Remarkable RESILIENCE
We all approach our challenges differently, but there are some universals, including the fact that we’re all on a path to get back to who we are—not necessarily who we were, but who we can be.”

Letter from the Executive Director

What’s revealed when “normal” isn’t an option

Life’s curveballs — whether rare like chordoma or universal like a global pandemic — have a way of revealing who we are and what we’re capable of. It’s fitting that 2020 was the year the Chordoma Foundation put resilience front and center with the launch of our Chordoma Survivorship Initiative, which focuses not on returning to life pre-diagnosis but on finding new ways to live well in the midst of our ups and downs and unwelcome changes.

This year also reinforced gratitude as adversity’s antidote. We’re grateful for healthcare workers’ heroic efforts during historic challenges, for our research partners’ extraordinary commitment to continuing their experiments, and for our community’s unshakable support of one another and of our mission.

As you’ll learn in the pages that follow, your steady generosity meant that progress against chordoma hardly missed a beat. Because of you, we’re heading into this next era closer than ever to our shared goals.

Josh Sommer
Co-Founder and Executive Director
15-year survivor

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Accelerating cures

In 2020, we invested $1.57M in research, bringing our cumulative research investments to more than $13M — plus millions more leveraged from the National Institutes of Health, other foundations, and pharmaceutical companies.

Despite 2020’s headwinds, our strategic research investments resulted in substantial and measurable progress across multiple priority areas, as described in the following pages. Your support of this research is rapidly changing the outlook for patients.

Currently funded researchers

Our grantees are pursuing top research priorities, including developing drugs that strike at brachyury, the Achilles’ heel of chordoma, applying powerful new technologies to harness the immune system to fight chordoma, and systematically identifying existing drugs that can help patients in the near term.

David Drewry, PhD
University of North Carolina

Adrienne Flanagan, MD, PhD
University College London

Hans Gelderblom, MD, PhD
Leiden University Medical Center

Opher Gileadi, PhD
Oxford University

Cigall Kadoch, PhD
Dana-Farber Cancer Institute

Santosh Kesari, MD, PhD
Saint John’s Cancer Institute

Michael Lim, MD
Stanford

Cassian Yee, MD*
The University of Texas MD Anderson Cancer Center

Stuart Schreiber, PhD
Broad Institute of Harvard and MIT

Paul Workman, PhD
Institute for Cancer Research, London

Yoshiya (Josh) Yamada, MD
Memorial Sloan Kettering Cancer Center

Stephen Yip, MD, PhD*
BC Cancer Agency

Gelareh Zadeh, MD, PhD*
University of Toronto

*Funded through partner organization

Publications

Our investments in research culminated this year in six original research publications, which contributed important insights into disease biology, potential therapeutic targets, and treatment approaches.

New understanding of how most chordomas lose a critical break on cell growth
Frequent alterations in p16/CDKN2A identified by immunohistochemistry and FISH in chordoma
From the Flanagan lab at University College London

Clues about how chordomas evade the immune system and what can be done about it
Defective HLA class I expression and patterns of lymphocyte infiltration in chordoma tumors
From the Schwab and Ferrone labs at Massachusetts General Hospital

A new indirect approach to attacking brachyury
Inhibition of histone H3K27 demethylases inactivates brachyury (TBXT) and promotes chordoma cell death
From the Flanagan lab at University College London with collaborators at Oxford University

Circulating tumor DNA can be detected in the blood of chordoma patients
The mutational landscape of spinal chordomas and their sensitive detection using circulating tumor DNA
From the Bettegowda lab at Johns Hopkins Medicine

New potential combination therapy identified through machine learning approach
Synergistic drug combinations and machine learning for drug repurposing in chordoma
From the UNC Catalyst for Rare Disease at the University of North Carolina at Chapel Hill

Preclinical evidence for a new potential therapeutic target
Rationale for the advancement of PI3K pathway inhibitors for personalized chordoma therapy
From the Prince and Brenner labs at University of Michigan
Research priorities

Despite historic challenges this year, our research collaborators and grantees went to great lengths to ensure that progress continued. Their dedication led to significant and tangible progress in each of our four research focus areas.

Drug repurposing

The fastest path to better treatments for chordoma is to find existing drugs that work. In 2020, considerable progress was made towards this goal.

- **Screened all ~6,000 existing drugs** against chordoma cell lines through a grant to the Schreiber lab at the Broad Institute of Harvard and MIT, yielding a number of promising leads to follow.

- **Tested 18 drugs and combinations in chordoma mouse models** through our Drug Screening Program, several of which significantly inhibited tumor growth.

