Anti-Cancer Campaign of The Scripps Research Institute
The Emperor of Maladies

In the past several decades of our war on cancer, there have been victories, large and small, and advances in detection, prevention and treatment.

While these triumphs are worth celebrating, there is still much left to learn about the large cluster of diseases we call cancer. Biomedical researchers such as those at The Scripps Research Institute (TSRI) share the belief that we are close to significant breakthroughs and that new approaches such as personalized treatments and methods for earlier detection are now within our reach.

Only when our scientific advances make cancer something we no longer fear will the Emperor of Maladies finally lose its power.
Widespread and Deadly

- One in two men and one in three women in the United States will be diagnosed with cancer at some time during their lifetimes.
- More than one million Americans develop cancer each year—a new case is diagnosed every 30 seconds.
- Cancer is the second leading cause of death after heart disease in the United States and the main cause of death in women between the ages of 35 and 74.
- In 2010, the economic cost of cancer was $125 billion; the human toll is immeasurable.
Many Mysteries Remain

- Cancer is not a single disease, but is a collection of more than 300 different disease types that are marked by the uncontrolled growth and spread of abnormal cells.

- Cancers form for many different reasons—hundreds of genes are known to contribute to cancer; other risk factors include smoking, poor diet, inactivity, environmental pollutants and ultraviolet radiation.

- The exact connection between risk factors and cancer’s formation often remains elusive.

- By the time most tumors are detected, they have grown to contain well over one billion cells.

- Metastasis—the spread of a tumor from its primary site to other locations in the body—is the principal cause of most cancer deaths, yet still one of the most enigmatic aspects of the condition. New drugs that block metastasis are a major focus of TSRI investigators.
Cachexia—muscle wasting in patients suffering from cancer—is a major but little understood cause of morbidity that is found in at least 40% of cancer patients. New agents to block this response are being developed by researchers at TSRI.

Overall survival of patients who suffer from several types of cancer—pancreatic, ovarian and lung cancer, brain tumors such as glioblastoma, many blood cancers, and advanced melanoma—has not improved over the last 30 years, despite intensive therapies. New approaches for early detection and therapy are needed, and these are the focus of researchers at TSRI.
When the U.S. boosted its government funding to beat back cancer 40 years ago, cancer mortality rates began to decline; between 1991 and 2006, they fell about 21% for men and 12% for women.

But, while cancer is still a widespread problem, over the past several years federal funding for critical basic biomedical research has decreased in real dollars—by 25% over the past 10 years.

What is especially important for scientific breakthroughs are high-risk, high-reward endeavors—the kind that are particularly difficult to fund through conventional government grants.

Pharmaceutical companies rarely invest in the basic biomedical research necessary to search for new classes of diagnostics and therapies.
The Anti-Cancer Campaign at TSRI

- TSRI proposes an organization that brings together varied scientific approaches to address these critical problems, funded aggressively to find breakthroughs in the shortest time feasible.

- The purpose is to find:
  - Novel therapeutic strategies—for both cancer prevention and treatment.
  - Early disease diagnostics (biomarkers).
  - New, safe and effective drugs—for refractory cancer types and metastatic disease, and for curing muscle wasting.
  - This will be accomplished by assembling a critical mass of scientists, each contributing their specific expertise to an interdisciplinary approach, creating synergies and expanding the base of information needed to find solutions.
Why TSRI?

TSRI has:

- A track record of basic discoveries translated into new therapies, including new and effective treatments for arthritis, lupus, hemophilia and cancer.
- More than 50 companies launched from TSRI discoveries.
- More than 800 patents on innovative technologies.
- 30 pharmaceuticals currently in clinical development.
- Recognition as a leader at the intersection of biology and chemistry—ranked number one in the world in chemistry, number two in microbiology (ranked by Thomson Reuters, citations per paper over a decade).
Building on TSRI’s commitment to scientific excellence and culture of innovation, TSRI scientists have already made many groundbreaking contributions, including:

- Developing and testing the anti-leukemia drug 2-CdA (a.k.a. cladribine or Leustatin®), an intravenous medication with remarkably few side effects; 2-CdA now cures or produces many years of freedom from hairy cell leukemia in almost all those receiving treatment.

- Inventing an advanced blood test for detecting and analyzing circulating tumor cells—breakaway cells from cancer patients’ solid tumors; the highly sensitive blood analysis provides information that may soon be comparable to some surgical biopsies.

