Report of the Sarcoma Progress Review Group: A Roadmap for Sarcoma Research

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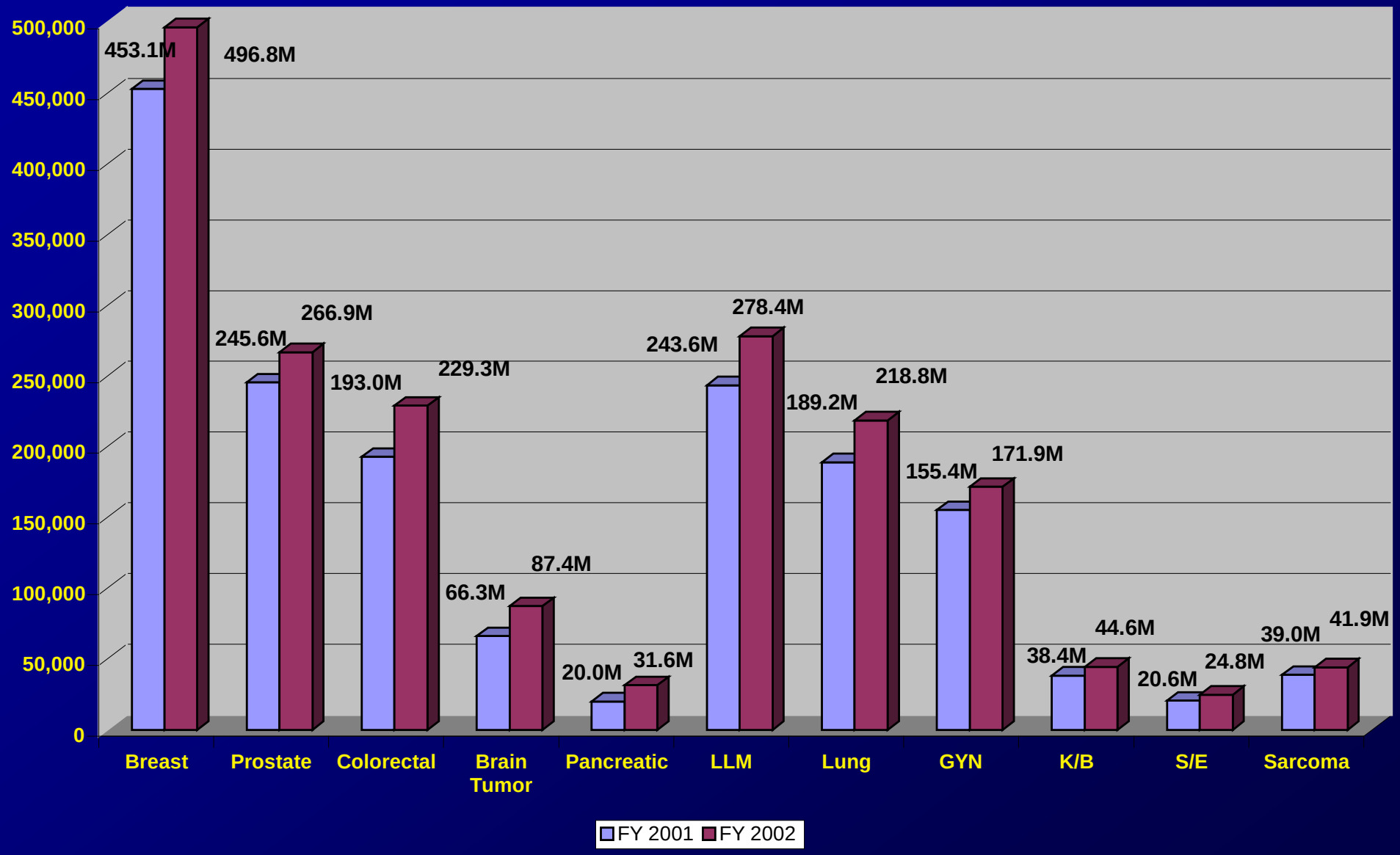
Sarcoma is a Rare Disease

