Improving the Path for Innovative Therapies

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www.c-path.org
The Critical Path Institute
Annual Progress Report
Fiscal Year July 1, 2005—June 30, 2006

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Mission
C-Path will create innovative collaborations in research and education that enable the safe acceleration of the process for developing new medical products.

Vision
C-Path is an independent, non-profit institute that serves as a “trusted third party” enabling scientists from the FDA, academia and industry to work together for the public good.
From the President & CEO

Dear Friends and Supporters:

On July 1, 2006, the Critical Path Institute (C-Path) celebrated its first official year in operation. We surpassed many goals this year and I hope that after reading this report you will agree that we have used the financial support of the community wisely in our efforts to create a world-class center for medical product development/regulatory science and to create it in Tucson, Arizona.

As I have said many times, we could not begin to accomplish our vision and mission without the incredible support of all of you. We have received (in cash and pledges) more than $10 million to make this Institute a reality. On behalf of all C-Path employees, I thank you. I also thank you on behalf of those patients who will benefit from your generosity and vision.

As you will see in this Annual Progress Report, the projects that we have begun this year will lead to the development of safer drugs, fewer strokes due to incorrect dosing of blood thinners and longer lives for patients with rare/orphan diseases and lung cancer.

Ultimately, everything we do is focused on making changes in the medical product development process that result in better care for patients, to ease their suffering and improve their quality of life.

I invite you to take time with our first Annual Progress Report and to let us know what you think because what we are doing has never been done before! We value your questions, suggestions and criticisms.

We don’t profess to have all the answers; indeed, we mostly uncover questions that need answers. As you will see in this report, all of our projects require collaborators and supporters, such as yourself. So, please share your thoughts with us.

Sincerely,

Raymond L. Woosley, M.D., Ph.D.
President and CEO
Leaders of The Critical Path Institute

Early support allowed us to attract and hire key employees

Raymond Woosley, M.D., Ph.D.
President and CEO
A noted medical administrator, scholar and researcher, Dr. Woosley was most recently Vice President for The University of Arizona (UA) Health Sciences Center and Dean of the UA College of Medicine. He was Associate Dean for clinical research and Chair of the Department of Pharmacology at Georgetown University School of Medicine. Dr. Woosley was a professor at Vanderbilt University Medical School and was one of the first scientists at Meyer Laboratories, now GlaxoSmithKline. Dr. Woosley earned his Ph.D. in Pharmacology from the University of Louisville, his M.D. from the University of Miami and completed post-doctoral training in pharmacology, internal medicine and clinical pharmacology.

Jeffrey Cossman, M.D.
Chief Scientific Officer and Director of Rockville, MD, Office
Before joining C-Path, Dr. Cossman was Vice President and Medical Director at GeneLogic, Inc. He co-founded Avalon Pharmaceuticals, a next-generation genomics cancer drug discovery company and was Chairman of the Department of Pathology at Georgetown University Medical Center. During the 1980s he was a senior investigator at the National Cancer Institute of the National Institutes of Health (NIH) where he founded and directed the Molecular Diagnostics Laboratory. Dr. Cossman has been recognized as one of the best doctors in America. He received his M.D. from the University of Michigan Medical School and a B.S. in human evolution, also at Michigan.

Lawrence “Larry” J. Aldrich, J.D.
Chief Operating Officer
As a former venture capitalist and President and CEO of Tucson Newspapers, Inc., Aldrich brought extensive business experience to C-Path. Prior to leading all business aspects for the two daily newspapers in Tucson, Aldrich was assistant general counsel for Gannett Co., Inc. He has also worked as senior trial counsel for the Antitrust Division of the U.S. Department of Justice. Aldrich has served as Chairman of the Southern Arizona Leadership Council and Chairman of the UA College of Public Health Advisory Board. He received his law degree from Tulane Law School and civil engineering degree from Georgia Tech.

