SOUTHERN RESEARCH

Conducting basic, translational, and contract research for pharmaceutical and biotechnology companies
Life Sciences

Located in Alabama and Maryland

Birmingham, AL
Main Campus

Frederick, MD
Partnering with Clients to Move Drugs Through the Pipeline

- Discovery
- Efficacy & Optimization
- ADME/PK
- GLP Toxicology
- Clinical Trials Support
Drug Discovery and Development Accomplishments

Southern Research discovered seven of the anticancer drugs that are currently being marketed for patients.

Twenty drugs discovered at Southern Research have entered clinical trials.

Over half of the FDA-approved anticancer drugs were evaluated at Southern Research.
## Drug Pipeline

<table>
<thead>
<tr>
<th>Drug Program</th>
<th>Therapeutic Use</th>
<th>Preclinical</th>
<th>IND Submission</th>
<th>Phase I</th>
<th>Phase II</th>
<th>Phase III</th>
<th>NDA Submission</th>
<th>Marketed By</th>
<th>Trade name</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amifostine</td>
<td>A chemotherapy and radiotherapy protective agent</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>MedImmune</td>
<td>Ethyol®</td>
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<tr>
<td>Fludarabine</td>
<td>Adult leukemias and lymphomas</td>
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<td>Sanofi-Aventis</td>
<td>Fludara®</td>
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<tr>
<td>Dacarbazine</td>
<td>Melanoma, Hodgkin’s disease, and soft tissue sarcoma</td>
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<td></td>
<td>Merck</td>
<td>DTIC-Dome®</td>
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<tr>
<td>Lomustine</td>
<td>Brain tumors</td>
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<td>Bristol-Myers Squibb</td>
<td>CeeNU®</td>
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<tr>
<td>Carmustine</td>
<td>Brain tumors, multiple myelomas, and Hodgkin’s Disease</td>
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<td>Bristol-Myers Squibb</td>
<td>BiCNU®</td>
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<td>Clofarabine</td>
<td>Leukemias, solid tumors, and autoimmune diseases</td>
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<td>Genzyme</td>
<td>Evolitra® Clolar®</td>
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<tr>
<td>Pralatrexate (PDX)</td>
<td>Lymphomas and solid tumors</td>
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<td>Allos Therapeutics, Inc.</td>
<td>FOLOTYN™</td>
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<td>Palifosfamide</td>
<td>Advanced sarcoma</td>
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<td>DEKK-Tec</td>
<td>ZIOPHARM</td>
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<tr>
<td>Thiarabine</td>
<td>Leukemias and autoimmune diseases</td>
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<td>Access Pharmaceuticals</td>
<td>Antisoma</td>
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<tr>
<td>DMPEN</td>
<td>Metastatic breast cancer and brain tumors</td>
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<td>Antisoma</td>
<td>Clomet™</td>
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<tr>
<td>PNP</td>
<td>Gene therapy treatment of solid tumors</td>
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<td>PNP Therapeutics</td>
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<tr>
<td>Bithionol</td>
<td>Solid tumors</td>
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<td>Champions Biotechnology, Inc.</td>
<td>ZIOPHARM</td>
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<tr>
<td>Isophosphoramidemustard analogs</td>
<td>Late stage cancers</td>
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<td>Southern Research / UAB</td>
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<tr>
<td>4’-ThioidU</td>
<td>Pox viruses</td>
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Full Range of Discovery and Preclinical Development Series

- Basic Research
  - Target Identification
- Lead Discovery and Optimization
- Preclinical Drug Development
- Clinical Trials

- Computational Chemistry
- Molecular Biology & Biochemistry
- Assay Development
- High Throughput Screening
- Animal Efficacy Models
- PK/ADME
- GLP Toxicology
- Bioanalytical Sciences
Chemistry

Drug design, synthesis & route selection for scale-up

Medicinal chemistry, SAR & lead optimization

Library design & combinatorial chemistry

*In silico* screening

Molecular modeling

Structural biology/protein crystallography

Cheminformatics, repository & database services
Discover Biology

Assay development & validation
High throughput screening
Mechanism of action
Target discovery and validation
Genomics
Proteomics
Cell biology
Immunology
Cancer Therapeutics Evaluation & Testing

