



MILLENNIUM[®]

THE TAKEDA ONCOLOGY COMPANY

The Takeda-Millennium Acquisition: The Clinical Outsourcing Roadmap to Market Leadership in Oncology

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**19th Annual Partnerships
in Clinical Trials 2010**

Millennium: The Takeda Oncology Company



- Fully integrated biopharmaceutical company
- Focus in oncology
 - Global product and marketing strategy
 - Global development function
 - Drug discovery
- Founded in 1993
 - Headquartered in Cambridge, MA
 - Approximately 1,200 employees
 - Wholly-owned subsidiary of Takeda Pharmaceuticals (May 2008)

Takeda Pharmaceutical Company, Ltd.



- Leading pharmaceutical company in Japan
 - Metabolic and cardiovascular
 - Oncology and urological
 - CNS, bone & joints
 - Gastroenterology
- Deep roots, more than two centuries
- Founded upon strong values
 - Perseverance, fairness, honesty
- Clear mission
 - Better health for individuals and progress in medicine by developing superior pharmaceutical products
- Global vision

Our Mission

- Build Takeda to a leading **global oncology company**
- Drive better patient outcomes and improve standard of care through a high quality portfolio of **clinically-differentiated products**
 - Strive for a development pipeline containing '**best-in-class**' or '**first-in-class**' compounds
 - Ensure **diversity in oncology target pathways** and treatment modalities (e.g., targeted therapeutics, antibodies)
 - Ensure consistently **full clinical development pipeline** of 11–14 ongoing projects
- Build a **strong reputation** as a science-driven, patient-oriented oncology company

Major inflection point in May 2008

- Became an autonomous oncology business unit responsible for worldwide strategy and execution of oncology development portfolio
- Pipeline growth required new operating model
 - Increase from 4 to 14 molecules in development
 - Expansion in broader tumor types (i.e. prostate)
- Global Responsibilities

The Millennium Pipeline

Global Oncology Pipeline

			Preclin	Phase I	Phase II	Phase III
Protein Homeostasis	MLN4924	NAE Inhibitor				
	MLN9708	Proteasome Inhibitor				
Anti-Angiogenesis	motesanib*	VEGFR/PDGFR Inhibitor				
	tandutinb	PDGFR Inhibitor				
	AMG386**	Anti-Angiopoietin Peptibody				
	TAK-593	VEGFR/PDGFR Inhibitor				
Growth Signaling Inhibition	TAK-285	HER2/EGFR Inhibitor				
	TAK-701*	HGF Antibody				
	TAK-733	MEK Inhibitor				
	AMG479**	IGF-1 R Antibody				
Cell Cycle Inhibition	MLN8237	Aurora A Kinase Inhibitor				
	SGN-35*	Anti-CD30				
	CBP501*	Cell Cycle Dysregulator				
	TAK-901	Aurora B Kinase Inhibitor				
Hormone Regulation	TAK-700	Androgen Synthesis Inhibitor				
	TAK-448	Metastin Analog				
Apoptosis Inducer	conatumumab**	DR5 Antibody				
Immunomodulator	mlfamurtide‡	Macrophage Activator				

ADDITIONAL INDICATIONS / NEW FORMULATIONS

Protein Homeostasis	VELCADE®	Proteasome Inhibitor (Follicular NHL, First Line MCL, Subcutaneous Formulation)				
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* In-Licensed

† Japan Only Developed by TBDC

‡ Approved in EU only

- Motesanib diphosphate is being developed by Millennium in collaboration with Amgen, Incorporated

- CBP501 is being developed by Millennium in collaboration with CanBas Limited

- SGN-35 is being developed by Millennium in collaboration with Seattle Genetics, Inc.

- VELCADE® is co-developed by Millennium and Johnson & Johnson Pharmaceutical Research & Development

These compounds are either investigational or studied in new indications. Efficacy and safety have not been established.

