Dear Friends,

Since attaining its non-profit status in 2002, the Life Raft Group (LRG) has served as a beacon for GIST patients and their families. Over the years, it has refined its focus to four major program areas: Research, Information and Support, Patient Outreach and Assistance and Advocacy.

It is especially notable that the LRG continues to break ground in research with the 2006 launch of the LRG Resistance Research Project.

This report is a glimpse of our prominent program areas. The LRG’s mission remains: To ensure the survival of GIST patients while maintaining the quality of their lives. The LRG reaches beyond the average cancer support group by working one-on-one with patients in trouble. The includes interceding on their behalf to overcome obstacles to treatment access. Many of our greatest accomplishments occur behind the scenes.

In 2006, the LRG reached a network of over 60,000 people through its newsletters, websites and educational materials. That number continues to expand on a daily basis with the incorporation of new initiatives. The goal is to reach and educate as many patients and doctors as possible to create a world where all GIST patients are treated with expert care.

We are grateful to all those who have given so generously, and in so many ways, to help the LRG carry out its essential programs.

ensuring that no one has to face GIST alone
To accomplish its mission, the Life Raft Group devotes its efforts to four major program areas: Research and Treatment Surveillance, Information & Support, Patient Outreach & Assistance, and Advocacy.

### Research and Treatment Surveillance

**Research:** The Life Raft Group has created a strategic plan to address GIST treatment resistance. We intend to identify the mechanisms of treatment resistance and the means to overcome them. We have established a sophisticated research team and developed a supportive grants infrastructure that will hold each researcher accountable for specific results, redirect resources when research dead ends and supplement them when new needs arise. Along the way, the LRG will create a new research paradigm that will help other patient groups to close the known information gaps to understanding and overcoming treatment resistance.

We conduct our own patient-based research to ensure that we have the most timely and relevant information that GIST patients need to survive. This internal research is designed to provide us with information that is not currently available from clinical trials, either because we are waiting for the trial to reach its research end point and for the researcher to share the information or because the perspective of the trial is just not geared to what patients need to know in order to survive. Patients, caregivers and the LRG cannot completely depend upon the profit drive of the normal drug development marketplace and traditional research funding to ensure patient survival.

A note about Life Raft Group research: Dr. Daniel Vasella, CEO of Novartis described our research as follows: “The Life Raft Group ... has provided various people, patients, doctors, investigators with a unique kind of data bank that cannot be replicated anywhere else, not even in patient trials.”

**Treatment Surveillance:**

In addition to our research, the LRG aggressively tracks new drugs and compounds before they even enter clinical trials for GIST. We seek out and publish clinical trial information in our newsletter and website before any other trial listing service, private agency or government. We then track these clinical trials via patient reports immediately after they begin and evaluate the efficacy and side effects of the new drugs on an ongoing basis. Subsequently, we share this information with patients and doctors through our newsletter and website.

### Information and Support

The Life Raft Group provides information and emotional support to more GIST patients and their families.
than anyone else in the world. Backed by an extensive surveillance program and the maintenance of key databases about treatment options, we prepare and distribute timely and critical information through our website, our monthly newsletter, our internet-based chat facilities, patient pamphlets, membership meetings and sister groups in the United States and around the world. To facilitate access to the best possible treatment, we created and continue to expand an international directory of GIST specialists. Finally, we dramatically impact the recruitment for clinical trials by referring significant numbers of patients to trials that hold promise.

Patient Outreach & Assistance

The Life Raft Group is the only organization in the world that provides real time consultation to GIST patients about treatment options through expertly staffed telephone consultation. Uniquely, we help patients understand how to navigate clinical trials for survival. We provide vital information to patients and their caregivers through our monthly newsletter, our websites, our internet-based chat facilities and our local groups.

Advocacy

The Life Raft Group is the major advocacy voice on behalf of issues vital to the medical and economic well-being of GIST patients. We have undertaken major initiatives to fight the use of placebos in clinical trials for patients that have no other treatment alternatives, to secure Medicare coverage for oral cancer drugs and to bring new drugs to clinical trials. We have begun to represent the GIST patient in the planning of clinical trials and we continue to represent the GIST patient in a growing number of forums both in the United States and abroad. We directly intervene with pharmaceutical companies, insurance companies, medical institutions and foreign governments to deliver life saving drugs, to help patients gain access to clinical trials and to help patients overcome financial and logistical obstacles to treatment.