William B. Mattes, Ph.D., D.A.B.T.
Director of Toxicology
Dr. Mattes has worked in toxicology for more than 23 years. He was Senior Scientific Director of Toxicogenomics at GeneLogic and served as Associate Director of Toxicogenomics at Pharmacia Corp. He was group leader of experimental toxicology at Ciba Pharmaceuticals and of molecular and cellular toxicology at Ciba-Geigy Agricultural Chemical Division. Dr. Mattes holds a B.A. from the University of Pennsylvania and a Ph.D. in biological chemistry from the University of Michigan. He did postdoctoral training in biochemistry at Johns Hopkins University, and was a staff fellow at the National Cancer Institute, NIH.
Joseph R. (Bob) Assenzo, Ph.D.
Executive Director for Education
Dr. Assenzo led the Drug Information Association from 1996 through 2004 as executive director. Prior to that appointment Assenzo was Vice President of Regulatory Affairs and Project Management and Senior Advisor for Novo Nordisk in Copenhagen, Denmark. Dr. Assenzo was also previously Executive Director of U.S. Pharmaceutical Regulatory Affairs, Medical Communications, and Pharmacovigilance at the Upjohn Company. Dr. Assenzo received degrees in civil engineering from Northeastern University and environmental engineering from Harvard University and completed his Ph.D. in biostatistics from the College of Public Health, University of Oklahoma.

On July 1, 2005, C-Path began its first year with four full-time employees, plus a number of consultants, part-time employees and volunteers. The fiscal year ended with 12 employees and several consultants and volunteers.

Ellen G. Feigal, M.D.
Director of Medical Devices and Imaging
During 2006, Dr. Feigal joined C-Path on a sabbatical from the Translational Genomics Research Institute (TGen)—where she was recruited in 2004 as Vice President of Clinical Sciences/Deputy Scientific Director. Dr. Feigal directed the National Cancer Institute’s Division of Cancer Treatment and Diagnosis from 2001 to 2004, was deputy director of the division, and senior investigator in the Cancer Therapy Evaluation Program. She is a research faculty member at the University of Arizona and Arizona State University. Dr. Feigal earned a B.S. degree in biology, an M.S. in molecular biology/biochemistry from the University of California (UC), Irvine, and her M.D. from UC Davis.

Marietta Anthony, Ph.D.
Director of Women’s Health
Dr. Anthony joined C-Path in the fall of 2006. Before joining C-Path, Dr. Anthony played a leadership role in health policy and oversaw large research programs for federal agencies and universities. Anthony directed research on women’s health at the NIH and the Food and Drug Administration. She was also the Deputy Director of the Office of Women’s Health for the FDA. She founded and directed the National Center of Excellence in Women’s Health at the University of Arizona and was director of Women’s Health Research at Georgetown University. Dr. Anthony received her Ph.D. in medical microbiology and immunology from UCLA School of Medicine and completed a postdoctoral fellowship in biological chemistry.

Board of Directors

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President and CEO

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The Critical Path Institute
Chief Operating Officer (COO)

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Janet Woodcock, M.D.
Food and Drug Administration
Acting Deputy Commissioner for Operations and COO

Bruce Wright, B.A.
The University of Arizona Science and Technology Park
COO
Creation of C-Path

Unprecedented community support made it possible

The Critical Path Institute (C-Path) filed for incorporation December 3, 2004, as a nonprofit 501(c)3 organization. It began as a concept and then a plan, and originally with the name “Institute for Global Pharmaceutical Development.” The U.S. Food and Drug Administration (FDA), The University of Arizona (UA) and SRI International, Inc., are C-Path’s founding partners.

C-Path’s mission from the beginning has been to serve as a “trusted third party” and to enable innovative collaborations between government regulators, the academic community and regulated businesses to come together to improve the process of developing new medical products, making the process faster, safer, smarter.

C-Path’s entire focus is on the “Critical Path Initiative,” the FDA report (available at www.fda.gov/oc/initiatives/criticalpath/) that was released in March 2004 and cited the need for innovations in drug development. To formalize a relationship with the FDA, C-Path entered into a Memorandum of Understanding that serves as an umbrella for all C-Path projects. C-Path also developed affiliation agreements to define its working relationship with other founding partners, SRI and UA.

During early 2005, the first steps of program formation were underway, including development of financial and work scope plans led by C-Path board member Jeff Jacob, CEO of Systems Medicine, Inc.