- Difficult to diagnose
- Sarcoma is a group of heterogeneous diseases- therefore clinical studies are very difficult to do in defined categories
  - Currently, this leads to sarcoma studies receiving low priority in the cooperative group structure
- Diagnosis is often delayed as patients with “lumps and bumps” often referred to general surgeons who don’t see these diseases
- Current diagnostic coding systems categorized by location, yet sarcomas are not site specific

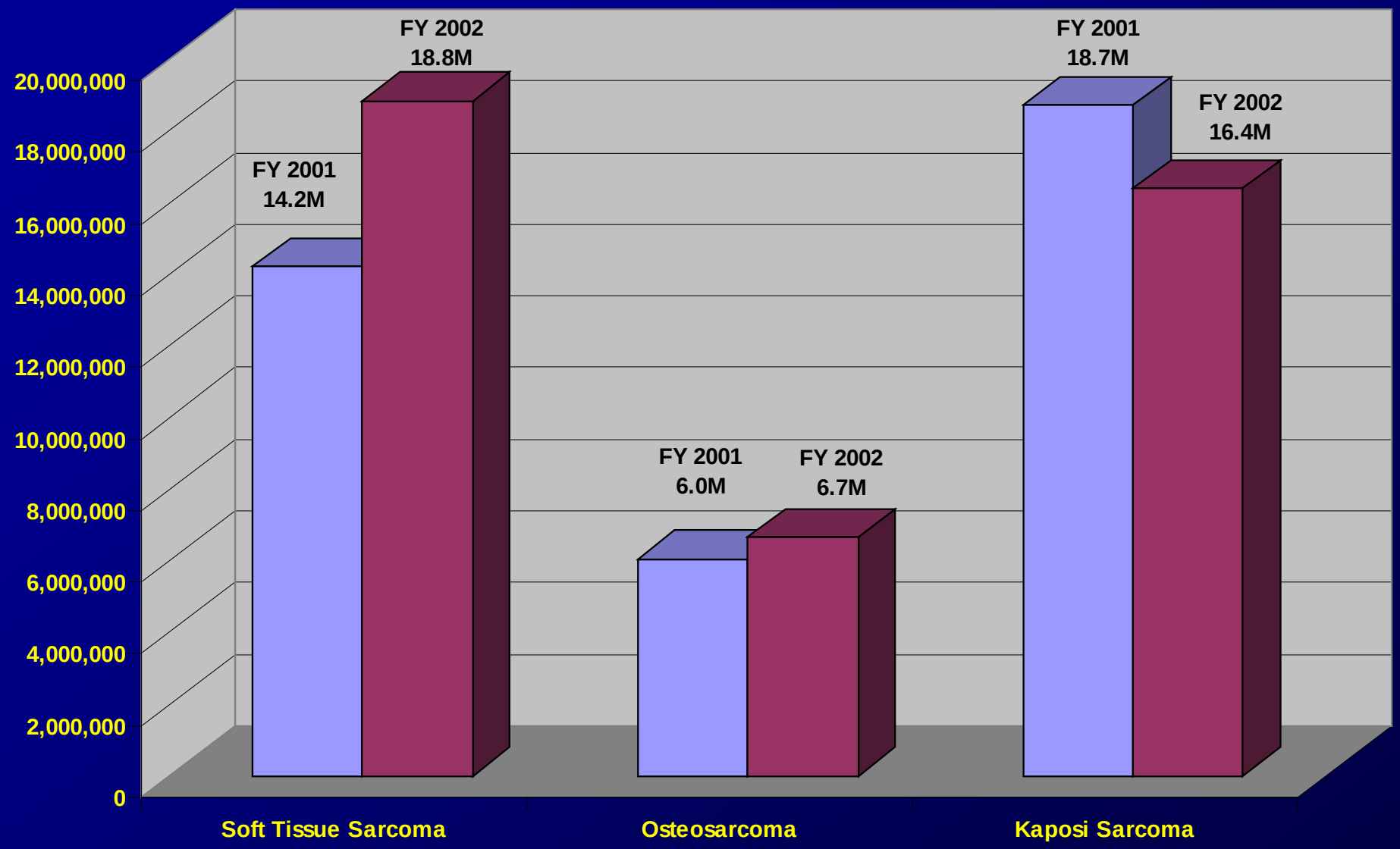
ACS Estimates: Bone & Soft Tissue Sarcoma