A major reason that many key people take a rare cancer advocacy group like the LRG so seriously is that we are able to do our own research and publish it in our own newsletter and website. That is a powerful tool which is permitting us, along with an astute use of networking and the media, to carve out a seat for GIST patients at the decision making table.
The LRG is committed to funding research programs for identification and validation of synergistic targeted therapies that counteract Gleevec-resistance in GIST. Despite remarkable clinical responses to tyrosine kinase inhibition, we are seeing relapses of GIST, even in patients with spectacular initial response to Gleevec. We expect that virtually all GIST patients currently benefiting from Gleevec treatment will eventually develop resistance unless we can find and overcome the reasons for such disease progression.

The ambitious plans and the impressive Year One progress outlined in this report would not be possible without a closely-knit and highly-interactive GIST scientist research group. Great pains have been taken to enable collaboration without redundancy, such that the team is emphasized over the individual. This carefully coordinated approach continues to maximize the LRG research productivity. The overall objective in this research is to identify combinations of therapies that can provide synergistic benefit with Gleevec in patients with GIST. The specifics of this progress report represents the input of each LRG research team member.

A series of ten “priority” projects were highlighted for immediate funding. The Year One progress for each of these projects is summarized below. With the exception of project B, all have made outstanding progress and are expected to continue in the same fashion for Year Two.

Project A: Oncogenic signaling mechanisms as novel therapeutic targets: Substantial progress has been made in identifying “downstream” proteins which play crucial roles in channeling the KIT activation stimulus into the GIST cell which are alternate therapeutic targets in GIST. The Year One research highlighted the crucial roles of PI3-K and AKT proteins in maintaining cell growth and has begun to catalog comprehensively the cell proteins that bind to the KIT/PDGFRA oncoproteins in GIST.

Project B: KIT/PDGFRA Wildtype GISTs: These studies have been hampered by the availability of frozen GIST specimens that lack KIT and PDGFRA mutations. The LRG board of directors and research team discussed strategies for obtaining additional frozen GIST specimens that lack KIT and PDGFRA mutations for Year Two. This project is suspended until suitable samples can be obtained.

Project C: Primary Resistance: Progress has been made in establishing laboratory models for GIST mutations that show primary resistance to Gleevec, and potent alternative KIT kinase inhibitors of such mutants. Future studies will continue to focus on the identification and validation of novel KIT kinase inhibitors that are effective against primary KIT/PDGFRA Gleevec-resistant mutations.

Project D: Stable disease after imatinib: Stable disease, i.e. GIST cells that are suppressed but not killed by Gleevec, remains a major problem for most patients. Year 1 studies show that clinically stable GIST – in patients receiving Gleevec or Sutent – can contain abundant KIT secondary mutations, which are the starting point for progression to eventual outright Gleevec resistance. Future studies of stable GIST will address KIT/PDGFRA mutational heterogeneity, evaluate new therapies that more effectively induce apoptosis (cell death), and identify new therapeutic targets by gene expression profiling and proteomic methods.
Project E: Secondary resistance mechanisms & clinical evaluation: Great progress has been made in the past year by developing new human GIST and non-GIST cell lines and mouse xenografts of human GISTs that contain various KIT and PDGFRA kinase domain Gleevec and Sutent resistance mutations. These diverse GIST "models" have enabled identification and preclinical validation of novel small molecule kinase inhibitors with expanded efficacy against the Gleevec-resistant KIT and PDGFRA mutations.

Project F: Kit Degradation: The Year 1 studies have validated the concept that HSP90, and similar proteins, are required to protect KIT in GIST cells. HSP90 can be inhibited by various drugs, resulting in substantial destruction of the KIT oncoproteins in all GIST cell lines tested to date, cessation of growth, and induction of death, in the GIST cells. Future studies will focus on identifying HSP90 inhibitors with greater potency and selectivity for KIT/PDGFRA in GIST.

Project G: Murine Models: The proposed studies are well underway, with Dr. Besmer’s group having shown that the PI3-K pathway is crucial to KIT oncogenic signaling in the murine GISTs, and that therapeutic inhibition of mTOR can reduce the growth of these GISTs. Continuing studies from Drs. Besmer and Rubin will produce mice with Gleevec-resistant inherited mutations, which will be very useful in screening for novel therapies against Gleevec-resistant GIST.