Larry Aldrich joined C-Path, initially part-time and then full-time December 1, 2005, as Chief Operating Officer. He helped set up the many essential structural components, such as an Operations Board (now our Board of Directors), bylaws, policies, payroll and benefits. In March of 2005, the first contributions were received and C-Path opened leased offices in Tucson’s St. Phillips Plaza, formed a National Advisory Board, created a website and worked with key leaders in government, academics and industry to determine the types of projects that should be undertaken by C-Path. These projects became

The Creation of The Critical Path Institute and First Year Highlights

- **March 2004** The U.S. Food & Drug Administration releases the Critical Path Initiative report. C-Path leaders enter into verbal agreement with the FDA.
- **September 2004** State of Arizona grants C-Path a $200,000 planning grant.
- **July 2004** Target for pledged funding is achieved.
- **December 2004** C-Path files articles of non-profit incorporation.
the foundations of our workscope (see website, www.c-path.org).

By July 1, 2005, C-Path was ready to begin operations with four full-time employees, plus a few consultants, part-time employees and volunteers. C-Path ended this fiscal year with 12 employees and several consultants and volunteers.

Early in 2006, the official name was changed to The Critical Path Institute to provide direct linkage with the FDA’s Critical Path Initiative.

C-Path developed more than a dozen contracts to work with its many partners, collaborators and funders. An audit was issued for the partial year ending June 30, 2005, so a clear standard for openness and accountability could be established.

As you will see on the following pages, the concept of a “trusted third party” that operates on “neutral ground” has been well received. C-Path’s mission requires the implementation and expeditious execution of collaborative projects that are part of cohesive programs. During the first year, C-Path made substantial progress on many projects in three program areas: Acceleration, Safety and Education. These are discussed in detail on the following pages and significant program milestones are noted on the timeline.

C-Path projects will yield results that improve the development process for new medical products. C-Path is using the community funding to plan these projects and is successfully identifying full funding for many of these projects. C-Path would never have been possible without the support provided by the founding partners, the public sector, individuals and private foundations. Detailed financial reports are on pages 21–23.

Once again, on behalf of all C-Path employees, and on behalf of patients who will be positively and permanently helped by our work, we thank you for your support.

—Raymond Woosley, M.D., Ph.D.
President and CEO
creating an environment for innovation and change through **COLLABO**

Led by C-Path, scientists from academia, biotechnology companies, the government and pharmaceutical industry are beginning to work together in new ways through pioneering partnerships. These powerful coalitions will lead to life-saving drugs, devices and biological products getting approved faster and ultimately reaching the people who need them most with greater safety.

C-Path is a trusted third party because it is a non-profit, unaffiliated with any single entity or interest group. This allows C-Path to serve as an effective and welcome facilitator among the government, academia and the private sectors.

Already in its first year, C-Path has forged key partnerships, created collaborations and hosted conferences leading to new working relationships. C-Path has enabled some of the largest pharmaceutical companies in the world to work together with the FDA to create the Predictive Safety Testing Consortium (PSTC). Through this consortium, industry competitors have joined for the first time as collaborators to share and verify testing methods. C-Path has also helped build new working relationships by hosting a conference for drug and diagnostic companies on cancer drug development. It is also partnering with the Drug Information Association for major conference collaborations with the FDA and other organizations.

- **October 2005** C-Path signs Memorandum of Understanding with FDA.
- **December 10, 2005** C-Path hosts ribbon-cutting ceremony at Tucson office to officially announce the start of the Institute.
- **December 16, 2005** FDA announces first-of-its-kind partnership with C-Path to fulfill the mission of the government’s Critical Path Initiative.
January 2006 C-Path officially changes name to “The Critical Path Institute.”

January 2006 C-Path announces that it will open additional offices in Washington D.C. and Phoenix.
Status of Projects

*Fostering developments that result in better care for patients*

As a country, the United States spends more than ever to do research and develop new drugs, and yet we aren’t seeing results proportional to the investment. Over the last 10 years, U.S. pharmaceutical companies have spent 250 percent more on research and development. The biomedical research budget for the National Institutes of Health has doubled in the last decade. However, the number of innovative new therapies submitted for approval by the Food and Drug Administration has actually declined by nearly 50 percent during the same time.

One of the major bottlenecks in drug development is the long and inefficient process for preclinical and clinical testing of drugs. It can require an investment of more than $1 billion and take 12 to 15 years to bring one product to market.

The Critical Path Institute exists to foster a collaborative environment where new therapies can be developed faster, where safer products arrive on the market, and where industry, the government and academia all work together in innovative ways that benefit the common good.