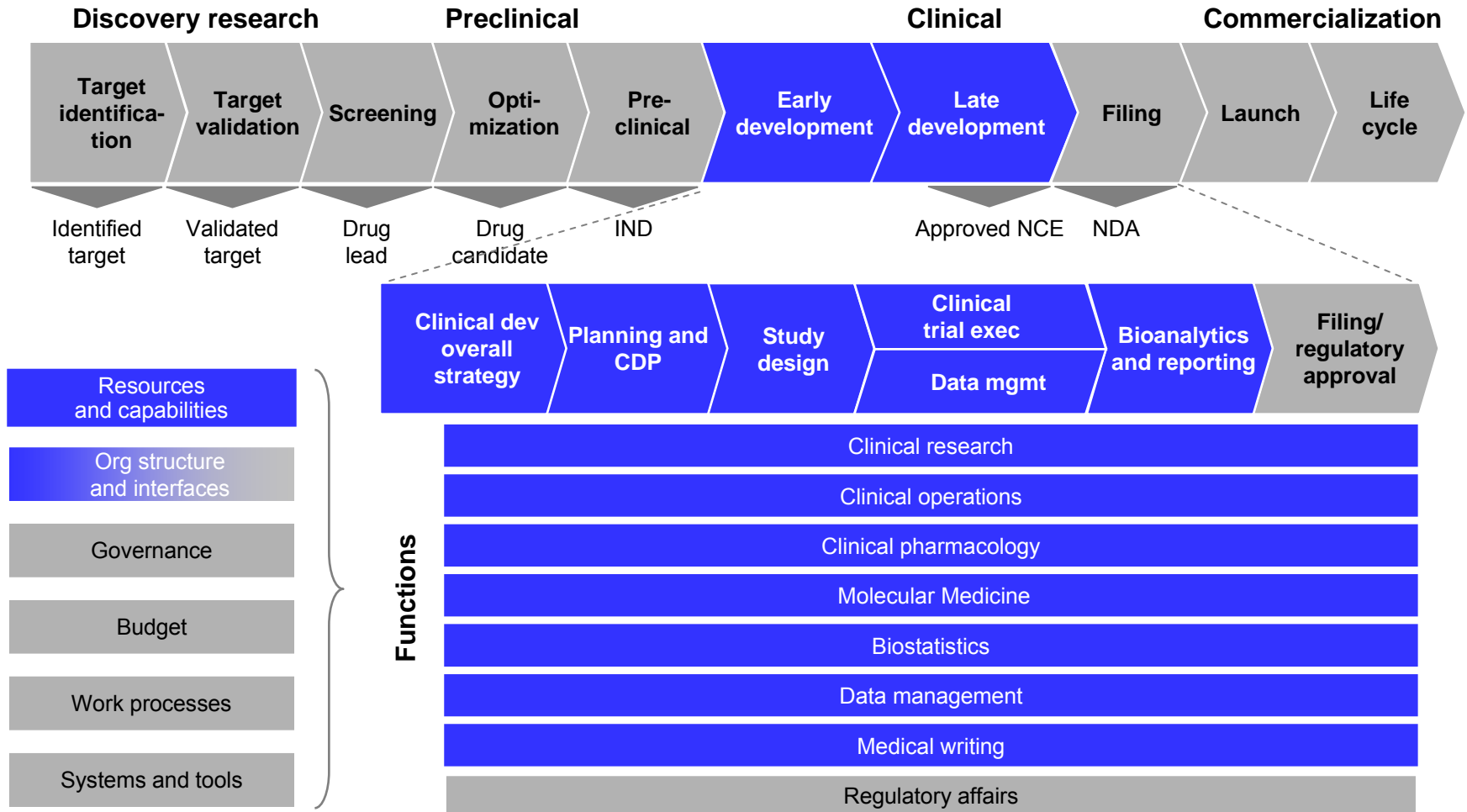
Key challenges

- 1 Shifting focus from local to global development
- 2 Dealing with a more complex set of interfaces (upstream and downstream, with Discovery and Commercial)
- 3 Expanding the scope of Development activities
- 4 Rethinking the capabilities required, and upgrading them accordingly
- 5 Rethinking and adjusting capacity needs in order to seamlessly prosecute the pipeline
- 6 Achieving scalability in conducting clinical development