- **Observed initial indications of some patients benefiting in 4 ongoing clinical trials** testing the cancer drugs afatinib, nivolumab, palbociclib, and pemetrexed.

- **Planned one new trial** testing the cancer drug cetuximab, an epidermal growth factor receptor (EGFR) inhibitor that has shown strong preclinical activity as well as anecdotal responses in patients treated off-label, and which may also stimulate an immune response against tumors.
Brachyury is the primary driver of chordoma, its greatest vulnerability, and a highly promising therapeutic target. It also plays a role in the progression of numerous other cancers such as breast, lung, and colon. Once thought to be “undruggable,” our research partners made unprecedented progress in the quest for the first brachyury drugs this year.

- **Created new compounds that bind to brachyury** and which could serve as the starting point for multiple classes of drugs, including a new and highly promising type called targeted protein degraders.
- **Demonstrated proof of concept for protein degraders:** in specially engineered chordoma cell lines brachyury degradation permanently stopped cell growth.
- **Developed critical open-access research tools** which enable the evaluation and optimization of emerging brachyury drugs, increasing the feasibility and reducing the cost for all current and future brachyury drug discovery programs.

There is growing evidence that developing drugs against brachyury could be beneficial not just for chordoma but for other cancers in which it appears to play a role as well.”

Bringing these drugs to fruition will set an important precedent for how emerging technologies can be applied successfully to the most challenging targets in oncology.”
Immunotherapy

Extraordinary advances are being made in the development of therapies that harness the immune system to fight cancer. Our goal is to ensure that chordoma patients everywhere benefit from these powerful new treatment approaches as quickly as possible. Key milestones in 2020 included:

- Development of the first cell based therapy for chordoma initiated by immunotherapy pioneer Dr. Cassian Yee and colleagues at The University of Texas MD Anderson Cancer Center. This research is made possible by a $200,000 grant co-funded by the Chordoma Foundation and Cancer Research Institute, the world’s leading nonprofit funder of cancer immunotherapy research.

- Identification of new potential targets for immunotherapy by the Kislinger lab at the University of Toronto, presented during our virtual International Chordoma Research Workshop.

Learning from each patient

Knowledge about how chordomas behave over time is critical for improving care, designing future clinical trials, and getting new treatments approved.

To generate this knowledge, we’ve partnered with the U.S. National Cancer Institute (NCI) to include chordoma patients within their ongoing Natural History Study of Rare Solid Tumors. Designed in consultation with our Medical Advisory Board and other leading chordoma clinicians, this study seeks to determine:

- How chordoma progresses in patients with various clinical profiles
- Clinical and biological factors associated with better or worse outcomes
- Treatments that are benefitting chordoma patients

Chordoma patients anywhere in the world can take part in advancing this important research.

Cell-based therapies have shown they can shrink or eliminate various types of tumors. Endogenous T Cell (ETC) therapy, in particular, can be developed and tested in clinical trials faster than certain other forms of cell therapy. Applying these approaches to chordoma represents one of the most promising paths to better treatments and, if successful, could lead to a clinical trial for patients within two to three years.”

Cassian Yee, MD
The University of Texas MD Anderson Cancer Center

“Studies like these are crucial to our understanding of how rare cancers progress and in building the scientific foundation upon which drug development programs are formed. All chordoma patients, including those in active treatment, are welcome to participate in the Natural History Study from the comfort of their home. They are also welcome to come to the NCI to meet with our experts directly.”

Brigitte C. Widemann, MD
Chief of Pediatric Oncology, NCI’s Center for Cancer Research
Keeping information flowing

Our biennial International Chordoma Research Workshops enable the rapid exchange of unpublished data, surface new research ideas and opportunities, and facilitate coordination and collaboration among researchers.

Adapting in the face of the pandemic, what would have been our seventh in-person gathering of the international chordoma research community turned into our first fully online research workshop.

320 doctors and scientists
31 presentations
25 countries represented

A silver lining of holding the event online was that it enabled many more investigators to participate: more than twice the number we’ve ever had in person and six times the number at the first workshop 13 years ago. We’re heartened to watch the field continuing to grow and to see the level of dedication and intellectual investment in our disease by so many talented physicians and scientists.
Improving lives

Managing life in a pandemic is challenging for everyone, but for those touched by chordoma, the worries are multiplied. We faced unknowns, asked tough questions, and wondered if things were going to be okay. Many patients and families turned to one another and to the Foundation as a source of support and guidance, and we were here to help address new needs and navigate new challenges.