In spite of scientific advances and increased spending for research, the efficiency and productivity of drug development has declined in the last decade. C-Path projects aim to facilitate positive change in the drug development process by addressing areas such as standards for data submission, methods for testing product safety, and unmet medical needs. Progress we’ve made on our major projects is detailed on the following pages.

- **Spring 2006** The Food and Drug Administration designates orphan drug status to potential cures for Valley Fever.

- **March 2006** C-Path creates an unprecedented collaboration between pharmaceutical companies and the FDA to form the Predictive Safety Testing Consortium (PSTC).

- **Spring 2006** C-Path coordinates the creation of Valley Fever Therapies, LLC, to advance a potential cure for Valley Fever into clinical trials.
June 2006 Federal funding of a collaborative cardiovascular drug safety and biomarker research program begins in partnership with the University of Utah.

June 2006 The Critical Path Institute Foundation is founded, with the sole purpose of creating long-term funding and endowments to support C-Path.

June 2006 C-Path assumes organizational responsibility and receives previous federal funding for the Arizona Centers for Education & Research on Therapeutics (AzCERT).
In the first year, three C-Path projects involve applied research and education to accelerate drug development. The projects concentrate on biomarkers (novel measures of drug effects), innovative clinical trial design and standards for data collection.

**Cancer Biomarkers**

C-Path is coordinating a project to bring pharmaceutical and diagnostic companies together with government agencies in a project that will help guide lung cancer therapy. The Cancer Biomarkers project is a significant part of a national collaboration called the Oncology Biomarker Qualification Initiative. This national Initiative was formed by the FDA, National Cancer Institute (NCI) and the Centers for Medicaid & Medicare Services with a mission to advance the development of personalized treatment and diagnostic testing.

As part of the Cancer Biomarkers project, C-Path has successfully brought competitors together as collaborators. Led by Chief Scientific Officer, Dr. Jeff Cossman, C-Path has assembled a group of approximately 18 pharmaceutical, biotechnology and diagnostic companies.

Together they are working to design and conduct a study in patients with lung cancer.

The goal of this working group is to undertake a clinical trial that will provide the FDA with evidence to guide the selection of tests (biomarkers) that predict response to the treatment of non-small cell lung cancer drugs that target novel proteins in cancers (EGFR).

C-Path brought the team together in Tucson on April 28, 2006, where the participating scientists decided to focus on lung cancer and the EGFR-inhibitor class of drugs. C-Path hosted a follow-up meeting in Atlanta during the American Society for Clinical Oncology Meeting, June 5, 2006. There, a project plan was developed and in the following weeks teams were created to address each of the candidate...
By forming this team project C-Path is creating new collaborative relationships that will help bring innovative cancer therapies to market faster.

**Collaborative Cardiovascular Drug Safety and Biomarker Research**

In partnership with the University of Utah, C-Path received an FDA grant for almost $2 million to evaluate genetic tests for their ability to predict safer and more effective doses of the anticoagulant warfarin (Coumadin®). Warfarin is a generic drug widely prescribed as a blood thinner to prevent dangerous blood clots. The optimal dose varies from patient to patient. If the dose is too high, the patient may have serious bleeding and conversely, if the dose is too low, the patient may suffer a stroke or...
embolism. In both these situations, death can follow. The intent of this grant is to reduce these adverse events from warfarin.

The three-year grant was announced in June 2006. The University of Utah is performing the clinical study and C-Path will evaluate the methods used in the study to assure the FDA that the results of the trial can be applied to write dosage recommendations for warfarin based on genetic testing. The FDA grant also supports work to evaluate biomarkers that predict the safety of drugs used in the treatment of cardiovascular disease, especially heart failure.

Research has identified numerous biomarkers that have the potential for predicting human response to new therapies. These biomarkers may also improve the ability of commercial sponsors to develop more effective treatments for cardiovascular disease. However, because of the overall low response rate without a predictive test, few of these reach the market and fewer become routine components of therapy. One of the factors that has limited development of biomarkers is the lack of a clear path to FDA approval for such assays. The results of this C-path project should identify such a path to approval and would aid pharmaceutical and diagnostic companies as they develop new drugs and diagnostics. The new process created by the FDA for this project could serve as a model pathway for other personalized medicines.

