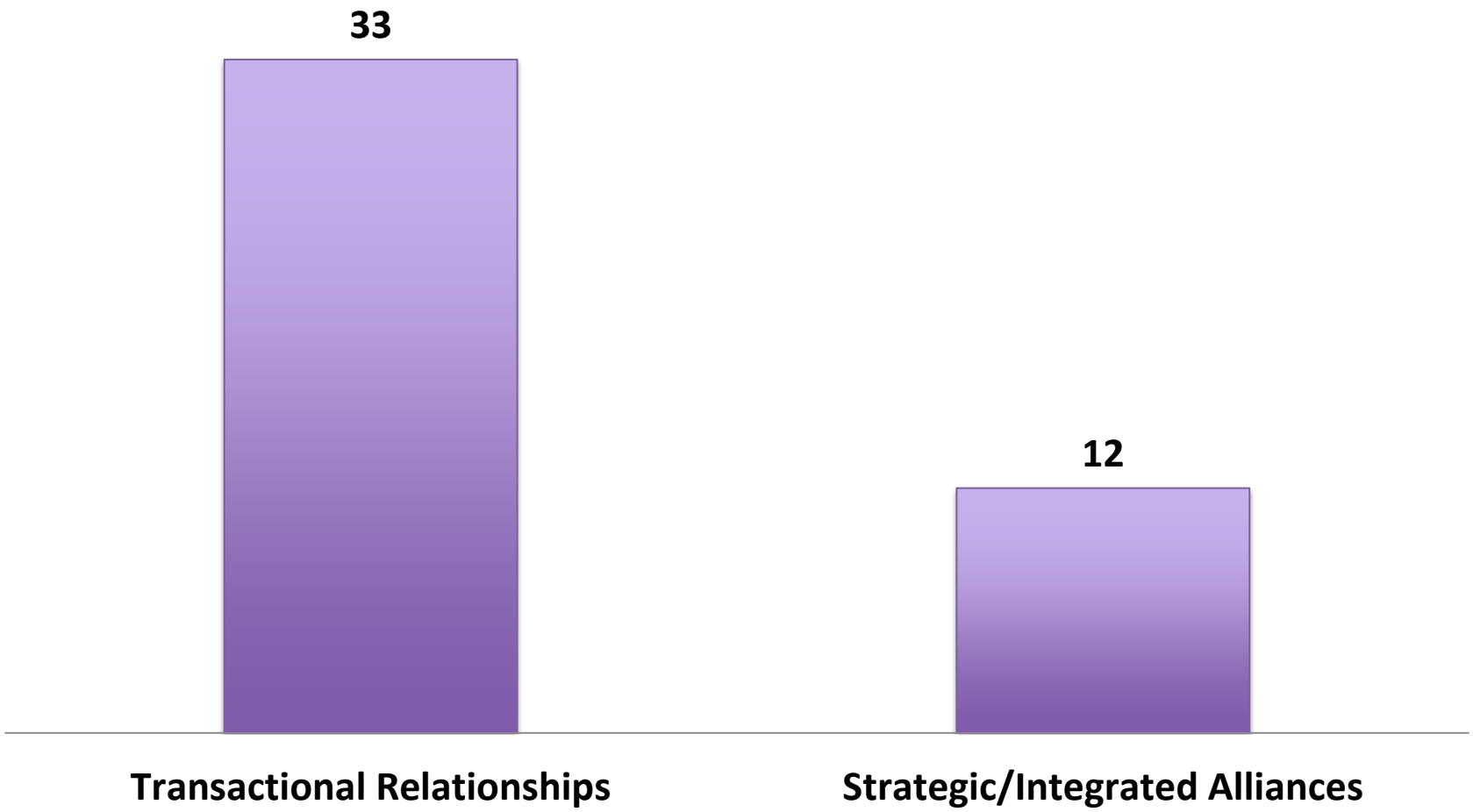
Early Measures of Integrated Alliance Impact

- **Tufts CSDD 2009 study** (N=116 Full Service vs. N=89 FSP/Alliance)
  - Significant start-up cycle time reduction
  - Significantly lower CRO staff turnover rates

- **Pfizer (2010)**
  - $20 million net annual savings from consolidating management of 150 to 17 preferred vendors
  - 18-20% cost savings compared to prior outsourcing strategy
  - 26% enrollment cycle time improvements
  - 80% reduction in number of contracts delayed >120 days

