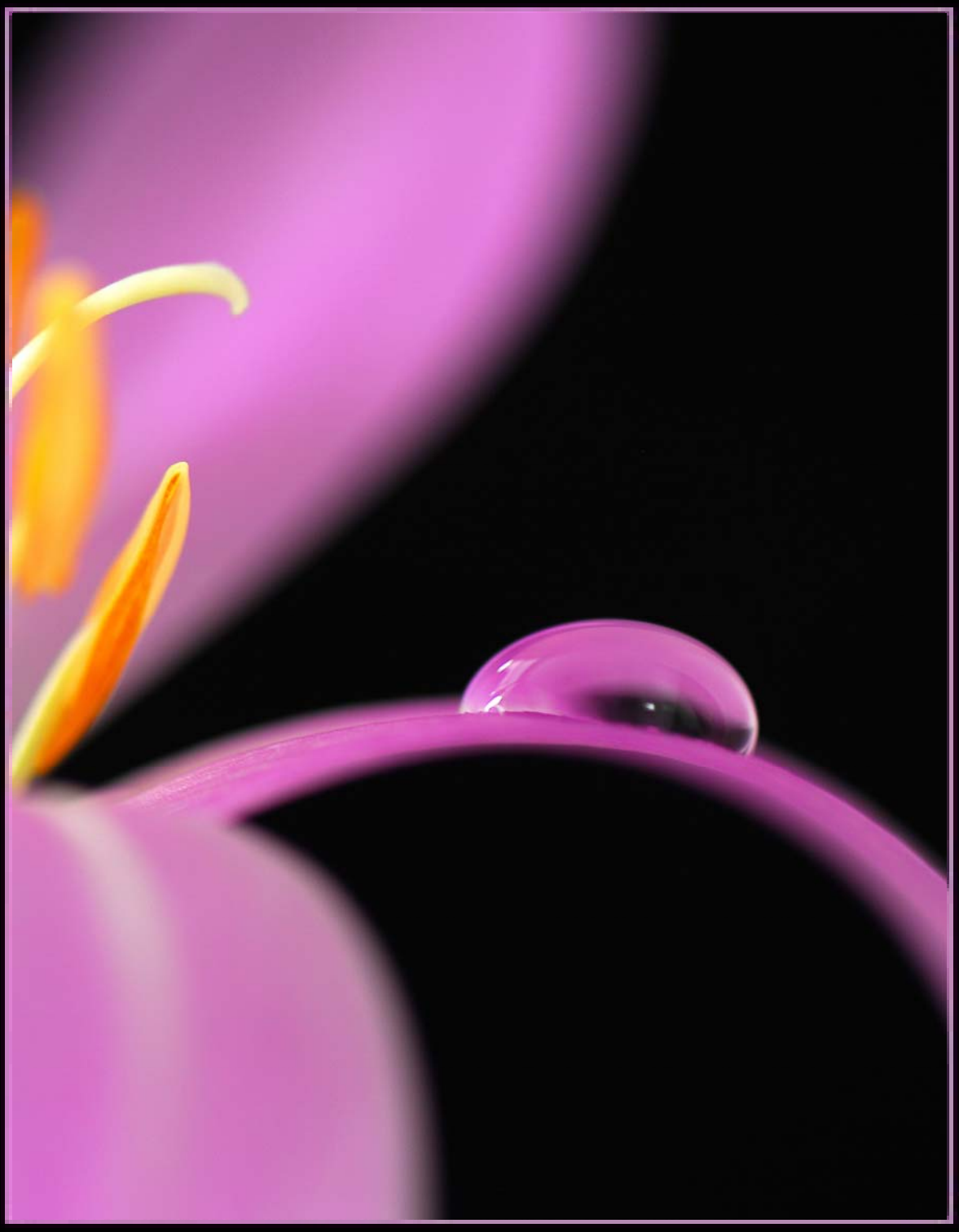


The Life Raft Group
2007 Annual Report

A note about the cover artist:

This picture is one of many stunning pieces of art from the collection of Rachel Gilbert. Rachel is a 21-year-old GIST patient from the United Kingdom. She has been living with GIST for almost seven years. She uses her art to channel beauty into the world to cope with her disease.

