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Some of New Haven's leading scientists and biotech industry leaders are on a personal mission to combat deadly diseases



Bindra's father died of esophageal cancer just three weeks before he graduated from medical school. PHOTO ANDREW VENDETTI

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In recent years, the New Haven region has seen an explosion of new biotech firms making strides on treatments for devastating diseases, from various cancers to Alzheimer's and ALS.

For many of the founders, executives and researchers working on these groundbreaking new treatments, it's about more than building fortunes or advancing science: It's personal.

Often, a loved one has been impacted by the disease. For others, past or current patients are the ultimate inspiration.

New Haven BIZ reached out to some of the people behind these young companies and asked them to share the personal experiences that are fueling their life-saving research. Here are

some of their stories.

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Grow old with me

While a cancer researcher at the University of Texas in 1998, Luca Rastelli had just given a speech to the American Brain Tumor Association when a woman in her 20s approached him with her young son.

"Is your research going to help me see my child grow older?" the woman asked him. She had been diagnosed with a brain tumor.

For Rastelli, who still gets emotional recounting that long-ago encounter, the question led to a promise. He decided to leave academia for private industry so he'd have a closer hand in developing new cancer drugs.

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"It's the reason why I go to work every day," says Rastelli, whose résumé includes a list of biotechnology firms, including CuraGen, the genomics company started by renowned Yale scientist Jonathan Rothberg.

Since April 2018, that work has been done at fledgling New Haven oncology biotech Kleo Pharmaceuticals Inc., where Rastelli now serves as chief scientific officer.

His mission at Kleo also hits close to home: his father-in-law, who lives in Hamden, suffers from multiple myeloma — the same deadly blood cancer that Kleo is targeting with its first immuno-oncology drug, CD38-ARM. If all goes as planned, human trials could begin early next year.

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Rastelli took the job at Kleo after moving back to New Haven from Boston last year to be closer to his father-in-law during treatment.

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"It was an amazing coincidence and opportunity," Rastelli says of the position and Kleo's disease target.

The Science Park-based startup is pioneering a synthetic compound, or antibody recruiting molecule (ARM), that it touts as more effective and less toxic than current treatments. The ARM "recruits" the body's so-called natural killer cells to go after tumor cells.

Based on the work of Yale scientist David Spiegel, the technology helps these antibodies "see" cancer cells that they previously did not recognize and target them for destruction, Rastelli explains.

Rastelli said animal studies show the drug has fewer toxic side effects than current treatments. Rastelli says his father-in-law ended up in intensive care twice for pneumonia-related issues exacerbated by his weekly IV infusions.

"What we are trying to do [eventually] is generate compounds that may be taken by mouth instead of injected, so they don't have this strong type of [negative] reaction," Rastelli said.

Rastelli says his father-in-law is hopeful about his work. "He jokingly says, 'I guess one day I'll take your medicine, Luca,' " says Rastelli. "[But] he realizes that we are years away and that for a variety of reasons, it may never happen for him."

Rastelli, too, is fully aware of the long odds of his industry (statistics show only one in 10 new drugs ever make it to market) but he is passionate about giving Kleo's compounds a place among the world's pharmaceutical success stories.

"Ultimately if you are working in this field you believe that what you are doing has a chance of success," he says. "Again, that's why I come to work every day. To actually see the research translated into helping people."

Donning the patient's shoes

When Marcia Dougan Moore was 13, she watched her grandmother succumb to breast cancer.

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"It was really a difficult thing to watch this happen to someone who was just a very vibrant, active person, really because there was no treatment available to her," Moore recalls. "It's something that really stuck with me."

The loss didn't spark her career in the pharmaceutical industry — a chance encounter with an industry executive on an airplane did that.

But it undoubtedly shapes the work she does every day for Science Park-based Arvinas Inc.

As vice president of development operations, Moore is overseeing two clinical trials the company has launched to test its potentially game-changing drugs for advanced breast cancer and a treatment-resistant form of prostate cancer.

Her own family's brush with the disease is never far from her mind.

"It gives me pause to think about the human aspects of clinical studies," she says. She instructs members of her team to view the trials "with an eye toward how it's going to feel if you're a patient."

"These people are absolutely essential to compiling the data we need to convince not only ourselves — but any regulatory agency — that we've got a good product," she explains.

"You're asking them to not only give up their time but to quite literally give of themselves," she says of the volunteers. "We take blood samples from them, we ask a lot of questions to get information about how they're feeling. And we're doing all that during a very stressful time in their lives."

The compounds Arvinas is testing in the trials, ARV-110 and ARV-471, use technology developed by Yale molecular scientist Craig Crews called PROTACs (short for proteolysis-targeting chimeras). Part of a new class of drugs known as protein degraders, they harness the body's own protein-disposal system to attack proteins that are causing disease.

Results of the trials are expected next year.

Moore is hopeful the work could one day improve life for people with cancer, giving them time and options that eluded her grandmother decades ago, even if a cure remains elusive.

"If we can help someone make it to their daughter's birthday, or the birth of their next grandchild, those are the kinds of things that are meaningful for people," she says. "And if we can get them there in good shape — not with a treatment that's going to take a huge toll on their quality of life — that's really important."

A brain vacuum cleaner

As the son of a pharmacist and a psychiatrist, Vlad Coric spent much of his childhood on the grounds of Norwich State Hospital, the state psychiatric institution that closed its doors in 1996.