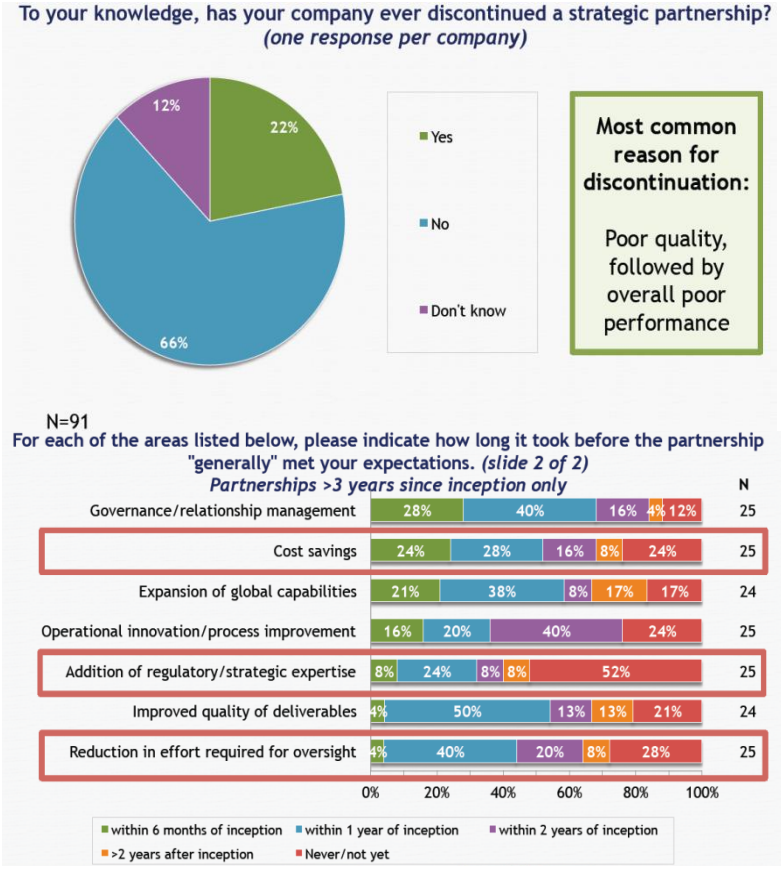
- **Lilly (2011) on DM and Monitoring FSP Relationships**
  - 20% cost savings
  - 50% improvement in probability of site success
  - 38% cycle time improvements
  - 93% improvement in monthly patient enrollment volume

Early Measures:
Average Number of Sponsor FTEs Assigned per Project



Source: Parexel, 2011

A More Complete and Mixed Picture Emerging…



2012 Avoca Group Study

- 22% of sponsors have terminated integrated alliances
- 16% report no cost savings realized
- 17% report no cycle time reductions

2012 Booz & Company Study based on interviews with senior executives:

- Misalignment between outsourcing strategies and the design and structure of relationships
- Suggest tying more explicit performance measures to objectives

Sources: Avoca Group, Booz & Co 2012

Vantage Partners 2012 Sponsor Survey (81 Companies)

- 65% of companies report using fewer than 5 CROs; up from 30% in 2007

- 60% of sponsors in established alliances report that their outsourcing relationships are a more effective way to manage costs vs. competitive bidding