The Life Raft Group

Dear Friends,

Since last year's annual report much has happened. The Life Raft Group (LRG) continues to grow in size and complexity to match the needs of today's GIST (Gastrointestinal Stromal Tumor) patient. Our program priority areas remain the same: Research, Information and Support, Patient Outreach and Assistance and Advocacy. However, in 2007, we expanded our capacity through innovative technologies and approaches to reach the evolving GIST community.

From a birds-eye view the Life Raft Group is a thriving young organization, its message reaching hundreds of thousands each year to help GIST patients and their loved ones in as many ways as possible. Here on the ground, the LRG is running a race against time, a relentless pursuit of survival. Faced with increasing cases of resistance to first-line treatment, the LRG continues its commitment to finding a cure through its work and funding the Resistance Research Project.

GIST is a rare cancer, but the struggle of cancer survivors is not uncommon in our world today. We will continue, with the help of our supporters, medical professionals and volunteers, to ensure that no one has to face GIST alone.

Stan Bunn
President

Norman J. Scherzer
Executive Director

The Life Raft Group's Major Program Ar-

To accomplish its mission, the Life Raft Group devotes its efforts to four major priority areas: Research, Advocacy, Information & Support, and GIST Outreach.

Research

In 2006, the Life Raft Group (LRG) set forth with a strategic plan and a team of expert researchers on the pathway to the cure. What is unique about this? The LRG not only funds this research but manages and facilitates communications of eight of the world's leading GIST researchers from six different institutions. Our innovative grant system dramatically reduces administrative costs, holds each researcher responsible for specific results and redirects funding when necessary.

This year marked the one year milestone for the LRG Resistance Research Project and although the cure is not yet in hand we are optimistic that it will soon be in sight. In 2008, we plan to obtain more funding for this project and expand the team to include other expert researchers. (Please see Fletcher's report for more details.)

LRG GIST Patient Registry

The LRG maintains a unique patient registry, tracking patients' medical status to allow us to provide information to GIST patients and caregivers. Timely knowledge and information are key to survival.

All of our information comes directly from patients and caregivers. Using this data, we examine questions that are not being answered quickly enough by current trials or not being examined at all. We monitor the latest treatments for early indications of a response. We look for treatment and response trends that can help our members reach tomorrow's cure.

WEBCASTS: **A new way to bring patients the information they need.**

Since the LRG is not limited by the design of traditional clinical trials, we have significantly increased flexibility over areas that we can examine. We are better able to follow patients over long periods of time and across institutional boundaries. Because the LRG was founded by patients and caregiv-

ers, we are in touch with the real life issues that come up on a daily basis. This connection allows us to track treatments and issues that are of concern to GIST patients today. In 2007, the LRG updated the 2004 Gleevec dosage study and revealed, for the first time, that patients on a higher dose of imatinib had significantly higher overall survival rates.

By fully embracing the role of patient advocate, we have now become patient scientists changing the medical research environment.

Treatment and Surveillance

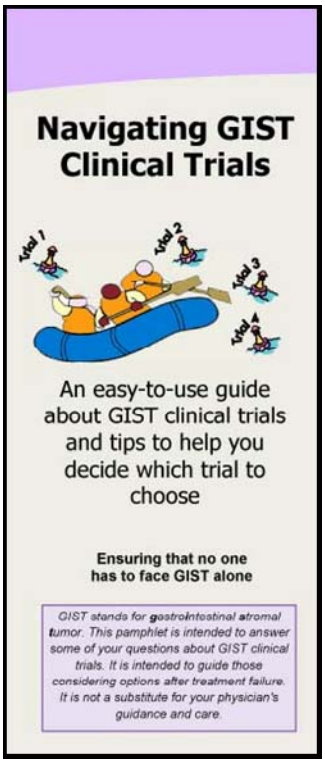
With a growing number of GIST patients looking for the next step in their treatment, we have strengthened our focus on rigorously tracking clinical trials and publishing monthly updates in the newsletter. The unique molecular targets for each trial are also listed so that patients are not repetitively trying similar drugs. The LRG continues to encourage patients to get mutational testing in order for their physicians to take advantage of that information when developing survival strategies.

Through our internal research, we also examine trends and preliminary reports so that patients can make informed decisions about the future of their care.