	Incidence	Death
Sarcoma	11,600	5,800
Hodgkin's	7,400	1,300
Testis	7,200	400
Lung	169,500	157,400
Colorectal	135,400	56,700
Breast	193,700	40,600

NCI Extramural Funding Estimates by PRG-focused Sites



NCI Extramural Funding Estimates by Sarcoma PRG-focused Sites



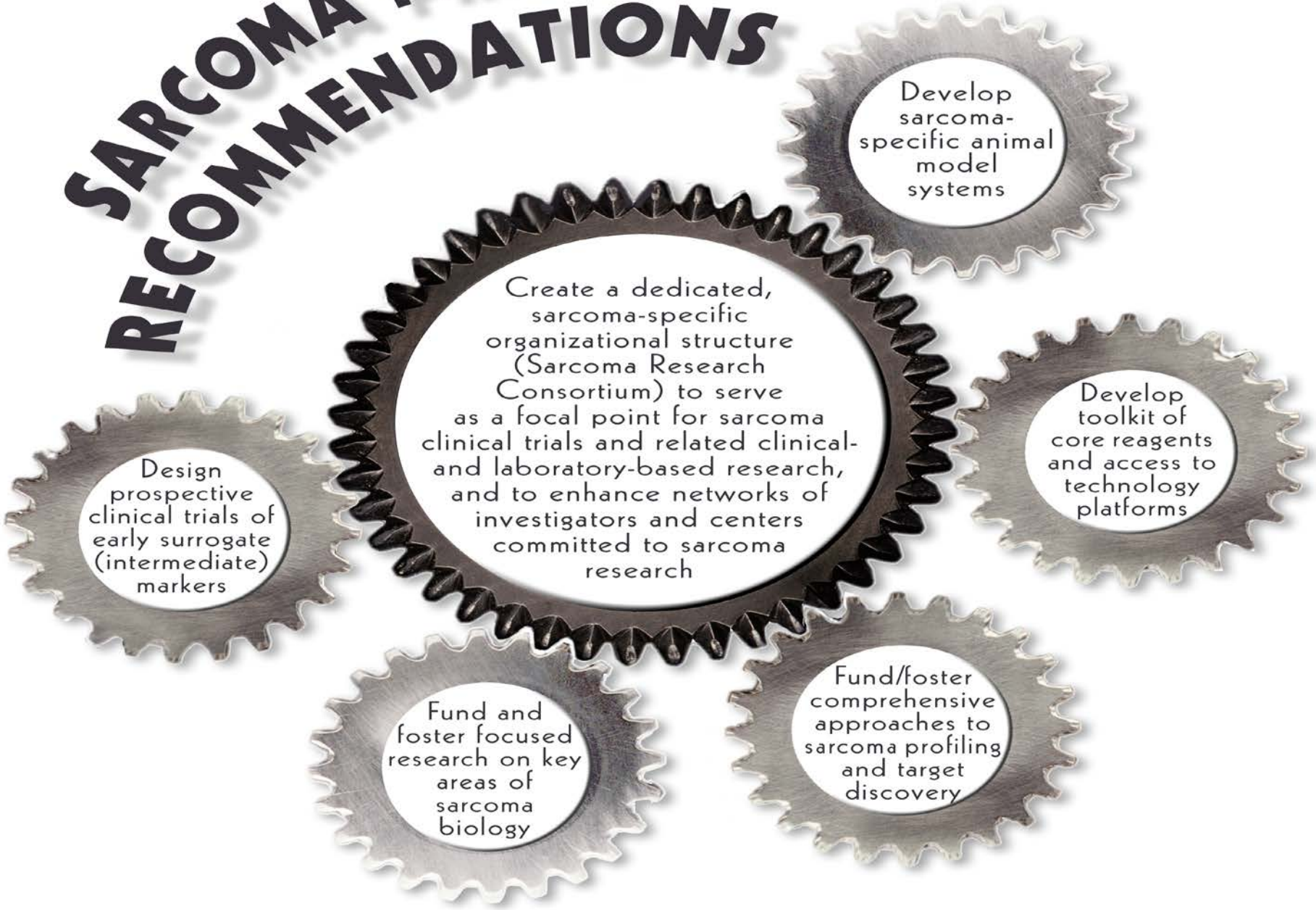
The Good News

- Genetic studies demonstrate sarcomas segregate into two major distinctive categories- those with tumor-specific recurrent chromosomal translocations and simple karyotypes, and those without specific chromosomal alterations, and complex karyotypes
- When diseases are defined by specific genetic characteristics, patient numbers may increase and clinical studies are better and easier to perform (GIST)

