STAT

‘I just white-knuckle it’: Hemophilia patients pin their hopes on the revival of Vioxx to fill a void in pain relief

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Vioxx was pulled off the market in 2014 after studies revealed that it roughly doubled patients’ risk of heart attack and stroke, leading to an estimated 60,000 deaths. *Spencer Platt/Getty Images*

After surviving hemophilia, hepatitis C, and HIV, Joseph Burke considers himself a walking miracle. But the medical odyssey that saved his life has also ravaged his joints, and now each day begins in pain, whether from his ankles, knees, shoulders, or all of the above.

“I just white-knuckle it, grit my teeth, and here I am, you know?” said Burke, 41.

Burke suffers from a side effect of hemophilia called hemophilic arthropathy, a buildup of blood in the joints that leads to pain, inflammation, and tissue damage.

There are no approved therapies, and the most commonly prescribed pain treatments are opioids. Burke's prescription is a single daily tablet of Percocet.

"There are days where I'm sitting there, like, 'What if I just take one more half?'" he said. "It's a constant mental battle. That part scares the crap out of me, honestly."

He wants a treatment that can soothe his pain without the anxiety of keeping an addictive drug in his home. And he's pinning his hopes on a decades-old pill more famous for class action lawsuits than medical miracles: Vioxx.

The pain drug became synonymous with pharmaceutical risk more than 15 years ago when studies revealed that it roughly doubled patients' risk of heart attack and stroke, leading to an estimated 60,000 deaths. That led to a congressional investigation, allegations of lapses at the Food and Drug Administration, and agreement by the manufacturer, Merck, to pay a nearly $5 billion settlement and pull Vioxx off the market.

For years, though, Tremeau Pharmaceuticals, a privately held Massachusetts drug company, has been seeking to resurrect the drug — Merck's patents have expired — and pressing forward with a plan to convince the Food and Drug Administration to approve Vioxx for patients with hemophilic arthropathy.

Earlier this year, the FDA signed off on Tremeau's plan to run a placebo-controlled trial that would support that approval, and the company has secured $110 million in financing from the blue-chip investment firm Gurnet Point Capital, which will fund the study in its entirety. Tremeau expects to begin recruiting patients this month.

For Brad Sippy, the company's founder, it's been a long time in the making. Sippy worked in Merck's marketing division in the 2000s, and one of his jobs was managing the Vioxx recall. He remembers receiving angry mail, accusing Merck of causing so much suffering.

"But then after about three or four months, it quickly flipped over to 'When's this coming back?' and 'I would do anything and sign anything to get it back.' And a

lot of that was people with hemophilia," he said.

Vioxx had long been the off-label drug of choice for hemophilic arthropathy, preferred by doctors because it could relieve pain without the increased bleeding risks inherent to other anti-inflammatory drugs. The cardiovascular issues were real but manageable with patient monitoring and careful prescribing, doctors said. Vioxx's recall "left a void in our arsenal," said Catherine Broome, a hematologist at Georgetown University Hospital in Washington, D.C.

"It was a sad day," Mark Skinner, who has hemophilic arthropathy, said of the Vioxx recall. Skinner, 60, counted on the drug for pain relief but now takes Celebrex. It has the same mechanism as Vioxx, but the results are inferior, he said.

"Is my memory perfect from 30 years ago? Probably not," Skinner said. "But my buddies and I think about the good old days, and Vioxx worked. There's no question that it worked and it was better."

Tremeau's plan is to enroll about 160 people with hemophilic arthropathy between the ages of 12 and 75 and randomize them to either placebo or Vioxx, whose generic name is rofecoxib. After three months, patients in the placebo group will be able to switch over to rofecoxib, and Tremeau will follow them for another year to study long-term safety.

The goal is to prove that rofecoxib can ease the burden of hemophilic arthropathy, which Tremeau is measuring using a patient-reported scoring system of daily pain. If the drug is significantly better than placebo at keeping those scores low, the study will be deemed a success.

But the answer won't come quickly. In order to properly isolate the variables, Tremeau is requiring that patients who enter the trial discontinue any pain treatments they're already taking before entering the study. For some patients, that would mean spending at least three months with no daily painkillers. Sippy acknowledged that it might prove discouraging for some eligible participants, and Tremeau expects it may take a year or more to recruit all the patients it needs.

Skinner, who was formerly president of the nonprofit World Federation of Hemophilia, said the challenge won't be insurmountable. The community of people with hemophilia has an abiding interest in participating in research that might improve the lives of fellow patients, he said. There's a group of people, affectionately known as "study boys," who are game for just about anything that might benefit the community, Skinner said. And for Vioxx, a drug for which he has such fond memories, "I'd be in that 'study boy' category," he said.

To Tyler Buckner, a hematologist who treats hemophilic arthropathy at University of Colorado Health, the potential return of Vioxx presents a welcome option for patients who are often forced to make do with mediocre pain treatment. About half of Buckner's patients with hemophilia deal with chronic pain. Celebrex works for some but is "frustratingly inadequate," he said. Opioids can be effective but require constant monitoring and present risks some patients find frightful. If Vioxx proves safe and effective, it would bring an eagerly desired alternative.

"It would be a huge boon to quite a few of my patients," he said. "If I could take my patients who are on opioids and replace some or all of them on a treatment that was effective, that would be huge."

For Burke, an effective treatment for hemophilic arthropathy would make the walking part of being a "walking miracle" a little easier. If the Tremeau trial is a success, rofecoxib would be the only medicine developed specifically for his condition; it would be "groundbreaking" for a group of patients accustomed to settling for whatever they can get, he said.

Burke has been in a reflective mood in recent months, as he's been using his pandemic downtime to get to work on a memoir, working title "Bloody Incredible." Growing up in southeastern Kentucky, caregivers didn't know much about hemophilia and the many precautions it required, and Burke's efforts to fit in with other kids led to frequent bleeding episodes. The treatment that kept him alive through childhood, one derived from donated blood, also made him one of the more than 10,000 hemophilia patients who unwittingly contracted hepatitis C and HIV. Thousands would eventually die of AIDS.

The advent of ever-more-powerful medicines means kids today won't have to go through what he did, and the prospect of gene therapy promises to bring a functional cure for hemophilia in his lifetime. He feels superlatively fortunate to witness that, and obliged to make sure the history of hemophilia isn't lost.

"I'm kind of a torch carrier," Burke said. "You read about Ryan White[8] and Ricky Ray[9], the hemophiliacs who succumbed to AIDS, and you just pause for a minute. They're not here. You carry the torch for a generation that won't know or understand what it was like."

The ensuing decades brought medical advances that would dramatically change his life: treatments that reduced his risk of bleeding, drugs that transformed HIV from a death sentence to a chronic disease, and a cure for hepatitis C, which he received in 2014. He hasn't had a bleeding episode since 2018.

All that remains is the joint pain. And to Burke, the potential return of Vioxx offers a chance at relief.

"That's the exciting part," Burke said. "There's potential. There's hope. Finally the veil has been torn away from this specific area of the bleeding disorder community."

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