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That exposure sparked a curiosity about the brain and inspired his career in neuropsychiatric research, most notably at Yale, where he led the medical school's neuroscience research unit as well as a research clinic for obsessive-compulsive disorder. It also forms the underpinnings of his work as CEO of New Haven's Biohaven Pharmaceuticals, which is developing drugs for neuropsychiatric diseases.

"I never had a stigma of mental illness," explains Coric. "I knew patients by first name who lived on the grounds of the hospital, and I became very interested in the brain chemistry that led to abnormalities."

As a physician, Coric became increasingly frustrated with the limited treatment options available to his patients.

"They wouldn't respond to our current therapies, so what do you have left for them?" he asks. "Either you say, 'I'm sorry, there's nothing left,' or 'I'll try really hard to find a new therapy.'"

Today, Coric and Biohaven are doing just that. The company, headquartered at 215 Church St., develops drugs that target mental illness and neurological disease, from OCD and generalized anxiety to Alzheimer's, migraine, ALS and others.

Coric's research at Yale led to the development of Biohaven's experimental drug troriluzole, a single compound that aims to treat four different diseases — OCD, generalized anxiety disorder, Alzheimer's and spinocerebellar ataxia, a condition marked by progressive loss of coordination — by regulating the brain chemical glutamate.

While the body needs glutamate for normal functioning, too much of it leads to disease, Coric explains, and the type of affliction depends on where in the brain it is accumulating.

"It's just a matter of where that pathophysiology is in the brain that tells you whether it's a behavior problem or whether it's a neurologic disease [such as ALS]," he explains.

Biohaven's compound acts as a vacuum cleaner of sorts, removing the glutamate from neurons in parts of the brain that are flooded, so it can potentially impact multiple different diseases, Coric explains.

The drug, one of several in Biohaven's pipeline, is now in clinical trials for all four indications, with results expected early next year. If successful, it could be available to patients by 2021.

(Biohaven's lead drug, a new migraine treatment called rimegepant that it licensed from Bristol-Myers Squibb, has gone through the regulatory process and is expected to win FDA approval in early 2020. Another drug targeting ALS, licensed from AstraZeneca, will be tested in a Massachusetts General Hospital-run trial next year.)

"When we go into a therapeutic area, we act as though an immediate family member was suffering from that [disease]," Coric says. "That's how dedicated and passionate you have to be because these are tough indications to solve."

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"It's not just about the science. It's about getting involved [with patient groups] and advocating for every one of those patients [suffering from] the disease that we're studying," he adds.

"Our team sacrifices their nights, their weekends, constantly working on these protocols in the hopes that one of these therapies will make a meaningful difference."

A 'heat-seeking missile' for tumors

Both Cybrexa Therapeutics CEO Per Hellsund and the New Haven company's scientific co-founder, Ranjit Bindra, MD, have witnessed the pressing need for kinder, gentler cancer drugs.

Hellsund's mother has been through multiple cancer therapy regimens since her breast cancer recurrence seven years ago, and she's been forced to abandon some that were working because the side effects were too toxic. The serial entrepreneur also lost his sister to lung cancer last year.

Bindra, meanwhile, watched his own father suffer through brutal chemotherapy treatments in the early 2000s; he was diagnosed with advanced esophageal cancer and treated at Yale while Bindra was there attending medical school. He died just three weeks before Bindra's graduation.

"My interest in finding new cancer treatments was, really, in large part motivated by that personal loss," Bindra says. "His parting words were: 'We need to get better treatment.'"

From Cybrexa's laboratory in Science Park, Hellsund and Bindra are now advancing a new class of cancer therapies that can target tumors while sparing healthy tissue, potentially eliminating the bone marrow toxicity, gastrointestinal distress, hair loss and other troublesome side effects their own parents endured.

Using technology developed at Yale and the University of Rhode Island, the three-year-old startup has created what Bindra describes as "a heat-seeking missile" for tumors.

Featuring a molecule known as pHLIP (which stands for pH Low Insertion Peptide), the compound forms a corkscrew-like structure when it comes in contact with an acidic environment, which happens to be a universal feature of cancer cells.

The structure then drills its way directly into the tumor cell, where it deposits a cancer-fighting agent and leaves the healthy cells around it unharmed.

Cybrexa's experimental drug, CBX-11, combines that technology with an already approved DNA repair inhibitor known as a PARP inhibitor, an anti-cancer drug that works by preventing the cancer cells from repairing themselves.

There are already DNA-repair inhibitors that, when administered with chemotherapy, can kill almost any tumor, Bindra says. But the combination is often too toxic to be given to patients safely.

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"By delivering these anti-cancer agents directly to the tumor, we're able to target the tumor and offset many or all of these horrible side effects," Hellsund says.

Another advantage of CBX-11 is that it's "tumor-agnostic," says Bindra. Current DNA repair inhibitors work only on tumors linked to specific genetic mutations, such as BRCA1 and BRCA2

"So many, many more patients now would be eligible for these really active drugs," he says. "Patients like my own father would have been eligible."

Although CBX-11 comes too late for Bindra's father, it could be just in time for Hellsund's mother, who told him she wants to take part in Cybrexa's upcoming clinical trial, which could begin in early 2020.

"The therapies we are developing would certainly apply to her," says Bindra. "We keep saying that we're going to make sure she gets a spot."

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