**What is a biomarker?**

A biomarker is a physical measurement of what is occurring in the body. Examples of biomarkers are the measurement of blood pressure, temperature or blood sugar. Biomarkers can be used to assess normal biologic processes, disease processes or response to a treatment. Genetic biomarkers are DNA sequences that identify persons who would react in a certain way to a treatment or a disease.
**Rare/Orphan Diseases**

An “orphan disease” is defined by the FDA as an illness that is present in less than 200,000 Americans each year. Because there are so many orphan illnesses, more than one in 12 Americans has an orphan disease. Focusing on three specific orphan diseases, C-Path is building collaborations to facilitate the development of effective and safe new treatments for Niemann-Pick Type C (NPC), valley fever and adrenocortical cancer.

The overall goal of the Rare/Orphan Diseases program is to help create the functional infrastructure for patients, providers, researchers, foundations and companies to work together to develop the clinical studies and scientific evidence needed for new treatments. A critical component of this demonstration project is developing “disease model registries” that describe the natural history of rare/orphan diseases. Disease models would enable scientists to more fully understand the basis for diseases and the pattern of symptoms and events that could be the target of new interventions.

Many clinical trials of new drugs fail because the natural history of the disease is not fully understood. Textbook descriptions are often out-of-date and the manifestations of a disease are often different in patients referred to medical centers compared to patients in the community-at-large. The FDA’s Critical Path Opportunities List calls for creation of disease models, and C-Path has made progress on establishing models for NPC and valley fever.

This project seeks to create collaborations to demonstrate the value of disease models and other modern clinical trial techniques such as adaptive trial design, on-line data analysis, and population enrichment using biomarkers. Successful use of these innovative methods with rare/orphan illnesses could demonstrate their value and result in FDA guidelines that encourage the industry to use these methods as routine tools in drug development.
Safer
Projects to improve drug safety

Two projects led by C-Path are designed to create the safety tools that enable the accelerated development of drugs. A novel research project explores new measures to ensure drugs are safer before they reach the market. The other focuses on methods to rapidly detect safety problems once new drugs are on the market and being taken by tens of thousands of patients.

Predictive Safety Testing Consortium

The Predictive Safety Testing Consortium (PSTC) brings pharmaceutical companies together to share and validate each other’s safety testing methods under advisement of the FDA. The 15 corporate members of the consortium have begun sharing internally developed pre-clinical safety biomarkers in four workgroups: carcinogenicity, kidney, liver and vascular injury.

The tests that are used to determine drug safety today have not changed in decades and many drugs that appeared safe in laboratory tests may be found later to have serious toxic effects in some people when large numbers of patients have taken the drug. Companies have developed newer safety testing methods, but these are not generally accepted by the FDA as proof of safety because the tests have not been independently validated by a third party. Also, the methods used by companies are often different, leaving the FDA scientists unclear about which methods should be preferred. In order to change this, C-Path has invited pharmaceutical companies to join the PSTC to share their internally developed methods and test the methods developed by another member of the Consortium. Ten FDA scientists participate as PSTC advisors, along with more than 120 scientists. C-Path serves as the “trusted third party,” collecting and summarizing the data. The process is expected to enable the FDA to write new guidances that identify more accurate methods to predict drug safety and identify less effective methods that should be discarded.

The Consortium was officially announced by the FDA on March 16, 2006, when Health and Human Services Secretary Michael Leavitt, FDA Commissioner Dr. Andrew von Eschenbach and FDA Deputy Commissioner Dr. Janet Woodcock announced the next phase for the FDA’s Critical Path Initiative. They identified this C-Path Consortium as “unprecedented” and a “shining example” of the type of work the FDA would like to see conducted.

Each member of the Consortium has begun sharing internally developed pre-clinical safety biomarkers in the four pathology areas. The safety biomarkers will be cross-validated by other members of the Consortium. Out of this work, data should be generated that will be the basis for an FDA Guidance to provide direction for the entire pharmaceutical industry on how to better test drugs for safety. Notably, the FDA scientists are not acting in their
usual role as regulators. Instead they are active participants, providing assistance and advice to the Consortium.

This project has gained international attention. The European equivalent of the FDA, the European Medicines Evaluation Agency, has agreed to appoint observers to work with the Consortium. The United Kingdom Academy of Medical Sciences—the UK equivalent of the U.S. National Academy of Sciences—has also asked to be kept informed of the progress and offered to share the results of a similar UK initiative that is being created and modeled after C-Path’s Consortium.