Millennium's Unique Opportunity

- Blank slate
 - Process of piece meal outsourcing needed to be redesigned
 - Existing processes not scalable to volume of work
 - Limited number of commitments to full-service global CROs in place
- Engaged BCG to work on sourcing strategy

Redesign Project



■ In scope ■ Out of scope

ICS framework

Innovative/Unique

Customized

Standardized

Classification

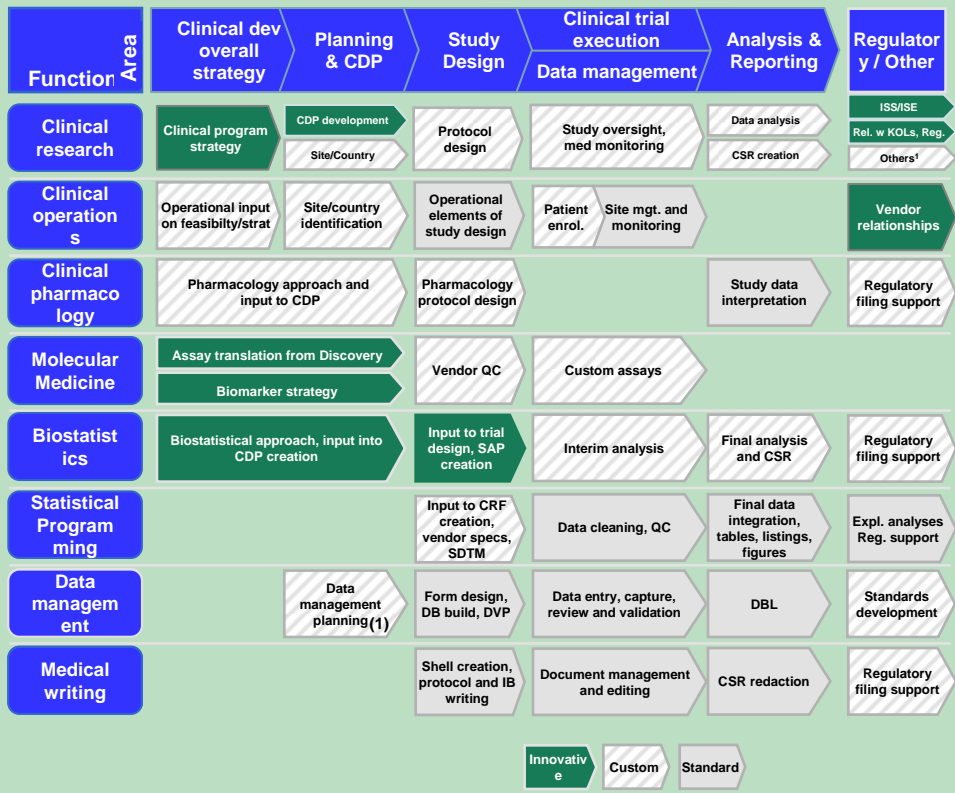
Common language

Defines the nature of an activity

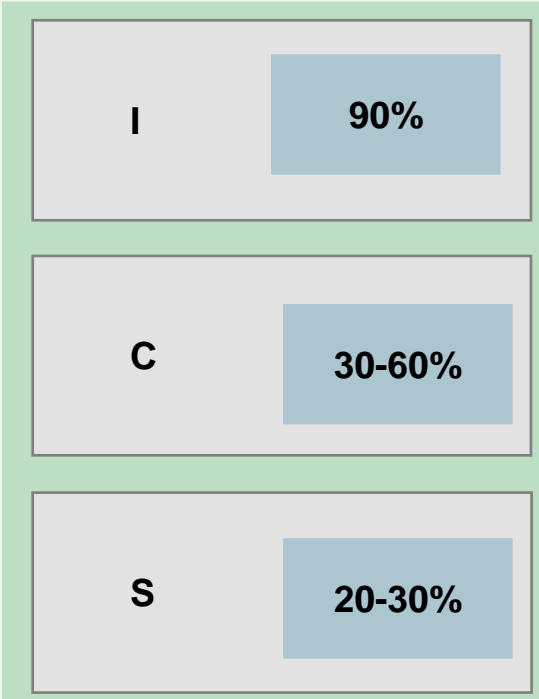
Helps guide goal, extent and nature of sourcing