1,165 members in Chordoma Connections, our online community

1,425 educational materials provided

584 responses to the Chordoma Survivorship Survey

498 patient navigation cases served

5 new Peer Guides trained

3 educational webinars held

2nd NCI MyPART Clinic (held virtually)

I knew as soon as I got my diagnosis that one of the things I wanted to do was help others struggling with chordoma. When I became a patient, I had to teach myself how to become comfortable accepting help, but learning that skill has been a gift. It’s critical for someone like me who is currently going through a recurrence, and for all of us in this pandemic.”
Chordoma Survivorship Initiative

Quality-of-life challenges are common for all those affected by chordoma: patients, survivors, caregivers, and co-survivors. Our Chordoma Survivorship Initiative, launched in 2020, is helping members of the chordoma community learn about these challenges and find ways to manage and overcome them. We do this by providing:

**Information**
Including guidelines for follow-up care after treatment, information on survivorship care plans, and guidance on managing quality of life issues such as pain and fatigue.

**Resources**
Including a Survivorship Specialist Directory within our online community, Chordoma Connections, which helps people find care to address the medical, emotional, and practical needs that may arise following treatment.

**Support**
A discussion forum in Chordoma Connections focused on quality of life and access to Peer Guides with shared experiences.

**One-on-one navigation**
Individualized assistance for survivorship needs through our Patient Navigation Service.

Ed Les, MD
Chordoma survivor and Chordoma Foundation Board member

“The launch of the Chordoma Survivorship Initiative is tremendous news for the chordoma community. It’s bringing dedicated focus to helping chordoma survivors live well — physically, mentally, emotionally, financially — after their initial intense battle with the disease and as they grapple with the reality of their diagnosis and all that it means.”
Listening to our community

We conducted the Chordoma Survivorship Survey to capture the physical, emotional, social, and practical experiences of our community members, including both survivors and co-survivors.

An incredible 584 individuals in 34 countries participated, contributing to the most extensive collection of chordoma patient experiences ever gathered. The following figures put into numbers what many affected by chordoma already know: major gaps remain in survivorship care. We’ll use what we’ve learned to guide the expansion of our survivorship offerings.

Who responded?

- 76% Patients or survivors
- 24% Caregivers or co-survivors

- 46% Skull base tumors
- 30% Sacral tumors
- 24% Mobile spine (cervical, thoracic, and lumbar) tumors or more than one tumor location at diagnosis

1 in 5 respondents were in active treatment

Experience with survivorship care planning

Only 7% of survivors and 5% of co-survivors say that a survivorship care plan was given when the patient completed their most recent treatment.

Fewer than half of survivors report that their doctors discussed current or possible quality of life issues, including how to seek care for those issues, at the end of their last treatment.

1 in 4 say that their chordoma doctor provided them with information about chordoma to give their primary care provider.

Ability to access care

Over 75% of survivors experience 5 or more quality of life challenges, such as fatigue, fear of recurrence, depression, pain, inability to go to work or school, etc.

But only 62% of those who do experience challenges say they accessed care for those needs.

And just 41% say that their needs were met by that care.
Expanding Peer Connect

Launched in 2011, the Peer Connect Program is a free, confidential peer-to-peer support program that connects anyone touched by chordoma with another person whose experiences are similar.

Over nearly a decade, it’s fostered hundreds of matches and cultivated life-changing relationships between affected individuals, including patients, caregivers, family members, or friends seeking to reduce feelings of isolation and stress.

In 2020, we introduced a new online training program designed to make the process of becoming a Peer Guide more accessible.

Become a Peer Guide or be matched with one

If you’re interested in talking to someone who has been through a similar chordoma journey or providing support for others, visit chordoma.org/peer-support or contact support@chordoma.org.

Susan Hall
Chordoma survivor and Peer Guide

“...My Peer Guide was by far the greatest source of hope and comfort to me when I was first diagnosed. If I can provide even a fraction of that relief to other people experiencing chordoma, it will have been worth it. And I was pleasantly surprised at how much I got out of the training personally and professionally. The skills it focuses on, listening and empathizing, can be applied to many different types of relationships.”
Thank you for your support

Our progress is possible thanks to your generosity, which was especially inspiring this year, and enabled our mission to continue uninterrupted despite the tremendous collective challenges we all faced.

2020 Fundraising Champions

We're grateful to the many Chordoma Champions who rallied their personal networks to fundraise for the Foundation, finding creative ways to raise funds in a socially distanced world. To learn how to become a Chordoma Champion, contact development@chordoma.org.