Nationally, C-Path’s Predictive Safety Testing Consortium has been praised by the regulators, the industry and the press as a successful model for a pharmaceutical industry collaboration. C-Path has been asked to report its experience at national meetings and to share the structure of the legal framework with other organizations forming consortia.

**Community Pharmacy Safety Network**

The goal of the Community Pharmacy Safety Network (CPSN) is to test the feasibility of obtaining reliable data for the FDA on the comparative safety and effectiveness of new medicines using information provided by patients receiving prescriptions from community pharmacies. The absence of a dependable early alert system to quickly detect serious rare adverse effects of new drugs after they are on the market is a barrier to accelerating the availability of important new drugs. The FDA’s current voluntary reporting system has been valuable, but it is not capable of systematically collecting reports on all adverse drug reactions, and therefore is unable to measure the incidence of adverse events for drugs. In addition to being very slow to detect adverse drug events, the current system is unable to compare the relative safety of alternative forms of therapy.

The CPSN project is investigating the practicability of an active surveillance system, using a previously validated model that may have the ability to detect and quantify adverse drug events for the FDA. Patients beginning therapy with specific drugs are asked to join a registry and contact a pharmacy call center to report any adverse events. The call center also contacts the registrants at specified times to solicit unreported adverse events.

A pilot collaborative project with funding from the federal Agency for Healthcare Research and Quality and the Arizona Center for Education and Research on Therapeutics (AzCERT) began on January 1, 2006, and will end in fall, 2006. The project includes 55 Bashas’ community pharmacies and the Arizona Poison and Drug Information Center. If the methods used in this investigation are found to be feasible and reliable, the next step is to consider the feasibility of expanding the program to a national scale.
In addition to providing a collaborative environment for innovative research programs, C-Path also seeks ways to share expertise and knowledge. In its first year, C-Path brought together participants, including students and university faculty, along with scientists and others working in the field of drug development, to share the latest innovations. Through these educational programs and brainstorming sessions, C-Path creates the venue for the advancement of more efficient ways to develop, review and use new therapies.

**Tucson Cancer Conference**

In April, 2006, C-Path convened a meeting of leaders from approximately 20 companies, the FDA and NCI, to discuss potential collaborations and research. It was decided at this meeting to focus on lung cancer and the EGFR-inhibitor class of drugs. The Cancer Biomarker Project outlined on previous pages grew out of this meeting.

**Information Technology Planning**

In order to gather advice and guidance for information technology needs, C-Path brought together industry leaders for a brainstorming session in February 2006. Dr. Patrick Lincoln, Director of the Computer Science Laboratory at SRI International, and employees from C-Path, along with faculty from The University of Arizona and Arizona State University, helped C-Path plan for information technology needs for the Rare and Orphan Disease Registries and biomarker database solutions projects.

**Education**

To gauge interest and begin discussions on developing a drug development curriculum at The University of Arizona, C-Path met with faculty members of five UA Colleges (Medicine, Pharmacy, Public Health, Science and Management) in June 2006. It was agreed C-Path would take an inventory of existing university courses that could be included in a curriculum, as well as identify gaps and other resources. The group plans to reassemble to further explore interest in a proposed Drug Development curriculum.

**National Presentations**

Executives from C-Path have made more than 30 formal presentations related to C-Path and CPI projects at various national conferences.
Financial Status

A strong financial beginning

C-Path’s existence and current success would not be possible without the financial support from the Arizona community. Through our founding partners—The University of Arizona, FDA and SRI International, Inc.—as well as the public sector, and individuals and private foundations, C-Path has received more than $10 million in cash and pledges.

C-Path began its first fiscal year in a strong financial position. Most of the first year pledges were paid in advance and all of the first two years of pledges have already been paid in full. In fact, a number of donors increased their pledge amounts.

This strong support allowed the hiring of staff and the ability to underwrite early phases of key projects, such as the Predictive Safety Testing Consortium.

To establish a clear standard for openness and accountability, an audit was issued for the partial year ending June 30, 2005.

In addition to the start-up funding from the community, several sources of long-term funding are being developed. In particular, the potential for endowment funding from national foundations is being explored as well as federal funding for C-Path as a permanent component of the federal budget.

