THE FUTURE OF BUSINESS
18 LEADERS AND LUMINARIES TELL YOU WHAT'S NEXT (PAGE 44)

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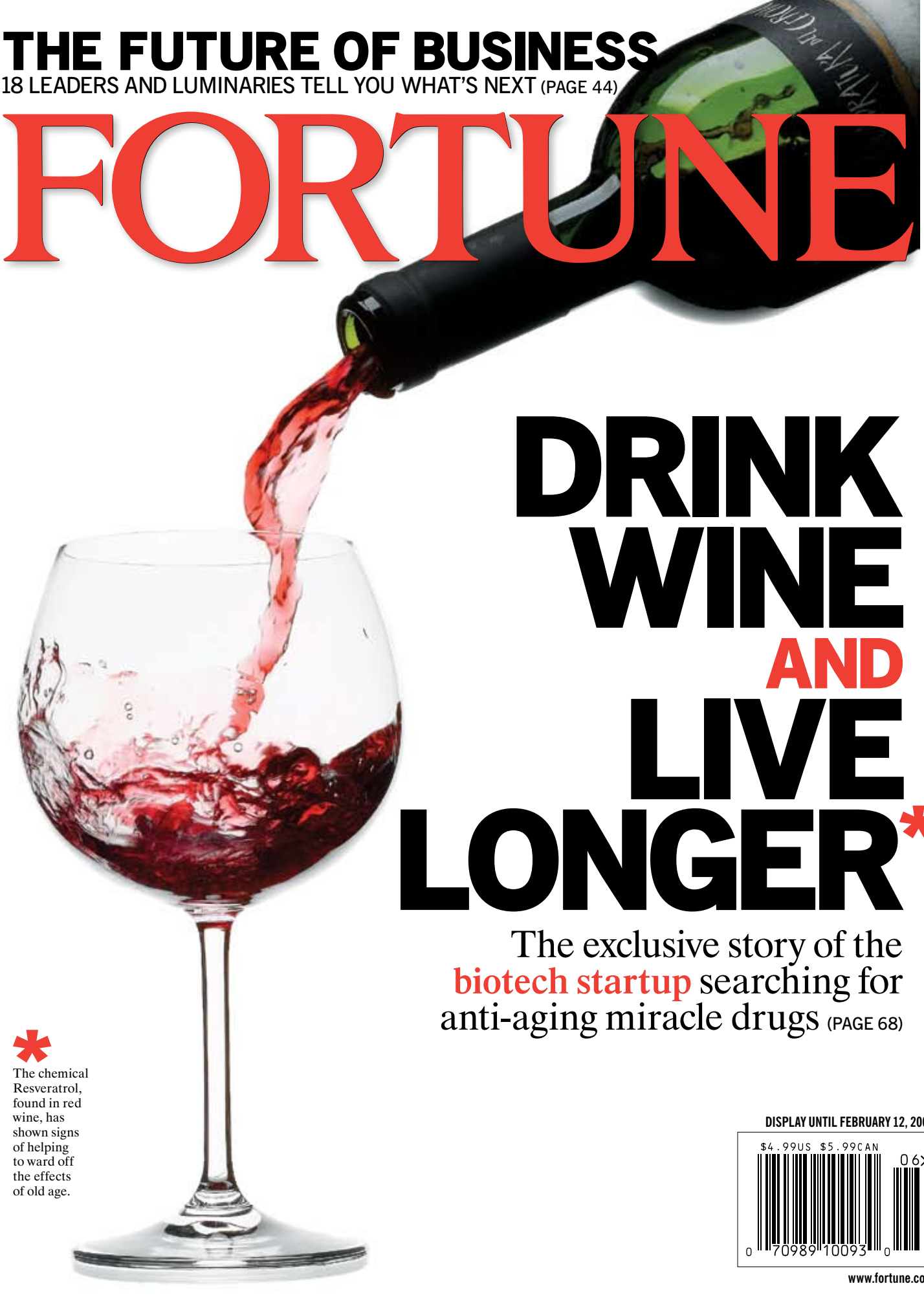

DRINK WINE AND LIVE LONGER*

The exclusive story of the biotech startup searching for anti-aging miracle drugs (PAGE 68)

* The chemical Resveratrol, found in red wine, has shown signs of helping to ward off the effects of old age.

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SO WHAT'S THE SCOOP ON THAT STUFF IN RED WINE THAT'S SUPPOSED TO LET YOU

LIVE FOREVER?

Turns out there's something to it. Here's the amazing, *real* story of the scientist and startup that have a shot at making it happen.

BY DAVID STIPP

PHOTOGRAPHS BY SARAH A. FRIEDMAN

Westphal, who earned a Ph.D. and an MD from Harvard in less than six years, gave up a lucrative career as a biotech VC to launch Sirtris.