Each activity was mapped

ICS classification

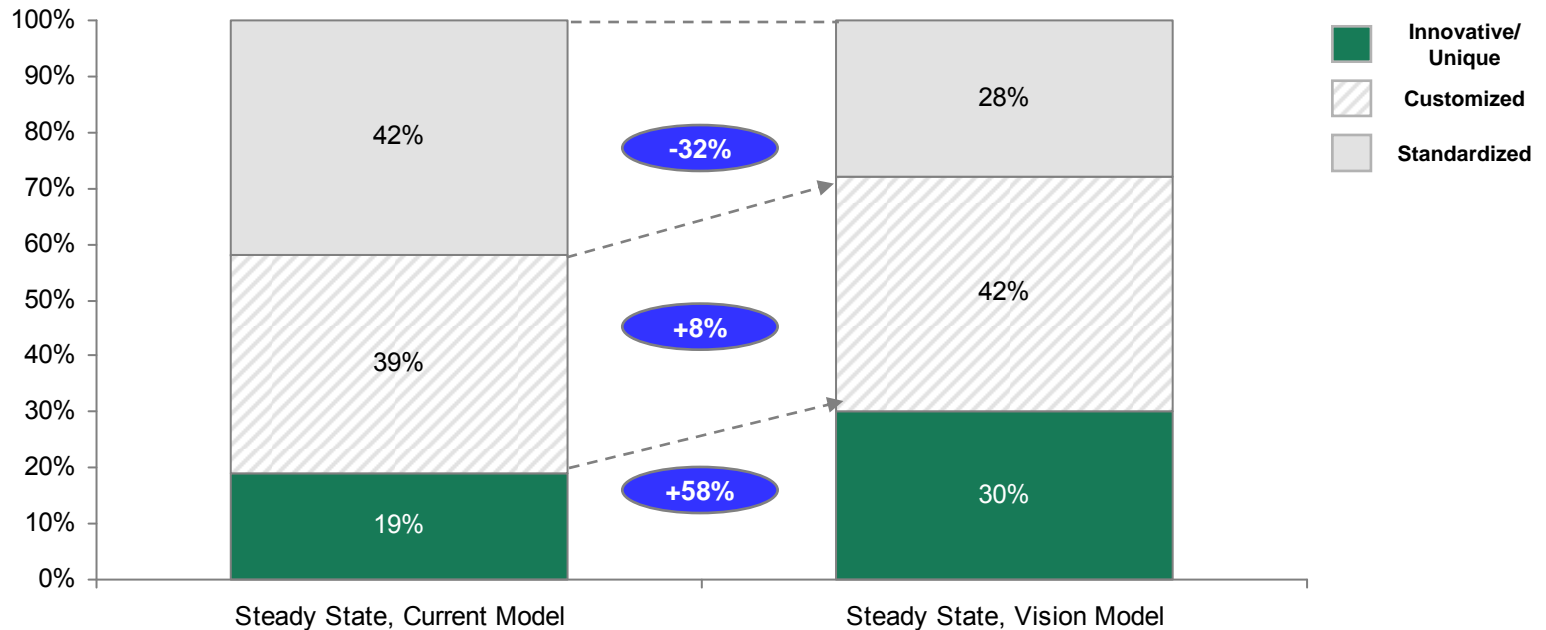


% Activities retained in-house



Shift of internal focus

- Under vision, standardized work decreases by a third, shifting internal focus to innovative activities



