NCI/CTEP Phase 2 Contracts: Early Therapeutics Development with Phase II Emphasis

James Zwiebel, M.D.
Chief, Investigational Drug Branch
Cancer Therapy Evaluation Program (CTEP)
Division of Cancer Treatment and Diagnosis (DCTD)

CTEP's Role in Drug Development

- Broaden development in relevant tumor types
  - Industry focus on limited number of indications dictated by market considerations
- Combinations of targeted agents a high priority
  - More than 100 trials initiated since 2000
- Explore
  - Alternative methods of drug administration
  - Mechanism of Action/Proof of Principle

CTEP: Therapeutics Development in the Public Interest

Phase 1 Program

14 Phase 1 sites
Cancer Centers, Brain tumor consortia

Phase 2 Program

9 Phase 2 consortia
Cancer Centers
Cooperative Groups
SPORES
Other: R01, R21

Phase 3 Program

Cooperative Groups
Community Clinical Oncology Program
Cancer Trials Support Unit (CTSU)

Drug Development Group (DDG)

- DCTD Drug Development Group (formerly the Decision Network) approves & prioritizes commitment of NCI preclinical or clinical resources
- Basis for approval:
  - Novelty of agent/target, supported by preclinical and clinical data
  - Acceptable toxicology
  - Agent availability
  - Need for NCI involvement
- Includes outside reviewers

Integration of Development

- Extensive opportunities for NCI staff, extramural scientists and clinicians to interact:
  - CTEP Early Therapeutics Development meetings held twice yearly
  - Translational research meetings
  - Cooperative Group meetings
- Broad CTEP solicitations for clinical trials
- Investigator-initiated proposals
- Input from the Investigational Drug Steering Committee (IDSC) for agent drug development plans

NCI/CTEP Clinical Trials Program - FY06

- Number of Active Investigators = 14,470
- Active Treatment Studies = 918
- New Activated Treatment Studies = 212
- FY ‘06 Accrual = 33,063