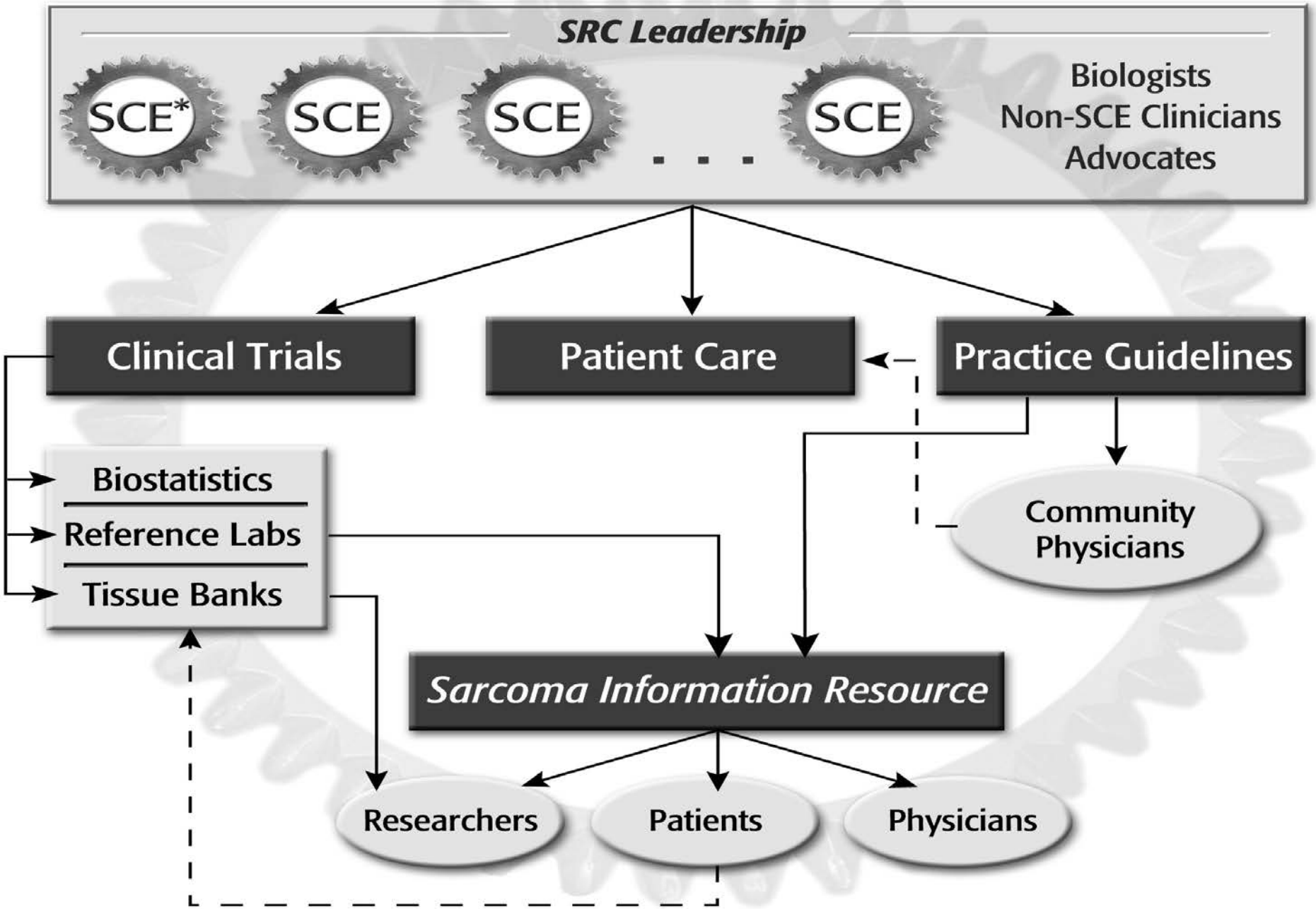
Opportunity

- We believe the development of an effective structure to accelerate the pace of progress in the treatment of sarcomas could serve as a model for many other rare diseases

SARCOMA PRG RECOMMENDATIONS



SARCOMA RESEARCH CONSORTIUM (SRC)



Priority: Fund and foster sarcoma biology research

- Mesenchymal developmental biology
- Targets of mutation in signaling pathways

  (e.g. Kinases)
- Downstream targets of fusion proteins
- Apoptosis pathways relevant to sarcoma
- Sarcoma immunology

Priority: Develop sarcoma animal models

- Capitalize on genetic understanding of many sarcomas
- Move study beyond simple growth assays

  (e.g. Metastasis)
- Toward biological understanding
- Toward pre-clinical development

Priority: Fund & foster comprehensive approaches to sarcoma profiling & target discovery.

Approaches include:

- **Comprehensive sarcoma profiling (genome, transcriptome, & proteome)**
- **High-throughput screens & functional genomic approaches**
- **Goals: to identify novel therapeutic targets, critical pathways regulating sarcoma growth & survival, markers for diagnosis, susceptibility, & prognosis, to predict treatment response & define intermediate endpoints.**

Priority: Fund & foster comprehensive approaches to sarcoma profiling & target discovery (cont.).

- Sarcoma profiling: currently fragmented; focuses largely on expression profiling.
- Understanding of specific sarcomas elusive.
- Because targeted screening of specific pathways is limited by current knowledge of sarcoma biology, screening (compounds, RNAi, & functional genomics) may identify novel targets associated with pathways not currently implicated in sarcomagenesis..
- NCI & NIH recognize molecular profiling & targeted therapeutic interventions as integral to future research & highlight them in their strategic plans & roadmaps.

Priority: Develop centrally available sarcoma research toolkit of core reagents (including cell lines, model systems, annotated tissue banks, biomarkers, & imaging) and access to technology platforms

- **Toolkit will enable new technology to define novel & valid biomarkers, imaging, & surrogate markers to take advantage of the unique biology of sarcoma subsets & encourage rational, targeted, & timely clinical development.**

Priority: Develop centrally available sarcoma research toolkit (cont.)

- NIH Roadmap (“New Pathways to Discovery” theme) highlights need for a “toolbox” that consists of technologies, databases, & other scientific resources.
- NCI’s Strategic Priorities include regional network of high-throughput laboratories for existing & emerging biomarkers of cancer risk, to facilitate collaborative development of national, regulatory-compliant, privacy-protected, standardized annotated biological samples.