Wendy Abbott
Leslie Adler
Irene Badura
Sharon Berlan
Sue and Gene Brenneman
Renée Butler
Tracy Clifford
Millie Cowles
Dawson’s Circle of Hope
Melodi Dunn
Peter Ernharth
Crystal Feldman
The Finley Family
Wanda Fuller
Robin Ho
John Mainey
Steven Mandel
Alexandra Muckey
Shyla Nash
Ruth O’Brien
Kimberly Ochs

Noreen and Mick Potempa
The Riccomini Family
Jeff Schilling, Maggie Bates, and Priscilla McInnes
Maureen Schroer
Joyce Spiegel
Team Mac
Todd Vallie
Hannah Wilson

“Fundraising for the Chordoma Foundation is such a meaningful opportunity. It’s easy, fulfilling, and so much fun. You feel like you’re changing the world.”

Renée Butler
Ultrarunner and mom of chordoma survivor
Special thanks to the members of our Accelerators Circle whose gifts of $25,000 or more over a period of up to three years accelerate our mission and make possible the multi-year investments needed to achieve meaningful long-term impact.

$1M+
The Beckman Family Foundation
The Marcus Foundation

$500,000–999,999
The Mark Foundation for Cancer Research
Moira and Gary Sinise

$25,000–99,999
Anonymous (3)
Roz and Adam Abram
Bruns Foundation

2020 Donors

$500,000+
The Marcus Foundation*
Gary Cole
James Counter
Charles and Martha Davis Foundation
Dawson’s Circle of Hope
Hester M. Digges Trust
Janet and Richard Fell
First Nonprofit Foundation
Fleisher Family Foundation
Eric Foss
Christine Albright and Lawrence Gill
David Hunt
Robert Irvine
Marion Johnson
Brian Kilmeade
Leikafsky Family Foundation
Frank Luntz
SBES Client Consolidated Charitable Foundation
Shared Health Alliance
Marcie and Avery Stein
Esta Stetcher*
Megan and Joseph Stewart*
Michael Torrey and Cheryl Kugel-Torrey
Tres Chicas Foundation
Mark Wahlberg

$100,000–499,999
The Beckman Family Foundation*
Lynette and Foster Friess
George Joseph
The Mark Foundation for Cancer Research*
Moira and Gary Sinise
Triad Foundation

$25,000–99,999
Anonymous (3)
Roz and Adam Abram
Bruns Foundation

$10,000–24,999
Anonymous (6)
American Online Giving Foundation
Amy Adams
Leslie Adler
Patricia and Randy Aker’s Joan Allen
AmazonSmile Foundation
American Endowment Foundation
American Express Foundation
Yoram Amiga
Alan Arnold
Trevor Balough
Bank of America Charitable Foundation
Shelba Barnes
Irish Adaba and Warren Barrett
Cristin Bartter
Jaynee and Eric Beckman
David Biondi
Judy Blume
Myma Blume
Boehringer Ingelheim
Jeremy Boreing
Donna and Timothy Borruel

K. Michael Ingram
Karyopharm Therapeutics
Todd Lannan
Bruce Marcus
McCann Foundation
Julie and Scott Moller
John Ondraski
Noreen and Mick Potempa
Christina Razzi
Bernard Rothman
Laurie and Mark Slepian
Jiliet Kim and Young-dahl Song
Thomson Giving Fund
Barbara Titus
Lauren Erb and Nicholas Vantzefield
William Wagasy

$1,000–4,999
Anonymous (6)
American Online Giving Foundation
Amy Adams
Leslie Adler
Patricia and Randy Aker’s Joan Allen
AmazonSmile Foundation
American Endowment Foundation
American Express Foundation
Yoram Amiga
Alan Arnold
Trevor Balough
Bank of America Charitable Foundation
Shelba Barnes
Irish Adaba and Warren Barrett
Cristin Bartter
Jaynee and Eric Beckman
David Biondi
Judy Blume
Myma Blume
Boehringer Ingelheim
Jeremy Boreing
Donna and Timothy Borruel

K. Michael Ingram
Karyopharm Therapeutics
Todd Lannan
Bruce Marcus
McCann Foundation
Julie and Scott Moller
John Ondraski
Noreen and Mick Potempa
Christina Razzi
Bernard Rothman
Laurie and Mark Slepian
Jiliet Kim and Young-dahl Song
Thomson Giving Fund
Barbara Titus
Lauren Erb and Nicholas Vantzefield
William Wagasy