But…

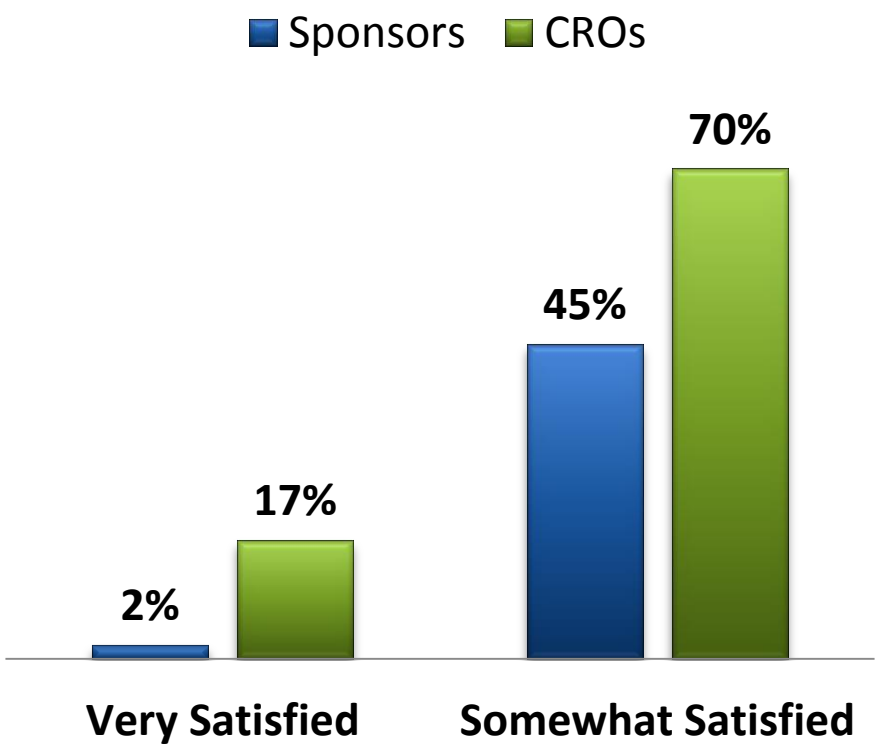
- 30% report that alliances are failing to deliver expected cost and time savings; 56% report that CROs are not delivering innovative solutions

- 48% report that CROs are unable to work collaboratively
  - (57% of CROs (N=88) said the same thing about their sponsor partners)

Avoca Quality Consortium 2013

- **Areas of high relationship dissatisfaction**
  - **Oversight of third party vendors**
  - **Poor communication of requirements and expectations**
  - **Poor communication and inefficient conflict resolution**

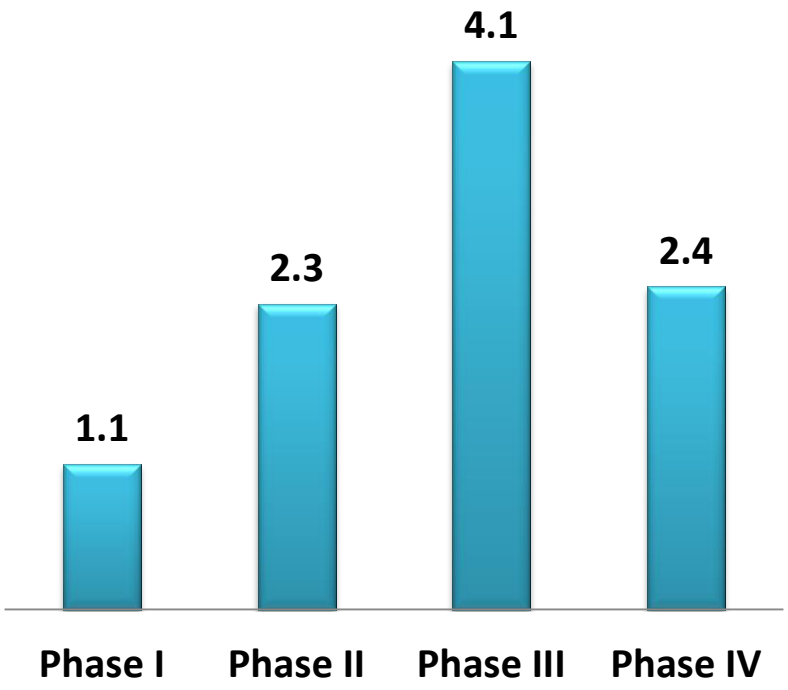
Satisfaction with Relationship Quality and Effectiveness