Patient Representatives came together from every corner of the world at the Patient Summit, Bad Nauheim, Germany. The Bad Nauheim Declaration was born!

Advocacy

The LRG has become a formidable advocate for GIST patients. As we grow, so does our ability to help GIST patients. This year the LRG's major efforts included the adoption of the Bad Nauheim Declaration, which aims to create a standard of care for all GIST patients in any healthcare system across the world so that all patients are treated equally. The LRG has also lobbied against the Medicare and Medicaid proposed restrictions limiting the use of drugs that treat anemia, a common side effect of most cancer medications. In addition to our public advocacy work, the most important efforts we carry out are done case by case for patients with nowhere else to turn. Many times patients or their loved ones contact the LRG for help from countries all over the world. They are facing obstacles that range from not receiving their prescriptions on time to outright refusal of treatment by their own government agencies. Often, patients are in dire need of treatment but, because of poor health, do not qualify for a clinical trial. The LRG works with those patients to gain access to a drug that will help them survive. The LRG goes above and



The LRG produces pamphlets to help patients cope with making decisions about their care.

beyond most patient organizations by stepping in as the patients' true advocate, using every method possible from persuasion to confrontation, to make sure that patients get needed treatment.

Information & Support

The LRG is committed to providing information and support to the GIST community including patients, their families, friends and medical professionals. With growing resistance to first-line treatment prompting the development of so many new drugs, it is of utmost importance for everyone to stay up-to-date.

This year the LRG focused on expanding our newsletter content; restructuring our website with new content and a focus on making it more user-friendly; and developing more education materials to address specific needs such as navigating clinical trials. The LRG also employed the use of webcasts as an educational tool. Webcasts allow attendees to go online and log on to important seminars such as "Living Well with Side Effects: A Guide to Side Effects Management"; "Mutational Testing: Broken Down"; "'GIST' the Basics" and many more. Through innovative technology, we have reached thousands of people in their very own homes. Webcasts are also stored in our new video library which is easily accessible on the LRG website.

The LRG was born on the internet and continues to provide patient support through our private email community. This forum allows only GIST patients and caregivers to discuss sensitive topics and exchange ideas to support everyone's quality of life.

GIST Outreach

In addition to the newsletter, webcasts, website and email community, the LRG fosters the development of local groups that meet in-person across the United States. This year alone we have added 11 new groups to our ever-growing list. We also work with international chapters and sister groups through the Global GIST Network which is funded by the LRG. This year we have added patient liaisons in Belgium, Lithuania, Thailand and Uruguay. These volunteers serve vital roles to help GIST patients with treatment issues specific to their countries. With the help of many outstanding volunteers distributing educational materials, hosting events and launching personal campaigns, we are able to cast a wider net to create awareness for this rare cancer.

We began working on pharmacy outreach this year hoping to reach all those patients who are on prescription drugs that treat GIST. So far, we have developed a pilot collaboration with a national pharmacy chain which has disseminated information about GIST to all of their locations.


Dr. Fletcher

The LRG Resistance Research Progress Report

GIST THERAPY RESISTANCE MECHANISMS

YEAR 2 PROGRESS REPORT:

Research to identify therapeutic methods that operate in synergy with Gleevec (imatinib) in achieving long-term remission and cure of GIST

In the past year, LRG research funding has enabled progress in identifying novel treatment strategies for GIST. Despite the remarkable clinical responses to KIT and PDGFRA kinase inhibition, GIST clinical progression can occur even in individuals with spectacular initial response to imatinib. For this reason, LRG is committed to funding research programs to develop synergistic targeted therapies that counteract imatinib-resistance in GIST. In the past year, research progress was made by studying new treatment methods in GIST surgical specimens, GIST cell lines, and mouse models of GIST. The urgent aims in all these studies are to identify therapies that function synergistically with imatinib in destroying GIST cells.

Each of the funded scientists performs GIST research that is coordinated with the efforts of the other scientists in this LRG program. Great pains have been taken to enable collaboration while eliminating redundant research efforts, such that team achievements are emphasized. This rigorous approach will continue to maximize the LRG research productivity, and – specifically – identify treatment approaches that synergize with imatinib and other KIT kinase inhibitors in enabling a higher cure rate for patients with GIST.