Perspectives on Standards

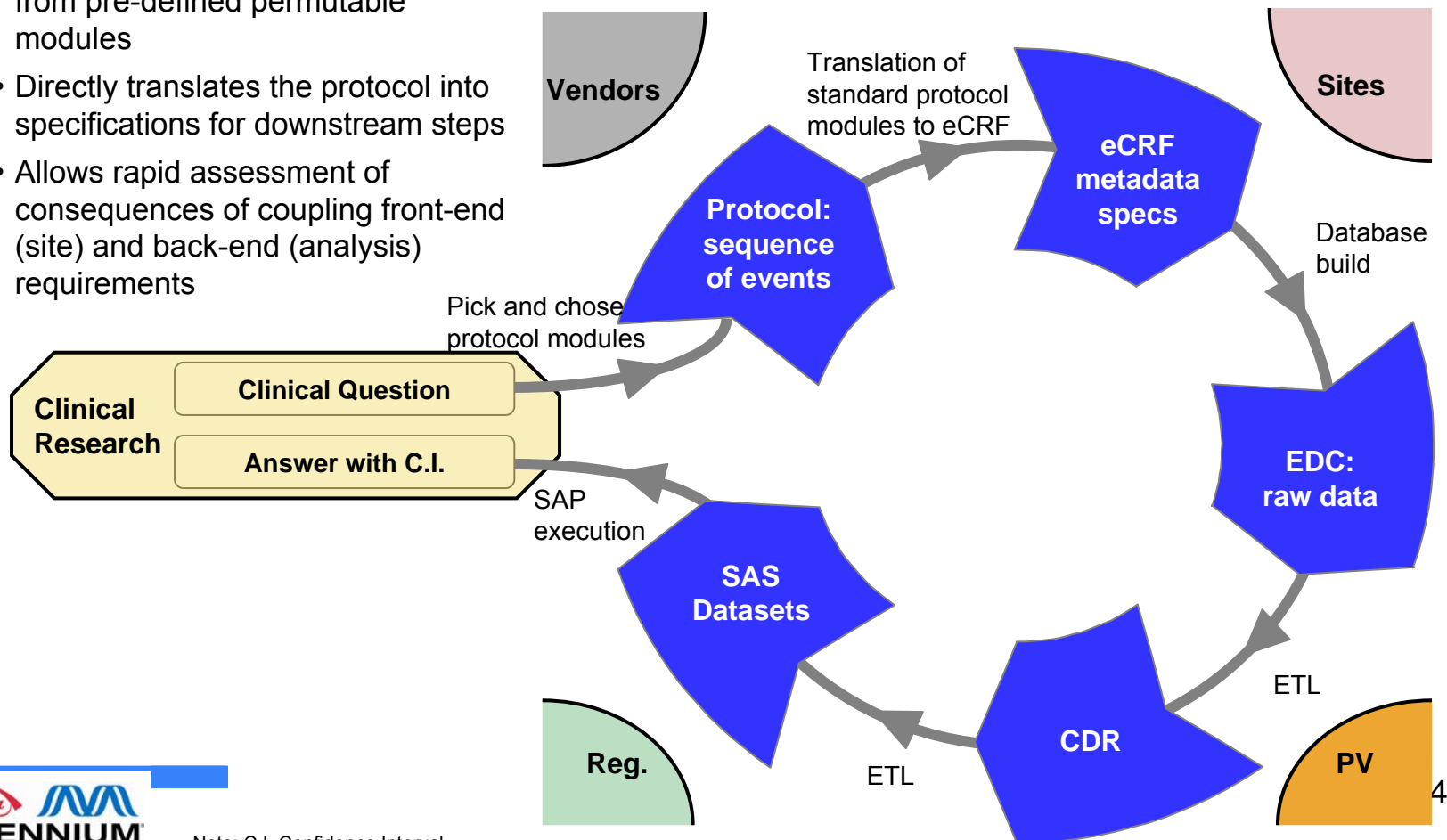
- Drive scalability by enabling a "build once, use many" approach
- Allow more extensive and more streamlined sourcing
- Enable clarity on beginning-to-end implications of a study data strategy prior to commitment to a specific plan
- Allow rapid testing and implementation of innovative technologies through modular Standards approach
- Reinforce Millennium branding and market differentiation with clinical sites through consistent usage of Standards