Tufts CSDD 2012 Study on Change Orders

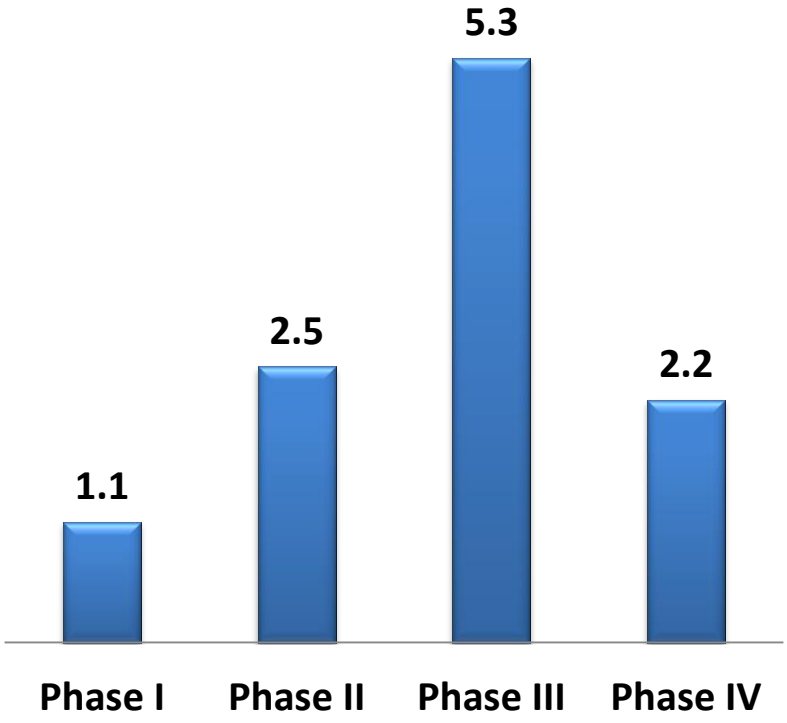
Transactional Relationships

(Average Number per Study)



Integrated Alliances

(Average Number per Study)



Source: Tufts CSDD, 2012

Lessons Learned

Cultural Baggage

- Lack of trust and willingness to transfer responsibility
- Unchanged mindset of CRO as commodity service provider

