“We’re on the cusp of clinical trials at Yale with a compound that was a concept here in Kline Biology Tower 17 years ago.”

counteractive therapy. “Basically it’s chemical castration,” said Dr. Crews. Arvinas has designed an oral PROTAC that eliminates the androgen receptor protein from cancer cells, degrades androgen receptor mutations, and slows tumor growth. Dr. Crews expects clinical trials to begin at Yale and elsewhere later this year.

The PROTAC against breast cancer works similarly. An estimated 80 percent of new breast cancer cases are positive for estrogen receptor alpha (ERα), whose proteins encourage tumor growth. Current therapies try to stop growth in ERα breast cancers by inhibiting the receptor, but many breast cancers become resistant, allowing signals from the receptor to break through and stimulate tumor growth. Arvinas’ PROTAC solves that by eradicating ERα proteins. Clinical trials will begin next year.

Another Arvinas project demonstrates how broadly the PROTAC technology can be applied, said Dr. Crews. When the protein called Tau aggregates, it causes neural death that leads to Alzheimer’s disease. Arvinas is working on PROTACs that drag Tau to its death.

Dr. Crews sees the company as the fruit of his lab are investigating leukemia, glioblastomas, lung cancer, and pancreatic cancer. “We’re very interested in some of these tough cancers that haven’t been easily addressed using the current drug repertoire,” said Dr. Crews. “It’s not an either/or thing. I hope other faculty can see that I’ve been able to maintain an active academic lab but also play a role through advocacy and consulting to further the development of real-world applications through these biotechs.”

He traces his interest in propelling discoveries out of the lab to his father, who worked on materials science at NASA. “He looked at alloys and composite materials for space wings, analyzing fatigue and fracture,” said Dr. Crews. “He would tell me about plane crashes where engineers had failed because the material had been too fastiged due to the pattern of the rivet holes. So it was clear to me early on that my Dad’s basic research had practical applications. As a basic researcher driven by my scientific curiosity, I love what I’m doing here, but I’m always asking how we can take what we’re learning into the lab and help people.”

Right now, Dr. Crews and the 18 members of his lab are investigating leukemia, glioblastomas, lung cancer, and pancreatic cancer. “We’re very interested in some of these tough cancers that haven’t been easily addressed using the current drug repertoire,” he said. “And we’re making progress.”

In May 2013, Joe Weber had just dropped his son off at Logan International Airport in Boston and was driving back to Connecticut when he decided to stop for a bite to eat. Before continuing his two-hour trip home, he visited the restroom and noticed an exceptional amount of blood in his urine. This came as a surprise to Joe as he had no indication that something was wrong in the weeks or days prior. He immediately made an appointment with his primary care physician.

His physician referred Joe to a urologist, who diagnosed bladder polyps as the cause of the blood, and recommended outpatient surgical removal. Joe went ahead with the surgery, and would continue to be checked every three months for the next year, only to have polyps recur and be removed in two additional surgeries. After his third surgery, Joe questioned whether the polyps could indicate a larger problem and he sought a second opinion.

It was then that Joe received the diagnosis of muscle-invasive bladder cancer. His new urologist recommended he immediately start an aggressive regimen of chemotherapy to precede surgery to remove his bladder and a portion of his small intestine. As testing continued, it was determined the bladder cancer had metastasized to Joe’s lungs, elevating him to a stage IV cancer diagnosis, and surgery was no longer an option. In consultation with his doctor, they decided to proceed with the standard of care for his bladder cancer, and for the next eight months, Joe received chemotherapy once a week. While his treatment did begin to shrink the tumors in his lungs, the side effects were too challenging and Joe decided to end treatment.

Knowing Joe would not be able to tolerate a return to this treatment regimen, his doctor advised he enter a clinical trial, and referred him to Dr. Daniel Petrylak, Professor of Medical Oncology and Urology, at Smilow Cancer Hospital. Dr. Petrylak is a leader in the development of new drugs to fight bladder cancer, and his success with clinical trials has expanded the treatment options for all patients, including many newly FDA-approved drugs.

Joe first met with Dr. Petrylak in July 2015, and for the next two years unsuccessfully participated in two separate clinical trials. In July 2017, Joe became eligible for a third trial touted as “targeted chemotherapy.” This trial combined an antibody targeted at a protein present in bladder cancer cells, with chemotherapy.

After three months, Joe had to again stop the treatment due to side effects, which in this case presented as neuropathy, or weakness and numbness in the feet. Joe paused his treatment for six months, but continued to have scans every eight
weeks during this break. Remarkably, the results of his scans began to show that his lung tumors were shrinking even while off treatment. It appeared that the three months of the initial treatment had been enough to cause tumor shrinkage.

Joe resumed the targeted therapy in April 2018 when his side effects improved, allowing Joe to resume his normal activities—working in the yard, albeit at a less rigorous pace, and playing golf.

Joe’s treatment team is thrilled with his progress and he shares their excitement, exclaiming, “Dan is the man!”

In the meantime, Joe aimed to check off a few big items from his bucket list: 1) to play a round of golf with Dr. Petrylak, and 2) complete a West Coast road trip with his son, Michael.

Squeezing in a trip between treatments, Joe and his son started their adventure by spending two days in Denver, Colorado before flying to San Francisco. As luck would have it, Joe’s wife, Maura, and daughter, Emily, were able to join them for the next three days, they made family memories across the Bay Area including a special trip to Muir Woods National Monument to see the redwood trees. After Maura and Emily headed back to Connecticut, Joe and Michael picked up their convertible and started south to kick off their special trip.

Their first destination was Los Angeles, but not before passing through some of the most scenic vistas in California: Monterey, Carmel, Malibu, and Santa Monica. Upon arriving in San Diego, where they visited the San Diego Zoo and swam in the warm waters of the Pacific Ocean.

After San Diego, Joe and Michael drove eight hours east through the Arizona desert to their next stop, the Grand Canyon. After one day of sightseeing, they concluded their trip with an extravagant steak dinner before turning in the convertible and flying home.

After a jam-packed journey of 1,400 miles through three states, Joe is looking back and he is thankful for these newfound opportunities to explore and enjoy life that did not seem possible a few years ago. But after such a memorable and successful trip that crossed one item off his bucket list, another has taken its place. On the eve of their return to Connecticut, in a conversation with his son at dinner, they realized that Joe has visited 43 of the 50 states. Upon learning this fact, son Michael is now inspired to get his father to all 50 states.

As the famous quote goes, “Life is either a daring adventure or nothing.” And thanks to his second chance at life, Joe can embark upon his daring adventure and continue to work on his bucket list.

“I am not sure whether a cure is in the realm of possibility, but I’m confident that we can arrest bladder cancer with as few symptoms as possible.”