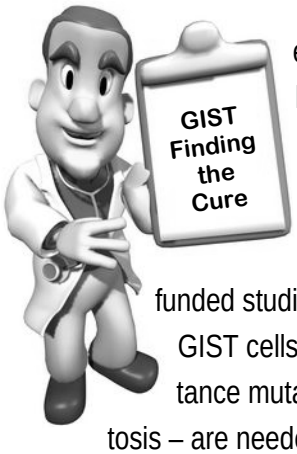
It is hoped that additional research priorities can be supported during the next several years of LRG funding. In particular, there is urgent need for therapies that operate in synergy with imatinib by increasing GIST cell apoptosis. The LRG resistance effort would be well-served by encouraging more studies of GIST survival and apoptosis mechanisms.

The imatinib-resistance studies described here are essential to therapeutic progress in GIST. These studies will likely reveal that combinations of GIST therapies are needed to consolidate initial remissions, forestall the emergence of clinical resistance, and lead to increased cure rates. At present, the LRG research program funds ten "priority" projects. Each of these projects has substantial, near-term potential for enabling development of novel GIST therapies. The Year 2 progress for each of these highest-priority projects is summarized below.

Oncogenic signaling mechanisms as novel therapeutic targets: These studies continue to highlight the crucial role of the PI3-K kinase protein in transmitting KIT and PDGFRA oncogenic signals in GIST cells. Specifically, the LRG research group have shown that a subtype of PI3-K, known as "catalytic alpha" is most relevant in GIST, and future studies will prioritize validations of new drugs that inhibit this particular PI3-K subtype. The LRG studies have also demonstrated several proteins that bind to KIT in GIST cells: one example is the protein kinase C theta protein, which in the next year will be evaluated as a novel therapeutic target in GIST.

Wildtype GIST: This project was suspended last year, because there were insufficient numbers of cases identified in the early months of the research program. Fortunately, substantial progress has been made in the past year, such that KIT/PDGFRA wildtype GISTs, as identified by mutational analyses of paraffin sections, can be used to identify the biologic mechanisms responsible for KIT activation in these cases. The recent work has identified several kinases, beyond KIT or PDGFRA, that are found at high levels in the wildtype GISTs, and that might serve as additional therapeutic targets.

Primary Resistance: Some GISTs are caused by KIT or PDGFRA mutations that do not respond well to imatinib. Research progress in the past year has highlighted that alternate therapies, including sunitinib, sorafenib, and nilotinib can be



effective against subsets of these imatinib-resistant primary mutations. In addition, some KIT kinase inhibitors have greater potency than imatinib against nonmutant KIT, and these inhibitors may be particularly effective against KIT/PDGFRA wildtype GISTs.

Stable disease after imatinib: Stable disease, i.e. GIST cells that are suppressed but not killed by imatinib, remains a major problem for most people with inoperable GIST. The recent LRG-funded studies show that a variety of imatinib-resistance mutations can be found at low levels in such stable GIST cells, accounting for partial resistance to therapy. However, other cells persist in absence of such resistance mutations, and new therapies – particularly those which are highly effective in inducing GIST cell apoptosis – are needed, in conjunction with KIT kinase inhibitor drugs, to destroy those cells. Future studies will focus on identifying drugs for stable GIST, and developing highly sensitive assays that can detect treatment-resistance mutations in blood samples.

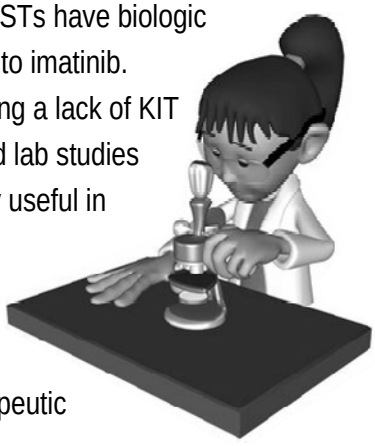
Secondary resistance mechanisms: Continued progress has been made in identifying drugs that can inhibit secondary imatinib-resistant mutations. In addition, novel and extremely sensitive assays have been developed to detect low-levels of imatinib (and other KIT kinase inhibitor) resistance mutations in GIST biopsy materials.