Study Standard & Implementation Group Formed

End-to-end consistency at set-up

A fully implemented Standards approach:

- Enables the creation of a protocol from pre-defined permutable modules
- Directly translates the protocol into specifications for downstream steps
- Allows rapid assessment of consequences of coupling front-end (site) and back-end (analysis) requirements



Outsourcing strategies considered

- Compound partnering
- Full-service CRO options
- Functional Service Providers (FSPs)

The Millennium Outsourcing Model

Large full-service provider model selected for program execution

- ❑ Global and therapeutic expertise
- ❑ Resources to meet rapid program expansion
- ❑ Integrated outsourcing more efficient

Specific strategic exceptions to the full-service CRO model are part of the strategy

- Pharmacovigilance – Functional Service Provider
- Regulatory Strategy – Specialty consulting engagements
- Medical Writing – Multiple FSPs for staff augmentation

Flexibility based on potential need for exceptions is built into the strategy

- Governance includes exception process built on business case
- Potential exceptions – joint ventures, First in Human, etc.

The Millennium Outsourcing Model

- Volume of work indicated need for three global full-service CROs
- Cross-functional Preferred Provider Selection Team
 - RFI, capabilities presentations, functional break-out sessions
 - Functionally oriented Business Terms
- Final selection based on evaluation that all three CROs can provide equivalent expertise
- Work allocated to keep CROs substantially equally engaged
- Relationships are evolutionary and expected to adapt to changing circumstances over time
 - Continuous improvement is integral to the strategy

Sourcing vision statement for Clinical Development

We aspire to be among the **top oncology development organizations** by 2020.

We believe that we will best achieve this by leveraging the drive of a **small core team focused on activities that enable competitive advantage**, while delegating all other tasks to an extended network of partners

Our key sources of competitive advantage will build on

- (i) **setting clinical strategy,**
- (ii) **developing and nurturing global relationships with KOLs, regulatory agencies and preferred partners in oncology,**
- (iii) **learning from innovative work in clinical development and translational medicine, and**
- (iv) **orchestrating and overseeing complex workstreams and vendor partnerships toward drug registration and approval.**

Given these areas of focus, **most late development studies will be sourced to select full service CROs**. Depending on level of pre-specification, early development studies will be addressed on a case-by case basis. Generally innovative studies will largely be retained in house

Activities that are generally executional in nature will largely be externally sourced. Our ability to **define rigorous and effective standards and build deep relationships with a small number of sourcing partners will therefore be key to our success**

Challenges of New Sourcing Vision

Gap between espoused sourcing strategy and execution

- Poor understanding of strategy
- Limited buy-in from key stakeholders
- Inadequate internal capabilities, including vendor management capabilities, to execute on strategy
- Lack of standardization, system and processes for smooth knowledge and data transfer execution
- Insufficient understanding of supplier capabilities
- Insufficient investment in relationship-building over time

Adversarial mindset and untrusting approach

- Duplication of work and driving high transaction costs

Implementation of new sourcing strategies based only on traditional or existing sourcing models