$100,000–499,999
Anonymous (3)
Roz and Adam Abram
The Cedar Street Foundation
Susan and Richard Friedman
Hirsch Family Foundation
George Joseph

$25,000-99,999
Anonymous (3)
The Alpert Family Foundation
Bavarian Nordic
Becherer Family Charitable Giving Fund
The Drew Barker-Wright Charity
Stanley, Marion, Paul and Edward Bergman Family Foundation
Boehringer Ingelheim
The Bruns Foundation
Belgine
Robert and Louise Cohen
Lorna and Stuart Cook
Charles and Martha Davis Foundation
Dawson’s Circle of Hope
Hester M. Digges Trust
Janet and Richard Fell
Robert Greenebaum
Illinois Tool Works, Inc.
Kit and Bob Lennon
Maria and Steven Mandel
Anthony Montalto
The Orokawa Foundation, Inc.

Reinhardt Family Trust
SBES Client Consolidated Charitable Foundation, Inc.
Erin and Jeff Schilling
Grace and Andrew Schoelkopf
Christy and Joel Shaffer
Megan and Joseph Stewart
Heather Lee and Steve Straus
Michael Torrey and Cheryl Kugel-Torrey
TrueScripts Foundation Fund
The Helen Van Sickle Fund
Karen and Richard Westin
Financials

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| Change in value of foreign currency pledges | $(19,022) |
| Change in net assets | -$24,840 |
| Net assets, beginning of year | $ 4,703,579 |
| **Net assets, end of year** | **$ 4,697,761** |

A copy of our 2020 IRS Form 990 and audited financial statements are available at chordoma.org/financials.

Onward
Chordoma is a solvable problem. Your support accelerates our focused quest for solutions. Our current priorities include:

**Brachyury drug discovery**
*Developing drugs that strike at the Achilles’ heel of chordoma*
- The moment we’ve been waiting for: Begin first preclinical efficacy studies of emerging brachyury drug candidates
- Begin studying safety of therapies targeting brachyury

**Immunotherapy**
*Applying powerful new technologies to harness the immune system to fight chordoma*
- Initiate and fund projects addressing top immunotherapy research priorities

**Drug repurposing**
*Identifying existing drugs that can help chordoma patients in the near term*
- Complete testing of all approved drugs in chordoma cells
- Initiate and support new drug repurposing clinical trials
- Identify new treatment approaches that show strong preclinical efficacy to pave the way for future clinical trials

**Patient experience**
*Helping patients and their families confidently take on health challenges and get the best care possible*
- Start new virtual support groups for patients and caregivers
- Host virtual community conference series focused on addressing quality of life issues
- Develop and translate educational materials addressing key questions identified by our community

**Clinical learning**
*Understanding how different treatments impact patient outcomes to continually improve patient care*
- Surpass 100 patients enrolled in the Natural History Study of Rare Solid Tumors
To keep pace with rapid advances and the growing set of opportunities in chordoma research, in 2020, we made several key additions to our research team. Dr. Dan Freed joined the Foundation as our new Head of Target Discovery and Translational Research, and Dr. Diane Ignar joined us in a consulting capacity as our Head of New Drug Development. Dan and Diane’s work at the Foundation builds upon the many achievements of Dr. Joan Levy, our former Director of Research, who moved on to an exciting new role and remains involved as an advisor. We also welcomed drug discovery and development leaders Dr. Paul Feldman and Dr. Sue Mahony onto the Board of Directors and brachyury expert Dr. Charles Lin to our Scientific Advisory Board.

Additionally, to bolster our ability to serve the full spectrum of needs within the chordoma community — particularly around survivorship — Andrea Locke joined us as our Patient Navigator, and caregiver and board-certified patient advocate Megan Stewart joined our Community Advisory Board.

This year also marked longtime director Joel Beckman’s retirement from the Board after 10 years. His dedication, leadership, and wisdom have left a lasting positive mark on our organization and on many in the chordoma community. We are deeply grateful to Joel for all that he has done and continues to do to support our mission.
The Chordoma Foundation was instrumental in my treatment. When I was diagnosed five years ago, it was through the help of the Foundation’s Patient Navigators that I was able to receive excellent care from chordoma experts. My family and I are forever grateful for the work of the Foundation in working towards a cure. They offer a wealth of information to those diagnosed with chordoma and are invaluable in helping us understand how this disease can be managed. Ultimately, the Foundation gave us tools, and those tools gave us hope.”

Joe Stewart
Chordoma survivor, pictured here with wife Megan Stewart, member of the Chordoma Foundation’s Community Advisory Board

“