- Devising a new technique for connecting drug molecules and antibodies to make highly targeted therapies called “antibody-drug conjugates”—that could be used, for example, to deliver toxic chemotherapy drugs to cancer cells while sparing most healthy cells.

- Finding a mechanism through which mitochondria, the powerhouses of a cell, control tumor aggressiveness.

- Identifying a new family of drug candidates with potential for treating breast, brain, skin and other cancers.

(continued)
Developing an innovative new method for economically synthesizing ingenol, a highly complex, plant-derived compound of interest to drug developers for its anti-cancer potential.

Developing technologies and constructing libraries to overcome challenges in natural product discovery, production and lead optimization that could contribute to anti-cancer drug discovery efforts.

Discovering a potentially beneficial use of a once-abandoned compound for the treatment of neuroblastoma, a devastating childhood cancer, and for preventing the progression of colon, prostate, skin and breast cancer—now in clinical trials worldwide.

Discovering new, safe and highly effective drugs that disable cancer cell metabolism across a broad spectrum of human malignancies.

Discovery of new strategies to overcome muscle wasting in cancer patients.
Some TSRI Cancer Researchers

- Thomas Bannister, PhD
- Phil Baran, PhD
- Michael Boddy, PhD
- Dale Boger, PhD
- Michael Conkright, PhD
- Benjamin Cravatt, PhD
- Eros Lazzerini Denchi, PhD
- Celine DerMardirossian, PhD
- Matthew Disney, PhD
- Derek Duckett, PhD
- Jane Dyson, PhD
- Tina Izard, PhD
- Brunhilde Felding, PhD
- Yangbo Feng, PhD
- Nathalie Franc, PhD
- Larry Gerace, PhD
- Patrick Griffin, PhD
- Min Guo, PhD
- Scott Hansen, PhD
- Wendy Havran, PhD
- Kim Janda, PhD
- Gerald Joyce, MD, PhD
- Katrin Karbstein, PhD
- Shuji Kishi, PhD
- Oktay Kirak, MD, PhD
- Joseph Kissil, PhD
- Thomas Kodadek, PhD
- Manson Law, PhD
- Jun-Li Luo, MD, PhD
- Lindsey Miles, PhD
- Kendall Nettles, PhD
- Takanori Otomo, PhD
- James Paulson, PhD
- Howard Petrie, PhD
- Matthew Pipkin, PhD
- James Quigley, PhD
- Christoph Rader, PhD
- Steven Reed, PhD
- Paul Robbins, PhD
- William Roush, PhD
- Erica Ollmann Saphire, PhD
- Karsten Sauer, PhD
- Louis Scampavia, PhD
- Paul Schimmel, PhD
- Peter Schultz, PhD
- Ben Shen, PhD
- Ryan Shenvi, PhD
- Linda Sherman, PhD
- Vaughn Smider, MD, PhD
- Andrew Su, PhD
- Peiqing Sun, PhD
- Mark Sundrud, PhD
- John Tainer, PhD
- Tim Tellinghuisen, PhD
- Peter Vanderklish, PhD
- Peter Vogt, PhD
- Luke Wiseman, PhD
- Dennis Wolan, PhD
- Xiaohua Wu, PhD
- Peter Wright, PhD
- Xiang-Lei Yang, PhD
- Changchun Xiao, PhD
A Collaborative and Focused Effort

To find novel therapeutic strategies, early disease diagnostics and effective drugs, the Anti-Cancer Campaign at TSRI will:

- Marshal an organized and focused collaborative research effort, turning the best scientific minds loose on the problem.
- Recruit talented young investigators working in the field and support their initial efforts.
- Create a collaborative, interdisciplinary, synergistic environment that expands scientific thinking about cancer from many perspectives—including genomics, molecular studies, immunology, chemical synthesis, drug candidate screening, development of new therapeutics, etc.
- Evaluate campaign-funded research aggressively on an annual basis to ensure that only promising pathways are pursued.
Supporting Innovative Research

Grants
- TSRI investigators submit requests for funding for innovative, out-of-the-box research.
- Accepted projects receive funding for three years to develop new approaches that will then be competitive for National Institutes of Health, Department of Defense and National Science Foundation funding to continue the work.

Oversight
- A scientist-director, appointed by the president of TSRI, holds an endowed chair to provide administration and scientific direction.
- An internal grant committee and outside evaluators review the proposals and provide granting recommendations.
Funding

The initiative will be funded by investments totaling $50 million.