Project H: Resource Development (imatinib sensitive & resistant): Exceptional progress has been made in developing new immortal cell lines. Future efforts will be devoted to expanding the panel of immortal cell lines available for drug testing.

Project I: Pediatric GIST: Dr. Antonescu has identified several genes that are uniquely active in pediatric GISTs, rather than adult GISTs. Future studies will determine whether these genes can be targeted successfully with drugs, producing therapeutic advances for pediatric GIST. This work is particularly crucial because pediatric GIST patients do not respond as well as adult GIST patients to Gleevec.

Project J: Tissue Banks: Excellent progress has been made in establishing a central repository for frozen and paraffin-embedded GISTs to enable the collective research efforts in the LRG program. Future efforts will focus on genomic and gene expression annotations for the banked specimens, and histopathologic annotation to assure that GISTs from patients already treated with Gleevec include both clinically stable and progressing specimens.

Gleevec resistance studies are essential to therapeutic progress in GIST. We hope to substantially expand select studies in the next two years. These studies will likely reveal that combinations of GIST therapies are needed to consolidate initial remissions, forestall the emergence of clinical resistance, and enable increased cure rates.
This past year the LRG held its third membership meeting in Dallas, Texas. Among the 175 patients, caregivers and medical professionals who attended were Dr. Daniel Vasella, CEO of Novartis and David Epstein, President & CEO of Novartis Oncology; the LRG Resistance Research Team members: Dr. Jonathan Fletcher of Brigham and Women’s Hospital, Dr. Christopher Corless of Oregon Health and Science University, Dr. Maria Debiec-Rychter of Catholic University in Leuven, Belgium, Dr. Matt van de Rijn of Stanford University and Dr. Brian Rubin of the University of Seattle; Monica Davey, Oncology Nurse at Fox Chase Cancer Center; Dr. Laurie Letvak of Novartis Oncology; Dr. Alberto Pappo of Texas Children’s Cancer Center and Dr. Jonathan Trent of MD Anderson Cancer Center.

The intention of this meeting was to bring patients, families, physicians and researchers together under one roof. Patients and families learned first-hand about GIST, current treatment options and the latest research findings. Physicians and researchers had the opportunity to network, share information and meet the patients to whom their work is so vital. Bringing people together from every corner of the GIST community assembles a united front of knowledge and drive to get to the cure.

The three day meeting boasted numerous presentations and workshops to help patients learn more about disease management and how to cope with different aspects of treatment. In addition to the educational value of the meeting, it provided community and support.

Our youngest patients (pictured below) participated in art therapy workshops, built their own teddy bears and learned how to ice skate while their parents were updated on pediatric GIST developments and research.

The LRG recognized greatness at this meeting by presenting two very special awards. The Researcher of the Year award was given to Dr. Fletcher for his outstanding dedication to GIST research. The Volunteer of the Year award was given to Richard Palmer for his long-lasting commitment as the LRG newsletter editor.

The LRG would like to express great appreciation to all the volunteers, medical professionals, and, especially, the Texas local LRG that pitched in to put this special meeting together.
This year, the Life Raft Group Board of Directors raised and donated over $182,000! We would like to take this opportunity to acknowledge these men and woman who are so instrumental to the LRG. Since its inception, the board has embodied the steadfast dedication it takes to guide an organization. They use their own means to attend each board meeting, give of their own resources and pound the pavement to raise funds.

This board is unique because every director is personally affected by GIST. Several have lost loved ones to this disease. One might have expected them to step down at that point but they have continued to help with our battle against GIST. Some are patients who must persevere through the trials and tribulations of dealing with their own disease. Others are caregivers. They all truly committed to finding the cure.

Many thanks to the LRG board, a group of extraordinary individuals, without whom 2006 would not have been such a successful year.
The Life Raft Group would like to express its deepest thanks to the donors whose generous support and partnership make our work possible. We are grateful for the following contributions and grants received for 2006.