Kit Degradation: These studies have identified small molecule HSP90 inhibitors that are exceptionally effective against the KIT oncoproteins in GIST cells. Preliminary studies show that greater efficacy, particularly in mouse GIST assays, is obtained with the combination of HSP90 inhibitor and imatinib, compared to using either drug on its own. Future studies will further evaluate these treatment synergies, and will determine mechanisms of HSP90 inhibitor resistance in GIST.

Murine Models: The laboratories of Drs. Besmer and Rubin have continued to develop mice that develop GIST and are therefore useful in testing new GIST drugs. Additional progress has included development of mice with imatinib-resistant GISTs, which will provide a system to test drugs of potential benefit for individuals whose GISTs have progressed while receiving imatinib.

Resource Development (imatinib sensitive & resistant): Exceptional continued progress has been made in developing new immortal GIST cell lines and mouse xenografts, which are indispensable for testing GIST drugs. The LRG scientists have shown that these resources provide biologically faithful model of GISTs in humans, and as such are highly useful in screening studies to identify new GIST drugs. Additional cell lines have been developed that permit drug testing against the wide variety of KIT and PDGFRA mutations found in GIST. These collective resources are, without doubt, one of the great strengths of the LRG research consortium.

Pediatric GIST: Dr. Antonescu's research group has continued to shed light on the biological differences between pediatric and adult GISTs. Studies in the past year have shown that the frequency of genetic syndromes, particularly the so-called "Carney's Triad", may be underestimated in children with GIST. A small subset of pediatric GISTs have biologic similarities with adult GISTs, and these tumors can be expected to respond better than others to imatinib. However, most pediatric GISTs have substantial biologic differences from adult GISTs, including a lack of KIT mutations. Activated KIT is nonetheless important in these KIT/PDGFRA-wildtype tumors, and lab studies suggest that newer-generation KIT kinase inhibitors, such as nilotinib, might be therapeutically useful in these pediatric wildtype GISTs.



Tissue Banks: The LRG central repository for frozen and paraffin-embedded GISTs supports the collective research efforts in this program. These specimens are studied to identify novel oncogenic mechanisms in KIT/PDGFRA-wildtype GISTs, and to identify additional therapeutic targets in GISTs with KIT or PDGFRA mutations.

The Life Raft Group

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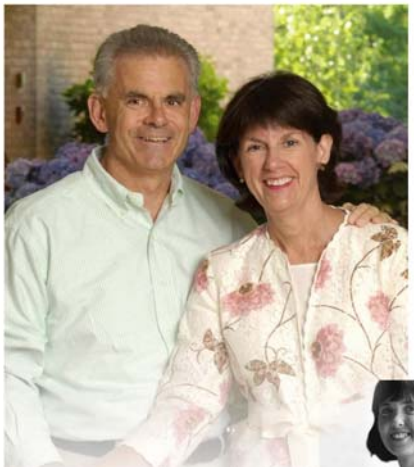

David Smith and Pat Brady donate stock each year in memory of their good friends' Jim and Marge Hughes' daughter, Nancy Hughes Welsh (right).