**Expenditure plan:**
- $9 million – Endowed chairs for three senior investigators and a director
- $6 million – A 10-year term endowment to ensure resources are available to follow up on top priority research projects
- Remaining funds of $35 million to be drawn down over 10 years to fund:
  - Projects, chosen on the basis of merit, funded at $300 - 500K each per year
  - Grants of $50K per year to exceptional postdoctoral fellows working on relevant research
A Lasting Contribution

We know so much more today than when war was first declared against cancer—however there is still much to learn. Scientists at The Scripps Research Institute are poised to develop new approaches to save lives from this malicious and complex disease.

Knowing what we now know about cancer, there will never be a single hero against the malady. Chances are there will be many heroes. Let's work together to make the next breakthrough a reality.
Appendices
Appendix 1: Drugs Developed from TSRI Discoveries

- **Humira®** for rheumatoid arthritis, plaque psoriasis, Crohn’s disease, ulcerative colitis and other inflammatory conditions
- **Benlysta®** for lupus, a debilitating autoimmune disease
- **Leustatin®** for hairy cell leukemia, an unusual cancer of the blood
- Purification of **Factor VIII** for the bleeding disorder hemophilia
- **Vyndaqel®** for transthyretin familial amyloid polyneuropathy (TTR-FAP), a rare, progressive and fatal neurodegenerative disease
- **Surfaxin®** for infant respiratory distress syndrome, a life-threatening condition affecting pre-term infants
- **Cyramza®** for gastric and non-small cell lung cancer
- **Unituxin™** for the childhood cancer neuroblastoma
### Appendix 2: Companies from TSRI Technology or Faculty

<table>
<thead>
<tr>
<th>Year</th>
<th>Companies</th>
</tr>
</thead>
</table>
| 2014 | Aldabra Biosciences  
|      | Padlock Therapeutics  
|      | Transplant Genomics, Inc. |
| 2013 | Blackthorn Therapeutics Inc.  
|      | iGenomiX  
|      | Sirenas Marine Discovery  
|      | Zebra Biologics |
| 2012 | Abide Therapeutics  
|      | Cypher Genomics  
|      | Vesper Biologics |
| 2011 | RQx Pharmaceuticals |
| 2010 | Ember Therapeutics  
|      | Epic Science |
| 2009 | Receptos Pharma  
|      | Protix, Inc.  
|      | Zyngenia |
| 2008 | aTyr Pharma  
|      | Curna |
| 2007 | Eyecyte, Inc.  
|      | Fate Therapeutics  
|      | Proteostasis Therapeutics  
|      | Sapphire Energy |
| 2006 | Fabrus, Inc.  
|      | Xcovery |
| 2004 | Affinity Pharmaceuticals  
|      | Calmune  
|      | Viriome LLC  
|      | Wittycell S.A.S. |
| 2003 | Achaogen Inc.  
|      | Motility, Inc.  
|      | Promosome |
|      | Rincon Pharmaceuticals (acquired by Sapphire Energy) |
| 2002 | CovX Research (acquired by Pfizer)  
|      | NanoRX (acquired by Adaptive Therapeutics)  
|      | VAXDesign (acquired by Sanofi Pasteur) |
Appendix 2 - continued

2001
- Kalypsys
- Phenomix
- Syrnx (acquired by Takeda)

2000
- ActivX Biosciences (acquired by Kyorin)
- Neurome

1999
- Geneformatics (merged with Structural Bioinformatics)
- Optimer Pharmaceuticals
- Prolifaron (acquired by Alexion Pharmaceuticals)

1997
- Epicyte (acquired by Biolex Therapeutics)

1996
- Digital Gene Technologies (purchased by Neurome)
- Discovery Labs (merged with Acute Therapeutics)
- Drug Abuse Sciences
- Sangamo Biosciences

1995
- PharMore
- Thrombosys

1994
- Apovia AG (formerly EVAX Technologies, originally Immune Complex Corp.)

- Applied Molecular Evolution (formerly Lxsys; acquired by Lilly, Inc.)
- CombiChem (acquired by Dupont-Merck Pharmaceutical and merged with Bristol-Myers Squibb)

1993
- Ciphergen Biosystems (acquired by Bio-Rad Laboratories)

1992
- Sequel Therapeutics (later acquired by Cytel, which was subsequently spun-out as Epimmune)

1989
- Avanir Pharmaceuticals (formerly Lidak)
- Corvas (acquired by Dendreon Corporation)
- UNASYN

1986
- MP Biomedicals (formerly Qbiogene and Bio101)
- NeoMPS (formerly Multiple Peptide Systems)