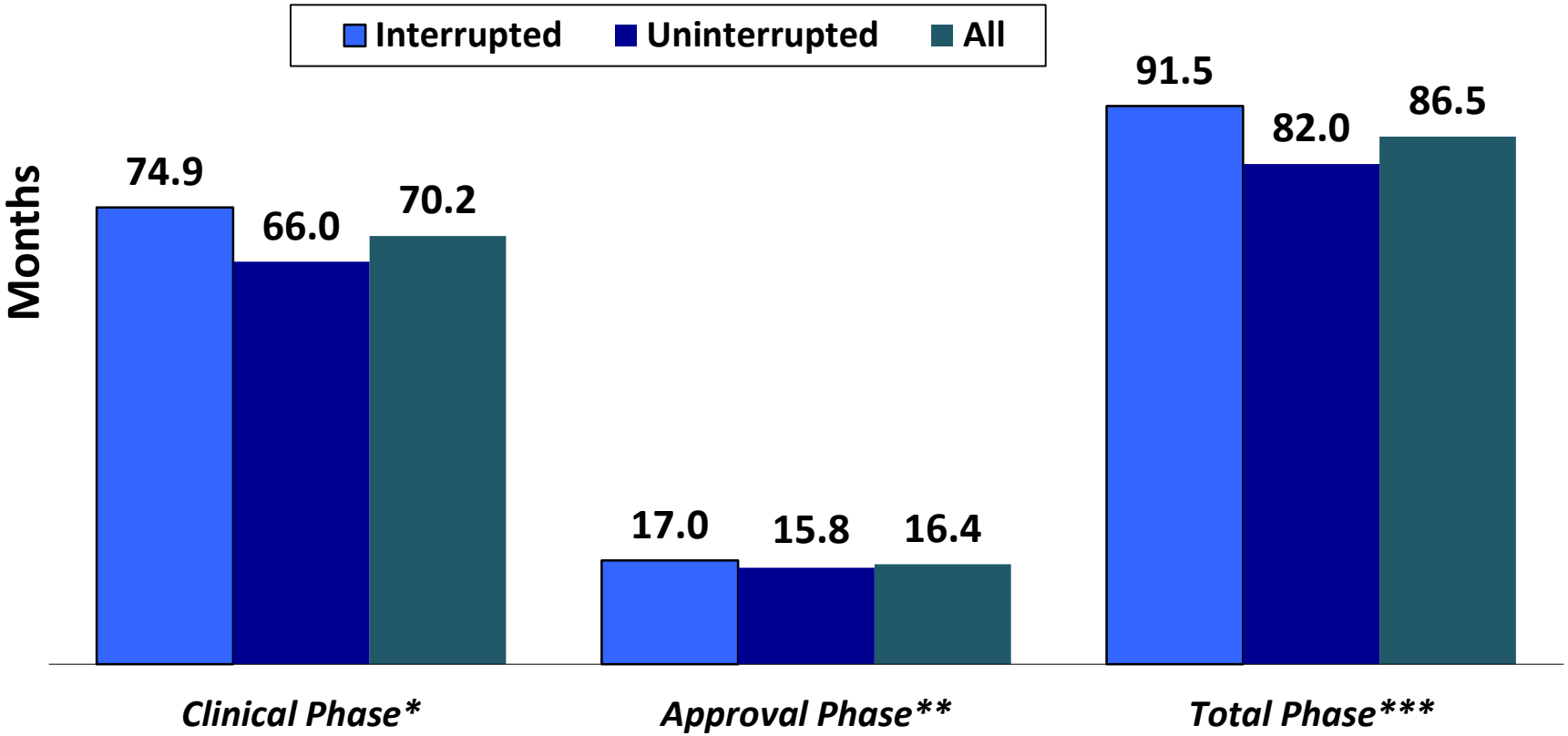
Poorly Structured Relationship

- Unclear and unrealistic expectations
- Poor alignment of policies and operating procedures
- Poorly defined and delineated roles and responsibilities

Poorly Executed Relationship

- CROs granted limited visibility and access to sponsor's development plans, timelines, and cross-functional resources
- Failure to engage headquarters and affiliate staff
- Failure to secure and maintain senior management participation
- Micromanaged or undermanaged collaborate activity
- Delay in addressing and resolving conflicts and issues

Risk-Sharing Collaboration Inefficiencies



* p=0.0131; ** p=0.4147; ***p=0.0116

Source: Tufts CSDD 2013

Customization and the Margin Squeeze

Functional Area	Activities/ Tasks	Proportion Keeping In-house	Proportion Outsourcing	Primary Relationship Models Used
Design & Planning		80%	20%	Niche
Site Operations	Selection	30%	70%	Full, FSP, Alliance
	Contracts & Budgets	40%	60%	Full, FSP, Alliance
	Start-Up	20%	80%	Full, FSP Alliance
	Enrollment	25%	75%	All
Data Management		25%	75%	FSP, Alliance
Statistical Analysis		30%	70%	All
Medical Writing		40%	60%	All
Regulatory	Strategy	85%	15%	Niche
	Support	45%	55%	All

Source: Tufts CSDD 2011 analysis of 36 major pharmaceutical and biotechnology companies

A Lopsided Landscape

Type of Relationship	15 Largest CROs	Midsize/Niche CROs
Transactional (full, niche) services	29%	59%
Functional service provider (FSP)/Multi-FSP services	33%	19%
Integrated alliance services	39%	22%

Source: CenterWatch (N= 40 CRO companies); December 2011

Anticipating Landscape Change

Small CROs

- Focus on small sponsors relying on transactional outsourcing
- Traditional role as specialty providers within fragmented collection of CROs
- Reliance on subcontracted relationships