*In Vitro* capabilities

- Over 200 human tumor cell lines
- 60 cell-line panel testing
- Cytotoxicity/anti-proliferative assays
- Mechanism of action (apoptosis, cell cycle, cell differentiation)
- Combination and/or sequencing studies including irradiation
- Custom cell-based assay development
Cancer Therapeutics Evaluation & Testing

*In Vivo* capabilities

- Over 80 human tumor xenograft models
- Extensive clinical drug efficacy database
- Numerous murine tumor models
- In vivo imaging with IVIS Lumina
- Combination therapy with clinically useful agents or irradiation
- Automated data acquisition
Immunoassays (e.g., ELISAs)
Immune function testing
Custom assay development
Flow cytometry
Immunohistochemistry
Infectious Disease Therapeutics Evaluation and Testing - Types

- Antibiotics
- Antivirals
- Antifungals
- Vaccines
- Topical Microbicidies
Infectious Disease Therapeutics Evaluation and Testing Capabilities

Custom assay development
Wide variety of pathogenic bacteria
*In vitro* models
*In vivo* evaluation of drugs and vaccines
BSL-3/ABSL-3 for select agents
BSL-3 aerobiology
Immunologic assays
Infectious Disease Therapeutics
Evaluation and Testing Agents

- Influenza viruses (including H1N1 and HPAI)
- TB (including multi-drug resistant)
- Pox viruses
- SARS-CoV
- HIV
- RSV
- Herpes viruses
- Hepatitis B & C
- Hantavirus
- Anthrax
- Tularemia
- Plague
- MRSA
**ADME/PK**

- Single and multidose
- Absolute and relative bioavailability
- Proportionality and linearity of absorption
- PK species-to-species extrapolations
- Toxicokinetic support
- Protein binding
- *In vitro* metabolic profiling
- Pathway definition
Pharmacodynamics

Target- or organ-specific enzyme activity
CBC alterations
Proteomic and genomic changes
Tumor growth
Cell permeability
Modulation of cell-cycle pathways
Bioanalytical Chemistry

Method development and Validation (GLP)

LC-MS/MS
LC/MS
HPLC with UV-VIS
GC with FID and ECD detectors
GC/MS with PCI, NCI, and EI ionization sources

Plasma and tissue drug-level determinations
PCR Laboratory

TaqMan® and Molecular Beacons™ assays

Isolation and purification of DNA and RNA

Quantitation using PicoGreen/RiboGreen

Biodistribution and gene expression
GLP Toxicology Studies
and
Preclinical Safety Assessment Evaluations
Toxicology Test Species

- Mice
- Rats
- Dogs
- Nonhuman primates
- Mini-pigs
- Rabbits
- Guinea pigs
- Hamsters
- Ferrets
<table>
<thead>
<tr>
<th>Toxicology Routes of Administration</th>
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</thead>
<tbody>
<tr>
<td>Oral Gavage/Capsule</td>
</tr>
<tr>
<td>Dietary admixture</td>
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<tr>
<td>Drinking water</td>
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<tr>
<td>Dermal</td>
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<td>Injection</td>
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<td>Infusion</td>
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<td>Intranasal</td>
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<td>Ocular</td>
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<tr>
<td>Rectal</td>
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<tr>
<td>Surgical implant</td>
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<tr>
<td>Intracranial</td>
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</tbody>
</table>
Clinical Pathology

- GLP-compliant
- BSL-1 - BSL-3
- 25 years experience
- ASCP certified
- CAP proficiency testing
Clinical Pathology - Analyzers

ADVIA® 120 Hematology
ACL™ Elite Pro Hemostasis
COBAS® 6000 Clinical Chemistry
Clinitek 500 Urine Chemistry
Anatomic Pathology

ACVP board-certified pathologists
Histopathologic examinations
Consultations
Peer review
Digital photography
Necropsy
Histology and histopathology
Quality Assurance - GLP Personnel

Registered Quality Assurance Professionals (RQAP-GLP)

More than 85 years collective experience

Hosted 20 regulatory inspections without an FDA Form 483
Quality Assurance - GLP Program

Audits/inspections conducted in accordance with US FDA, US EPA, OECD, MOHW, UK Compliance Programme

More than 60 internal audits/inspections conducted biennially

18 internal facility inspections conducted annually

Vendor/Supplier audits conducted biennially

GLP training annually and as needed
Proven Science.
Experienced People.
Trusted Results.
Since 1941.