Priority: Design prospective clinical trials whose principal objective is to compare early surrogate (intermediate) markers to conventional endpoints

Tightly linked to appropriate tissue banking & incorporate novel statistical methodologies appropriate to sarcomas

Conducted concurrently with a series of innovative therapeutic trials

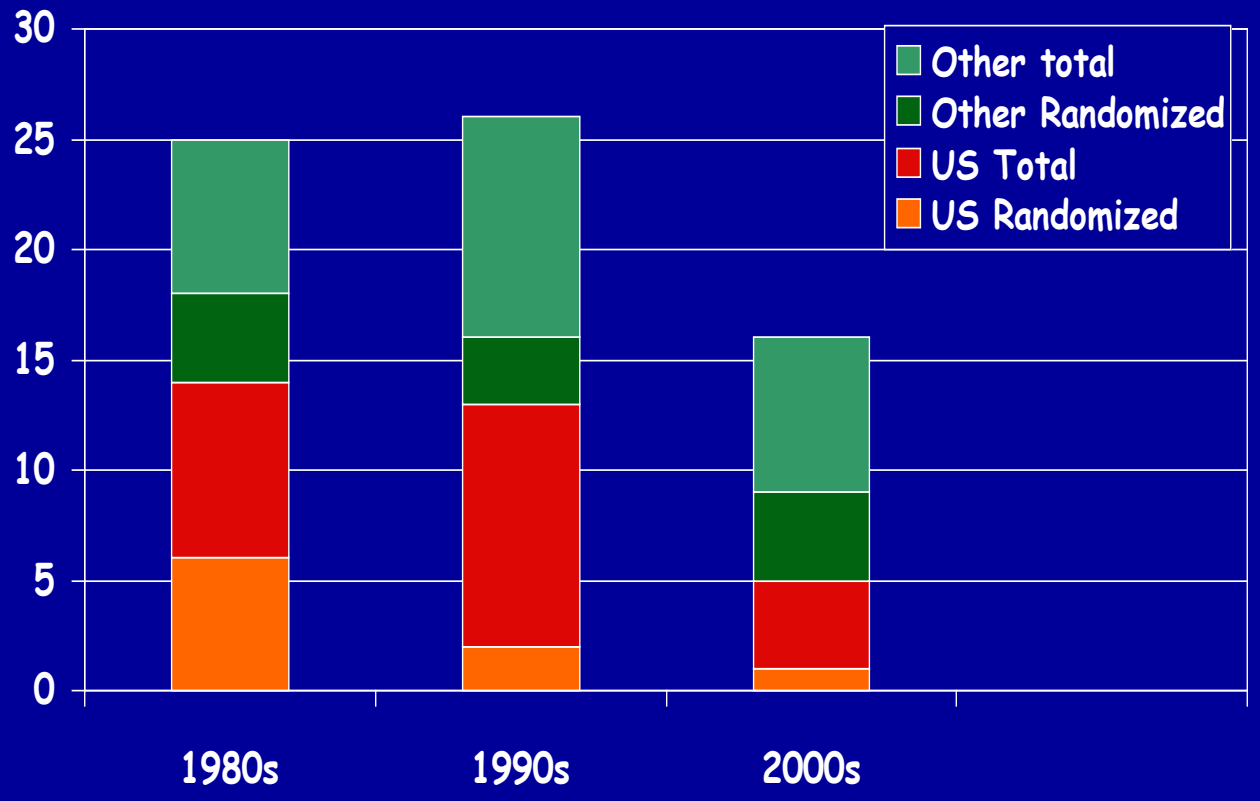
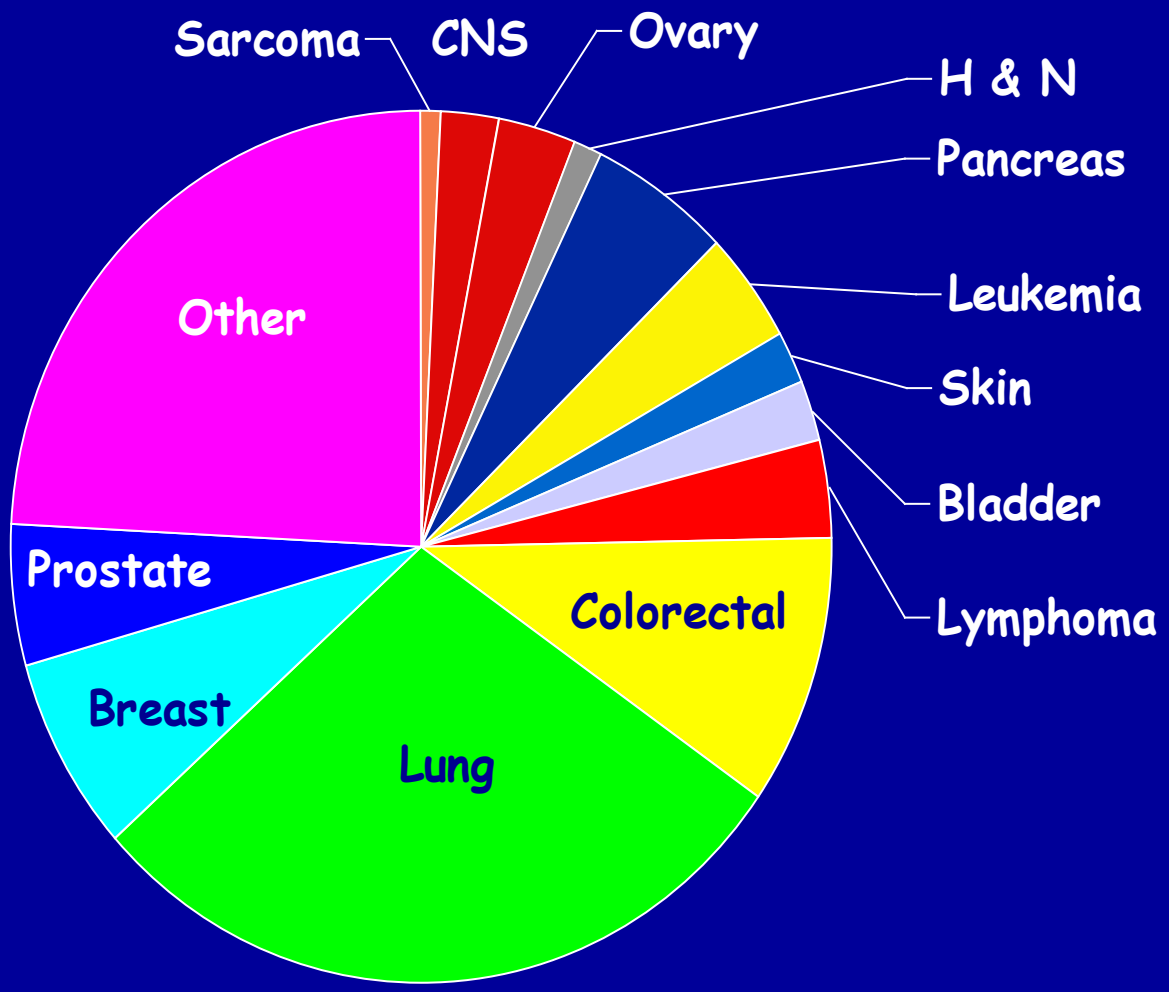
Surrogate (intermediate) endpoint may be viewed as innovative & therefore attractive to patients & their physicians

Allow more rapid conduct of clinical trials & be attractive to the pharmaceutical industry

Priority: Design prospective clinical trials (cont.)

- An NCI objective in its Strategic Priorities for 2015 is to develop, validate, & approve surrogate markers as endpoints to shorten the time necessary for conducting clinical trials.
- In NIH's "Re-engineering the Clinical Research Enterprise" Roadmap the need for improved assessment of clinical outcomes is highlighted

Published Sarcoma Studies



Half of all cancer deaths are from lower incidence sites