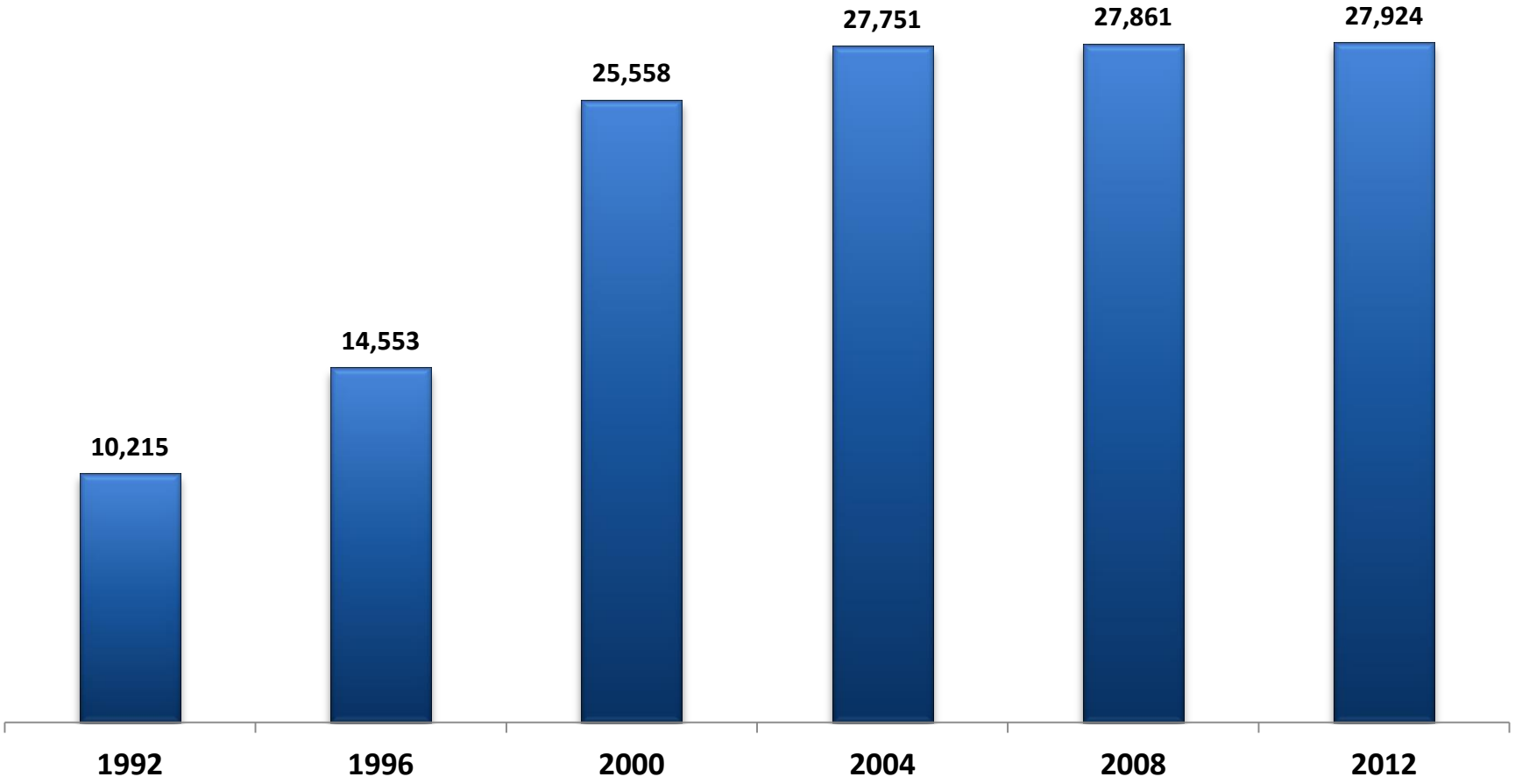
Mid-Sized CROs

- Mixed strategies: focus on transactional market or enter integrated relationship market
- Consolidation (M&A)
- Partnering with specialty and niche service providers

Major CROs

- Aggressive pursuit of market share
- Declining margins; higher fixed costs
- Divestiture and/or expansion into higher margin service areas
- Consolidation
- Focus on more control over performance and efficiency
- Differentiation through novel partnerships

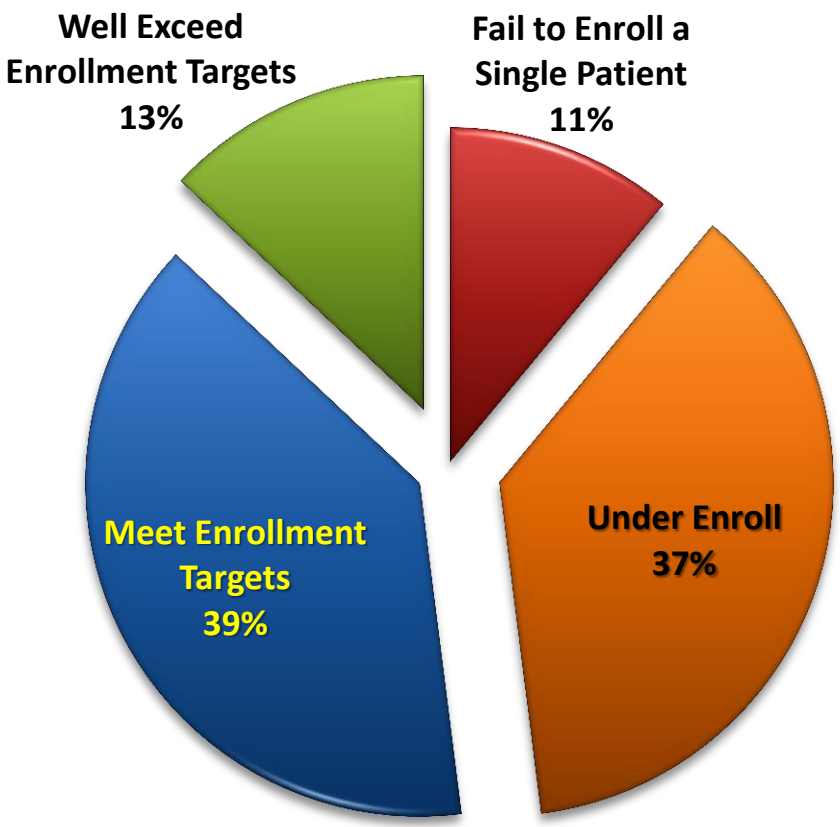
Active Unique Investigators Filing Form 1572s World Wide