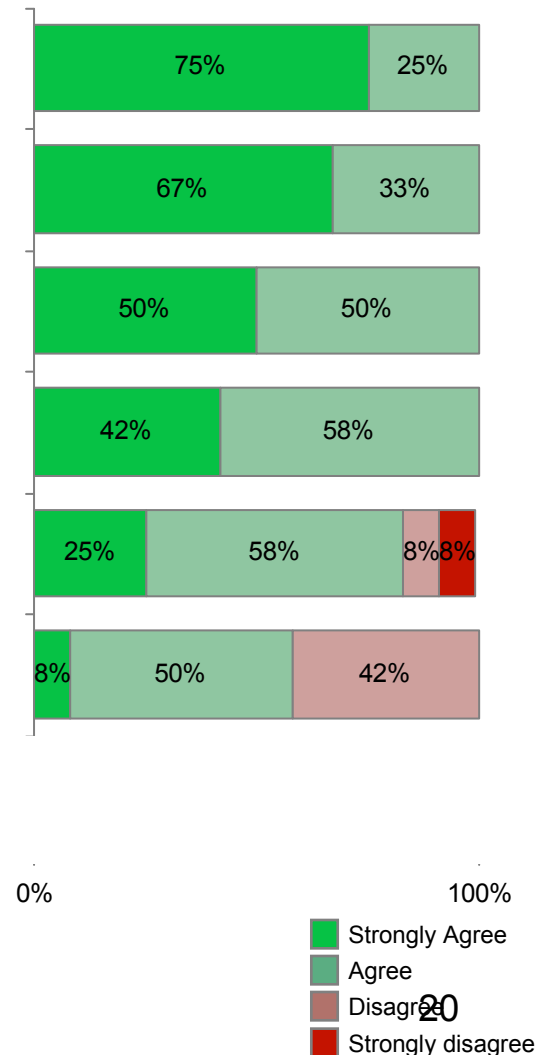
- Reliance exclusively on past experiences
- Unwillingness to experiment and challenge common beliefs

Becoming a sponsor of choice

Building a Millennium reputation as an ideal sponsor to work with

Change Management: Surveys

1. I believe change is required
2. I would like leadership to further provide and communicate a clear plan and pathway for changes that need to occur
3. Given that the new organization is likely to rely significantly more on outsourcing, I believe it will continue to provide challenging and stimulating environment for me
4. I am willing to accept changes to my role to enable the vision.
5. We have the capabilities to execute on the vision
6. My colleagues are ready, willing and committed to change, included any necessary change of their role and realignment of the organization



Multi-faceted Change Management Process

- Creation of Clinical Outsourcing group
- Communications Strategy
 - Medical Sourcing Vision Portal
- Governance committees
- Revised job descriptions
- Training on new roles, outsourcing

Sponsor of Choice: Survey with investigators

Promise of drug

- ❑ Trumps most other considerations – KOLs will work with anyone if the molecule/target is of interest to them, and will avoid programs that they see of limited promise
- ❑ Contacts with scientists who truly understand the molecule and the pathway are important, *"Academic bent of Millennium is a plus"*