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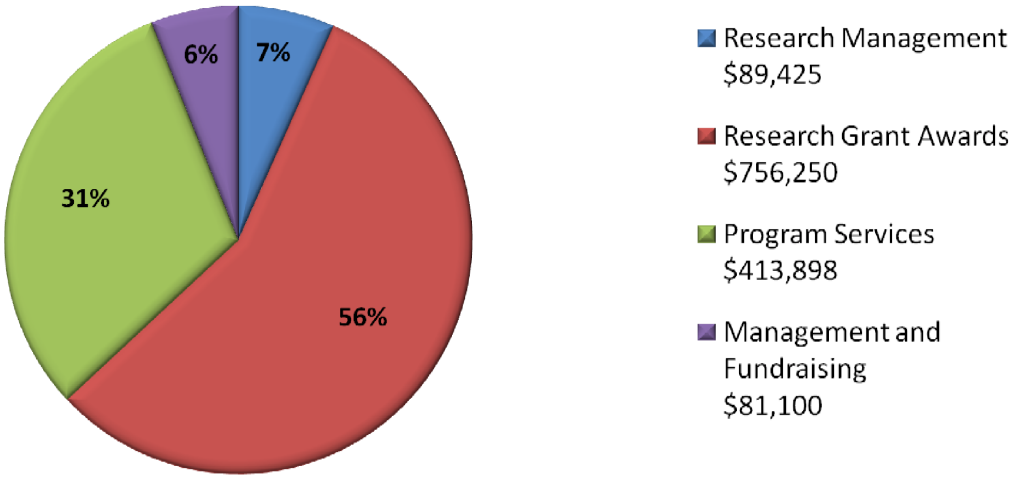
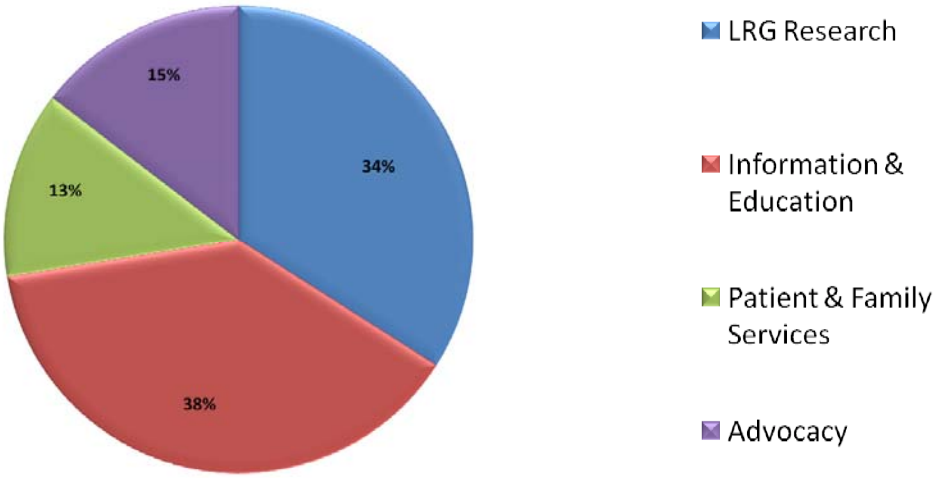
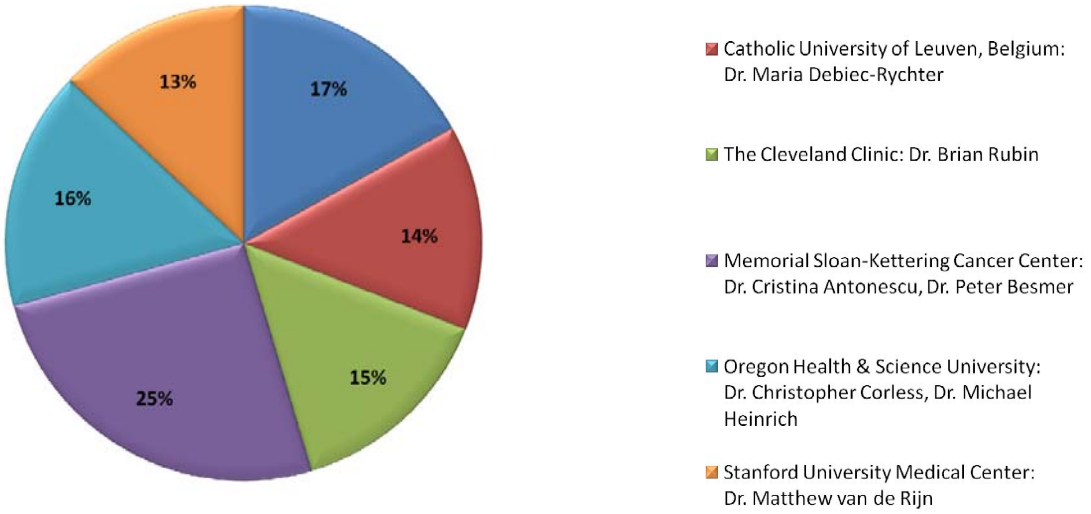


Allocation of Program Service Expenses



Allocation of Research Grant Awards for 2007



The Life Raft Group (LRG) is an organization that provides support, information and assistance to patients and families with a rare cancer called Gastrointestinal Stromal Tumor (GIST). The LRG achieves this by providing an online community for patients and caregivers, supporting local in-person meetings, patient education through monthly newsletters and webcasts, one-on-one patient consultations, and most importantly, managing a major research project to find the cure for GIST.

ensuring that no one has to face GIST alone

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