Source: FDA's Bioresearch Monitoring Information System File (BMIS)

Key Cost and Cycle Time Driver: Site Performance

(N= 15,965 sites participating in 153 global phase II and III clinical trials)



Source: Tufts CSDD, 2011

Doubling the Time to Complete Enrollment

	2012 Screen to Completion Rates	Increase in Planned Study Duration to Reach Target Enrollment
Overall	56%	94%
Cardiovascular	59%	99%
CNS	61%	116%
Endocrine/Metabolic	41%	113%
Oncology	78%	71%
Respiratory	59%	95%

Source: Tufts CSDD, 2012

Clinical Trial Process Inefficiencies

Phase II/III Programs	Coefficient of Cycle Time Variances
Study Design and Approval	.8
Site Identification	.9
Pre-Visit to Contract/Budget Sent to Site	1.1
Contract/Budget Sent to Site to Contract Execution	1.0
Contract Execution to Site Initiation	1.2
Site Initiation to FPI	1.4
LPLV to Data Lock	.8

Source: Tufts CSDD, 2012

Major CRO Strategies - Short-Term

- More rapid adoption of technology solutions and practices
  - Drive higher levels of coordination and operating control
  - Improve access to investigative sites and study volunteers

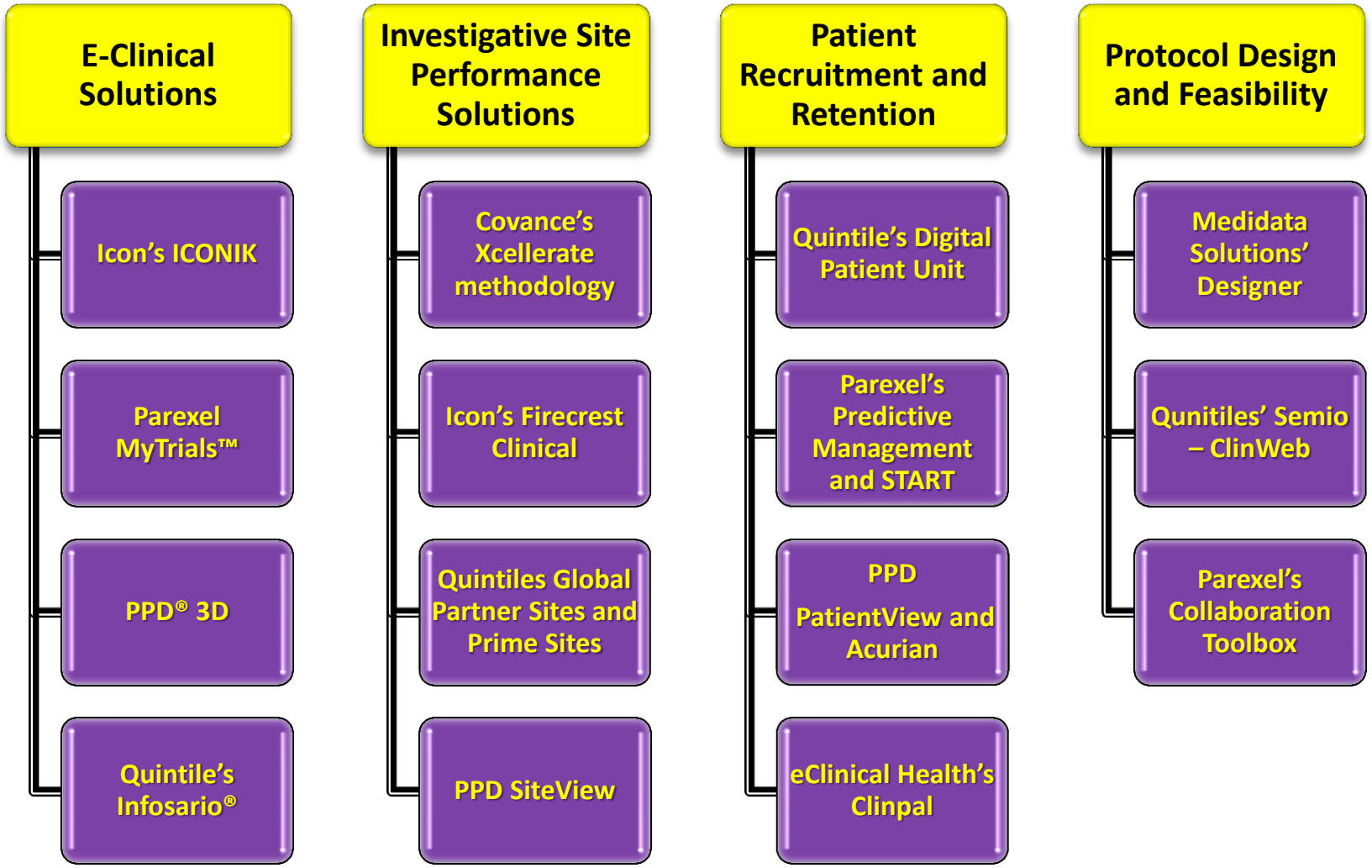
- Reduction in operating complexity
  - Fewer countries
  - Smaller and concentrated numbers of ‘preferred’ investigative sites
  - Improvements in protocol design feasibility