$100,000 & Above

Amgen
Novartis Pharmaceuticals

$20,000 - $99,999

Stan Bunn
Jerry Knapp

$10,000 - $19,999

Carlos & Liana Baldor
Jerry Cudzil
Jim Hughes
OSI Pharmaceuticals
John Poss
Rodrigo Salas

$5,000 - $9,999

Bristol-Myers Squibb Company
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Peter Leonard
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2006 Contributors

Board Member Jerry Cudzil raised over $85,000 at his third annual Poker Tournament

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Anthony Perrotta
Ben Quinones
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Robert Spellman
Andrew Tarica
Richard Vandermass
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Thomas Carroll
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Lyon Carter III
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Matthew Cherwin
Nicholas Chiara
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Andrew McSweeney
Katharine Merriman
Michael Meyer
Robert Miller
Mark Moskowitz
Jeff Mouland
Vincent Murray
Hemanth Nagaraj
Anatoly Narn
Allen Oppici
Life Rafters raised $30,000 for the 2006 Thanksgiving Campaign
Our top fundraisers who reached out on behalf of the LRG were:

Doris Dallow, raising a total of $3,150
Pat Lemeshka, raising a total of $1,525
Rachel Tate, raising a total of $1,035
Gail Mansfield raised over $300 by auctioning off this quilt created especially for the Life Raft Group.

$50 - $99

Doug & Sharon Aach
Patricia & John Abbott
Bina Ahmed
Cheryl L. Anderson
Joan Angerer
Anonymous
Amy Bachelder
Dorothy Barton
Marilyn & Calvin Bayles
Alan Bennett
Louis & Joan Berge
David Blender
Bill & Deanna Book
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Noell Design Group
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Deborah Ohanian
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Allison & John Pappas
Roselina Wong-Parlove
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Pentagon Gallery
Rod Bender Charters
Marilyn Rodgers
Sally Rogow
Miguel Romero
Murray Rosenthal
Harold & Isabel Ross
Bill & Frances Roth
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Carol Schlesinger
Bill Schwanke
Kevin Shanley
Darlene Shaw
Robert Shaw
Sign-A-Rama
Dick Singelton

SJMHN Dept. of Psychiatry
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Billie Zwolinski

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Julie Anne Licktieg
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Salvatore Luongo
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Robert Madsen
Wendy Mahas
Sue Stinson Mathios
Karen Merriam
Barbara & Ken Meyers
Brett Miller
Elizabet & Keith Miller
Norman Miller
Susan & Ian Miller
Robert & Hedy Miller
Dominic Monterosso
Kathy Moore
Jack & Holly Moran
Carole Morgan & John Frank
Christopher & Erin Norrissey
John & Joann Mull
Patricia Mullen
Hope & Alex Neuberger
Steven & Mary Nims
Oakland County Speech &
Hearing Association
Robert & Laura Olin
Barbara Opper
Michael Kilbourne
Fern Parks
Evelyn & Earl Philo
Jennifer Pierce
Debbie M. Preacher
Robert & Jean Ramseyer
Mary E. Ready
Mary Lou Rensberger
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Albert & Torvy Hord
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Pam Lewkovich
Amy Lewkovich
Gloria Lindemeyer
Abbe Lindenbaum
Elizabeth & William Litt
Maxine Litvinoff
Jeanne Livermore

Up to $49

Life Rafter Robert Kinsey raised over
$500 by betting on a horse and
directing the winnings to the LRG!!

Lori Hilder
Denise Holley
Ronald & Susan
Honeycutt
Albert & Torvy Hord
Ann & Richard Hughes
Stephanie & Jeremy Hull
Erma & Bruce Hutchins
Patricia Ickes
Marcia Jackie
Linda Jackson
Howard Janosky
Patricia & Robert Johnson
Madeleine Joubrel
Lisa Katzman
Elissa & Larry Kaufman
Marcia Keane
Moira Kehoe
Mary Kerwin
Sita Khufu
Richard & Maryann Kijewski
Jaime & Chrissy Kilmer
Paul & Cathy Knoop
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Fred & Risa Levitan
Pam Lewkovich
Amy Lewkovich
Gloria Lindemeyer
Abbe Lindenbaum
Elizabeth & William Litt
Maxine Litvinoff
Jeanne Livermore
Allocation of Funds for 2006

Total Expenditures $1,347,018.60

*If you feel we have made any errors in disclosing this information please contact us at: liferaft@liferaftgroup.org
Mark Thomas
January 16, 1960 ~ December 25, 2006
May his brilliance live on.

A note about the cover artist.
Mark Thomas, a professional photographer & Life Raft Group member, joined his fellow GIST patients at the Life Fest Meeting in September 2006. He arrived a little late, having spent Friday evening in an emergency room, but still jumped in and took photos for the LRG. Mark then offered to donate his photos for auction to raise funds for the LRG.
Mark passed away in December 2006. Although he is not here to see this today, his talent lives on.
ensuring that no one has to face GIST alone