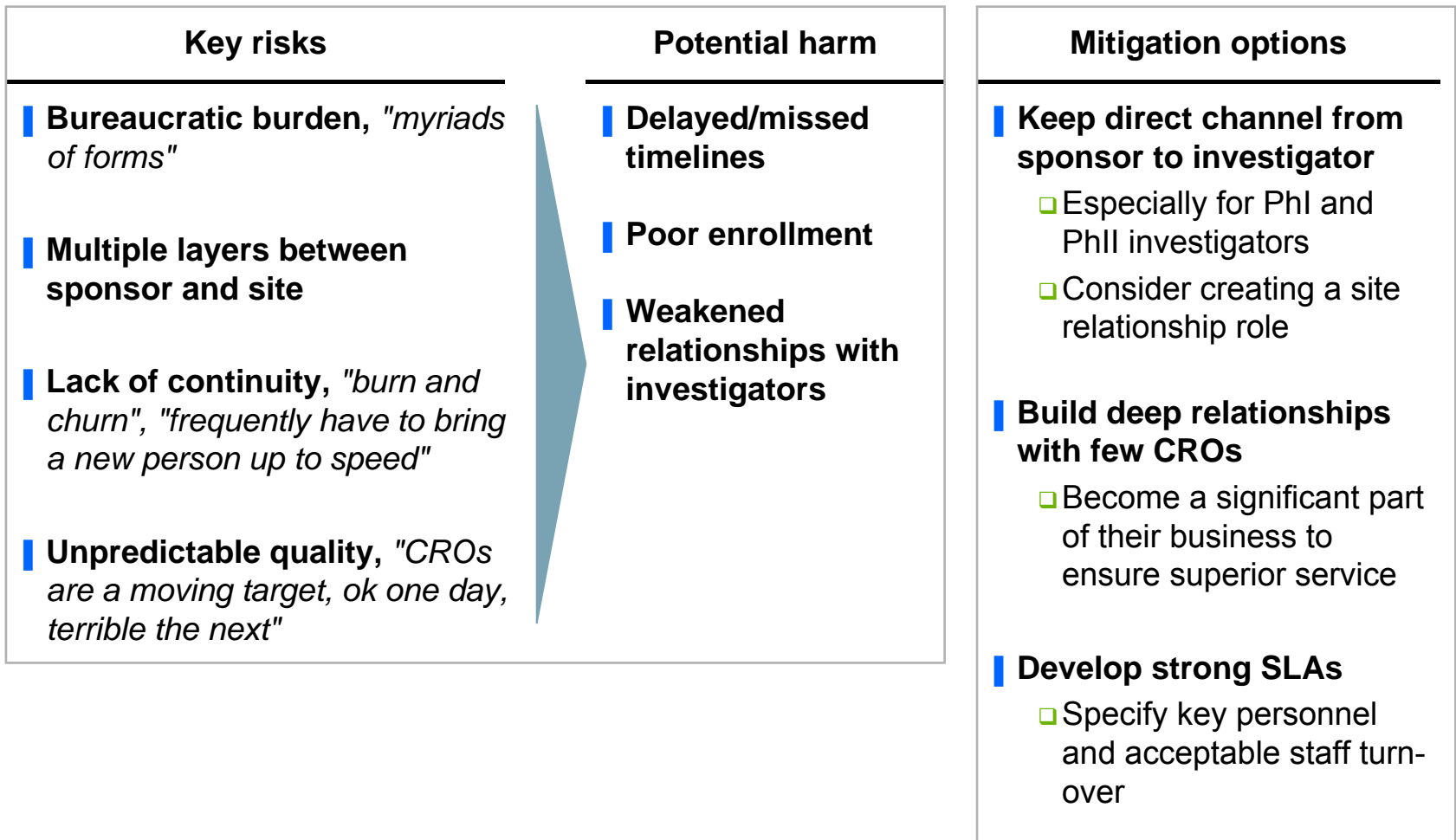
Patients come first

- ❑ Full disclosure of preclinical and on-going clinical information relevant to patients
- ❑ Credibility enhanced by liberal publication policy

Being heard

- ❑ Input to study design – *"Most pharmas ask for my input but don't seem to take it into account in any way"*
- ❑ Input for modifications of an ongoing study
- ❑ Consistent answers from staff across the organization (Clinical Research, Medical Affairs/MSLs)

Impact of using CROs on investigative sites: risks and mitigation



What differentiates the MLNM approach?

- Significant focus on change management
 - Reoriented job descriptions and organizations
 - Created Clinical Outsourcing group
 - Created SSI
- Strategy of integrated working relationships
 - Between Millennium and each CRO
 - Between CROs on Millennium processes
- Functional integration
 - Technology and CTMS
 - Standards for data and programming
 - Business Operations with CROs

Where are we today?

- Finalizing Master Service Agreements
- Awards under new relationships already underway
 - Program awards
 - Integrated teams being formed
- Governance implementation initiated
 - Steering and Operating Committees
 - Senior Relationship Managers

Vision for the future

- Ongoing program of process improvements
- Joint “learnings” forums across partners
- Implement metrics
- Millennium-specific career opportunities within CROs
- Millennium will work to become “Sponsor of Choice”
- Achieve continued efficiencies without continuous pressure on CRO margins



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We Aspire to Cure Cancer[™]