Assistance Reducing Protocol Complexity

Typical Phase III Protocol	2002	2012
Total Number of Endpoints	7	13
Total Number of Procedures	106	167
Total Number of Eligibility Criteria	31	50
Total Number of Countries	11	34
Total Number of Investigative sites	124	196
Total Number of Patients Randomized	729	597
Proportion of data collected that is 'Non-Core'	N/A	25%
Total Number of Data Points Collected*	N/A	929,203

*Source: Tufts CSDD; *Medidata*

Innovate to Add Value and Advantage



Integrating Real-World Data Elements

- Electronic Health Records
- Claims-data
- Payer data
- Patient reported outcomes and perceptions data
- Socioeconomic, Psychographic and demographic data
- Environmental data
- Digital and Social Media data
- Mobile Health applications data
- Operating data

Longer-Term Landscape Changes

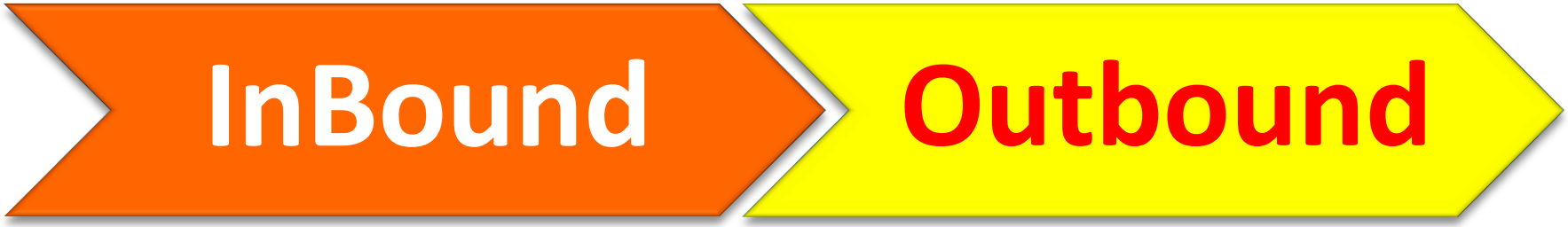
- Changing CRO-Site relationships
    - Acquisitions
    - End-run to major health care provider settings

- New entrants from major life sciences solutions and services companies serving massive health systems (e.g., Cerner, Siemens, Philips)

- New relationships with patient advocacy groups

- Backward and forward integration throughout R&D continuum (e.g., Wuxi Pharmatech; Jubilant)

Open Innovation-Driving Drug Development



Areas of Focus	**Target Identification and Validation** **Lead Identification and Optimization** **Preclinical Testing**	**Clinical project management and operations** **Study Conduct** **Data collection, management and analysis** **Post-approval project management and operations** **Learning health system informed development**
Partners	**Universities** **Small biotech** **Niche/specialty providers**	**CROs** **Investigative Sites** **Patients** **Health Systems**

Q&A and Thank You!

Ken Getz, Director of Sponsored Research and Associate Professor

CSDD, Tufts University School of Medicine

617-636-3487

Kenneth.getz@tufts.edu