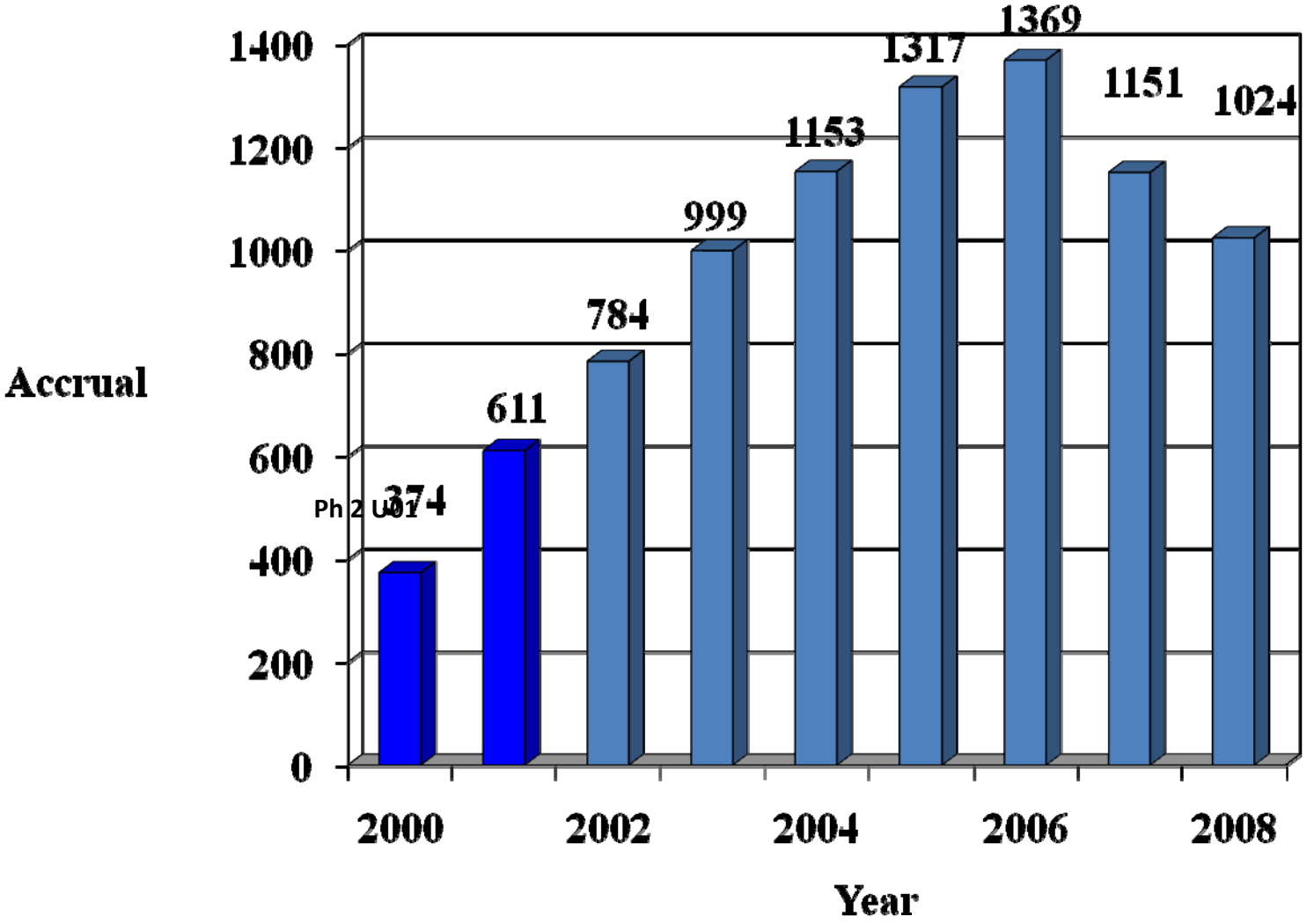
Phase 2 Program Objectives

- Conduct the clinical trials necessary to carry out the development plans for NCI-sponsored agents of varying classes, many of which are directed at new cancer targets
- Characterize the effects of new agents on their targets through biopsies and suitable assays, functional imaging, and other appropriate technologies
- Correlate those effects with clinically-relevant endpoints
- Develop new scientific insights into drug mechanisms and determinants of response

Phase 2 Program

- Converted from grants to contracts in 2000
  - 8 three-year contracts awarded
  - 7 contracts given option for years 4-5
- Re-competed with 9 contracts awarded as of CY2006, with plan to increase accrual up to 2000+ patients/year over the 5-year period of the program
- Most contracts involve multi-institution consortia, all with capability to carry out correlative studies for targeted agents
- **Incentive**: payments to contractors based on actual accrual (per-patient reimbursement)
  - Core Costs permitted (up to 20-40% of total costs) to support infrastructure, fixed costs
  - 3 sites without core costs; reimbursement for pt. accrual only