1984
- Stratagene

1982
- Synbiotics

1981
- Quidel
# Appendix 3
## Therapeutic Pipeline

<table>
<thead>
<tr>
<th>MARKETED PRODUCTS</th>
<th>PHASE I</th>
<th>PHASE II</th>
<th>PHASE III</th>
<th>NDA</th>
<th>MARKET</th>
</tr>
</thead>
<tbody>
<tr>
<td>Humira Autoimmune</td>
<td>Abbott</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Benlysta Autoimmune</td>
<td>Human Genome Sciences</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cyramza Oncology</td>
<td>Lilly</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vyndaqel Amyloidoses</td>
<td>Pfizer</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Leustatin Oncology</td>
<td>J&amp;J</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Monoclate-P Cardiovascular</td>
<td>Sanofi Aventis</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Surfaxin Respiratory</td>
<td>Discovery Labs</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unituxin Oncology</td>
<td>United Therapies</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>LATE STAGE PRODUCTS</th>
<th>PHASE I</th>
<th>PHASE II</th>
<th>PHASE III</th>
<th>NDA</th>
<th>MARKET</th>
</tr>
</thead>
<tbody>
<tr>
<td>Solithromycin Antibiotic</td>
<td>Cempra</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RPC-1063 Autoimmune</td>
<td>Receptos</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>OTHER CAT PRODUCTS</th>
<th>PHASE I</th>
<th>PHASE II</th>
<th>PHASE III</th>
<th>NDA</th>
<th>MARKET</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tralokinumab Respiratory</td>
<td>Medimmune/AstraZeneca</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CAM-3001 Inflammation</td>
<td>Medimmune/AstraZeneca</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rozrolimupab Cardiovascular</td>
<td>Symphogen</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GC-1008 Multiple Areas</td>
<td>Genzyme</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BI-505 Oncology</td>
<td>Bioinvent</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MT-203 Inflammation</td>
<td>Micromet</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bertilimumab Allergy</td>
<td>iCo Therapeutics</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>SANGAMO PRODUCTS</th>
<th>PHASE I</th>
<th>PHASE II</th>
<th>PHASE III</th>
<th>NDA</th>
<th>MARKET</th>
</tr>
</thead>
<tbody>
<tr>
<td>SB-728 HIV</td>
<td>Sangamo</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SB-313 Oncology</td>
<td>Sangamo</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>CLICK CHEMISTRY PRODUCTS</th>
<th>PHASE I</th>
<th>PHASE II</th>
<th>PHASE III</th>
<th>NDA</th>
<th>MARKET</th>
</tr>
</thead>
<tbody>
<tr>
<td>AZ-01 Autoimmune</td>
<td>Allozyne</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### Ambryx Products

<table>
<thead>
<tr>
<th>Compound</th>
<th>Therapeutic Area</th>
<th>Company</th>
</tr>
</thead>
<tbody>
<tr>
<td>ARX-201</td>
<td>Growth Deficiency</td>
<td>Ambrx</td>
</tr>
<tr>
<td>ARX-424</td>
<td>Autoimmune</td>
<td>Ambrx</td>
</tr>
<tr>
<td>ARX-618</td>
<td>Diabetes</td>
<td>Ambrx</td>
</tr>
<tr>
<td>ARX-328</td>
<td>Lipodystrophy</td>
<td>Ambrx</td>
</tr>
</tbody>
</table>

### Other Early Stage Products

<table>
<thead>
<tr>
<th>Compound</th>
<th>Therapeutic Area</th>
<th>Company</th>
</tr>
</thead>
<tbody>
<tr>
<td>IC-14</td>
<td>Respiratory</td>
<td>Implicit</td>
</tr>
<tr>
<td>ALT-801</td>
<td>Oncology</td>
<td>Altor</td>
</tr>
<tr>
<td>Shok-Pak</td>
<td>Organ Failure</td>
<td>InflammaGen</td>
</tr>
<tr>
<td>RG-2833</td>
<td>Friedreich’s Ataxia</td>
<td>BioMarin</td>
</tr>
<tr>
<td>HSC-835</td>
<td>Oncology</td>
<td>Novartis</td>
</tr>
<tr>
<td>3K3A-APC</td>
<td>Cardiovascular</td>
<td>ZZ Biotech</td>
</tr>
<tr>
<td>VS-4718</td>
<td>Oncology</td>
<td>Verstem</td>
</tr>
<tr>
<td>Resokine-IV</td>
<td>Autoimmune</td>
<td>aTyr</td>
</tr>
</tbody>
</table>