In June 2006, The Critical Path Foundation, a separate 501(c)3 organization was formed. The Critical Path Foundation will focus exclusively on raising endowment funding to support the mission of C-Path. Legislation was also recently introduced in the U.S. Senate to authorize “one or more Critical Path Institutes.” C-Path will work closely with Arizona legislators to see that the Institute becomes the first and foremost candidate for this permanent designation.

Because of timely payment of second year pledges and new grant revenue, C-Path is pleased to enter the new fiscal year in a strong financial position.
Financial Support

Generous support built a solid financial foundation

C-Path’s mission to improve the path for innovative therapies would not have become a reality without the generous support of the Institute’s founding partners and donors. A public thank you is needed to those who made it possible to begin the work of The Critical Path Institute on such a solid foundation. The Institute wishes to acknowledge donors who gave during calendar years 2005 and 2006 and offer its deep appreciation for their support.

$500,000 to $1 million
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Pima County

$200,000 to $499,999
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Diamond Foundation and Diamond Ventures
Thomas R. Brown Foundations
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The Cottrell Foundation of Research
  Corporation Technologies
Tucson Electric Power

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Bank of America
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Town of Marana
Town of Oro Valley
Tucson New Car Dealers Association
Wells Fargo
C-Path gratefully acknowledges the following grants received through June, 2006

<table>
<thead>
<tr>
<th>Grant</th>
<th>Amount/Details</th>
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<tbody>
<tr>
<td><strong>US Agency for Healthcare Research and Quality</strong></td>
<td>$631,000 (including a sub-award of $213,000 to the University of Arizona)</td>
</tr>
<tr>
<td><strong>US Food and Drug Administration</strong></td>
<td>$675,000 (including a sub-award of $225,000 to the University of Utah)</td>
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<tr>
<td><strong>Flinn Foundation</strong></td>
<td>$500,000 to date</td>
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<tr>
<td><strong>Commerce and Economic Development Commission, Arizona Department of Commerce</strong></td>
<td>$200,000</td>
</tr>
<tr>
<td><strong>Mary Alice and Thomas D. O’Malley Foundation</strong></td>
<td>$50,000</td>
</tr>
</tbody>
</table>

**$1,000 to $9,999**
- AAA Landscape
- Jennifer and Enrique Aviles
- Bourn Partners, LLC
- Campus Research Corporation; Bruce Wright
- Linda and David Cohen
- Executive Connection
- Finley Distributing Company
- Raphael Gruener
- KB Home; John Bremond
- Mary Jane and Richard Kurkjian
- David and Leesa Lane
- Edward and Christina McComb-Berger
- PICOR Commercial Real Estate Services
- Patty and Tom Richardson
- Jim Strickland
- The Caliber Group, Inc.; Linda Welter Cohen
- Tucson Realty & Trust, Co.; Hank Amos

**Up to $999**
- Anita Bell
- Randall Brookshier, CPA
- Monrad Engineering, Inc.
- Nicolina Pistacchio
- Sue and Red Redlazyk
- The Janzen Wahl Group, LLC
- Franklin Wilson
Future Directions

In its first year, C-Path has initiated projects that have successfully brought together scientists and others from the FDA, NIH, NCI, the pharmaceutical industry, diagnostics companies, and academia. Three projects (Predictive Safety Testing Consortium, Cardiovascular Biomarkers and Cancer Biomarkers) have adequate funding to proceed and are well underway. In the near future, C-Path hopes to identify funding for the Rare/Orphan Disease project.

Exploratory discussions are underway to consider forming consortia to develop testing methods for vascular stents and biomarkers for Alzheimer’s Disease. It is anticipated that C-Path will focus on the projects that are currently funded while leaving open the possibility of adding new, high-priority funded projects.

Looking forward, a key focus is on attaining long-term, sustainable funding sources. C-Path is exploring the potential for endowment funding from national foundations and federal funding of the Institute as a permanent component of the federal budget. The Critical Path Foundation will focus exclusively on raising endowment funding to support the mission of C-Path. C-Path also is pleased by the potential for legislative support.

C-Path is expanding its Tucson presence with additional office space located in the city and opening a Rockville, MD, office near the FDA and NIH.

The basic premise of C-Path as a trusted third party has been welcomed by government agencies including the FDA, NHLBI and NCI, as well as the medical product industry. Significant programs are underway and attractive financial alternatives to sustain C-Path are being pursued. Though, as these alternatives are developed, the community support that made C-Path possible will continue to be essential over the next four years.