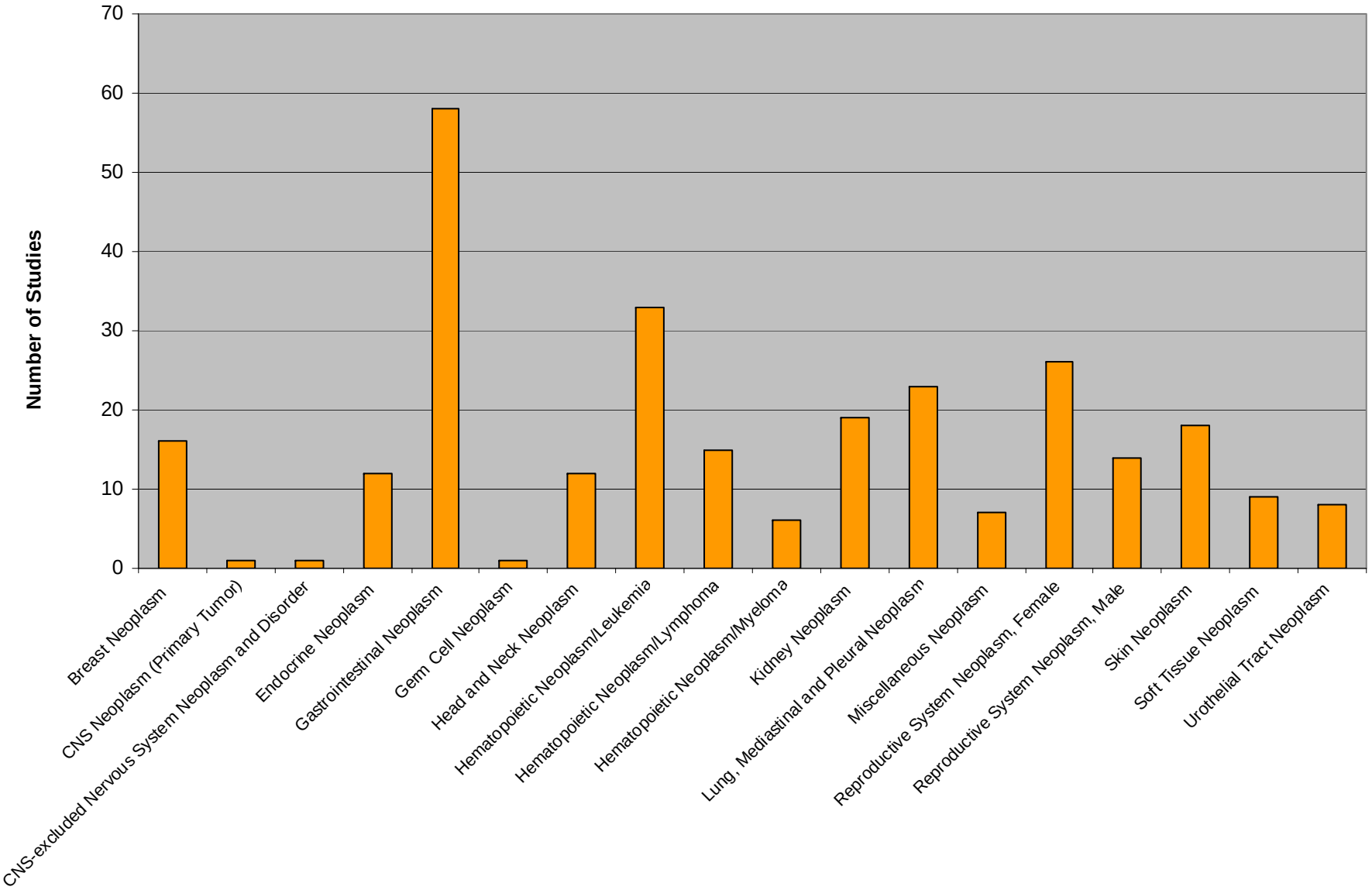
N01 Accrual by Year (2001-2008)



Phase 2 N01 Program
2006 Summary

- 44 protocols in review
- 32 protocols approved
- 37 trials activated
- 94 trials currently open

CTEP N01 Treatment Trials Activated in CY 2000-2006 by Disease Category



Inter-consortium Phase 2 trials

- Per-patient reimbursement has provided an incentive for trial participation by non-lead contractors
- Accelerates accrual to and completion of trials
- 19 trials with multi-site participation in 2006
- CTSU-FLEX
  - Expansion of CTSU to Phase 2 N01 program and to symptom control trials (DCP)
  - Formed to implement CTWG recommendation to enhance enrollment to trials by fostering inter-consortium collaboration ("consortia within consortia")
    - Large randomized phase 2 trials
    - Rare populations
  - Supported by the Center for the Coordination of Clinical Trials (CCCT)
  - One trial open; 2 others about to be activated