IF YOU HAVEN'T HEARD OF RESVERATROL, YOU'RE PROBABLY TOO YOUNG TO HAVE HAD THE EXPERIENCE OF GAZING IN THE BATHROOM MIRROR IN THE MORNING AND THINKING, "DAMN." RESVERATROL

is the ingredient in red wine that made headlines in November when scientists demonstrated that it kept overfed mice from gaining weight, turned them into the equivalent of Olympic marathoners, *and* seemed to slow down their aging process. Few medical discoveries have generated so much instant buzz—even Jay Leno riffed about it in his opening monologue.

But the key question raised by the news—whether the discoveries will lead to pharmaceutical payoffs before we're too old to care—won't be answered in the Harvard lab from which the news sprang. Instead look to a boxy, low-rise building a couple of miles away, an unprepossessing biotech hatchery that got little media attention in the wake of the resveratrol findings. This is the Cambridge home of two-year-old Sirtris Pharmaceuticals. Its stated goal is to develop medicines that have the same health-boosting effects in people that resveratrol had on mice. But that hardly captures the company's sweeping promise: If it succeeds, its medicines may retard the onset or progression of a whole slew of age-related diseases, from diabetes to Alzheimer's to cancer. The drugs may also have an extremely provocative side effect: They might extend life span (see box, page 72). You have to go back to the advent of antibiotics in the first half of the 20th century to find such broad therapeutic potential.

For all that to happen, Sirtris, like most biotech startups, must wend through a minefield that will take many years to traverse. And no biotech gets very far through the minefield without a kind of walking contradiction leading the way—a dreamer with feet planted firmly on the ground, a science whiz who could pass as a circus ringmaster, a riverboat gambler with a passion for minimizing risk. Three years ago one such paradox strolled into the Harvard lab that put resveratrol on the map and set in motion events that may in time radically transform the way we age: Meet Christoph Westphal, Sirtris's co-founder, CEO, and dreamer-in-chief.

A former venture capitalist, Westphal, 38, was known for conjuring up dreams that spellbind investors before he joined forces with David Sinclair, 37, the charismatic Harvard Medical School researcher who spearheaded the research on resveratrol. Between 2000 and 2004, Westphal co-founded five companies and served as CEO of four of them, including two hot biotechs that have gone public and now have a combined market value of over $1.4 billion. But Sirtris is probably his entrepreneurial *pièce de résistance*, and he quit his meteoric VC career to lead it.

MIT professor Phillip Sharp, a Nobel laureate biologist who advises Sirtris and has known Westphal for years, says he's excited about the startup's science. But it was Westphal's involvement that largely persuaded him to put his imprimatur on Sirtris. (Sharp, one of the biggest names in science, helped launch the biotech industry in 1978 by co-founding Biogen, now Biogen Idec.) "Christoph's combination of skills is very rare," Sharp says. "I haven't seen his equivalent in 30 years of working in biotech."

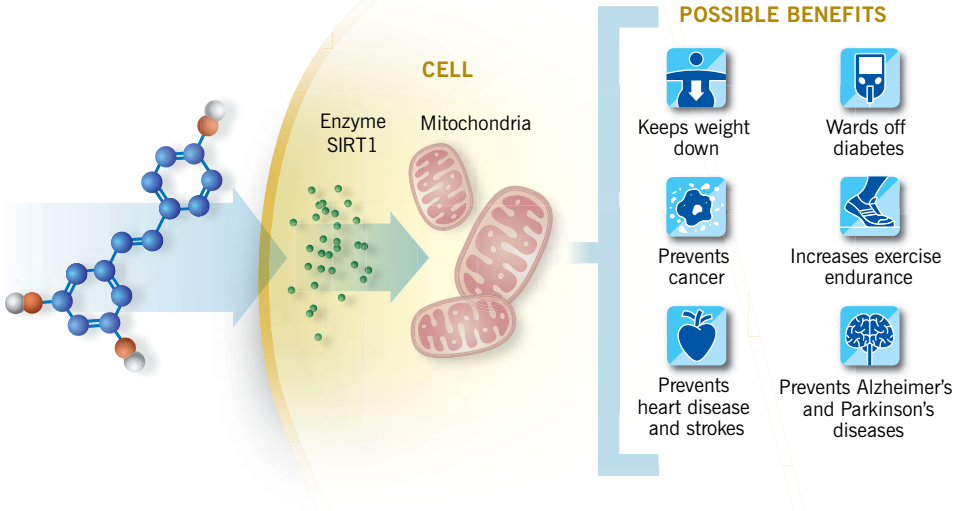
Venture capitalists have been equally enthralled by Westphal,

Sinclair at the lab. Sirtris is making a major bet that his theory of how resveratrol works is right.

judging by the $82 million they've pumped into closely held Sirtris over the past two years. That's a remarkably large sum for a high-risk, early-stage biotech, and it has helped fast-track the company's drug development—it is already clinically testing its first medicine, a resveratrol-based drug that promises to help keep diabetic patients' blood sugar under control. The drug contains concentrated resveratrol and gets far more of it into the bloodstream than drinking red wine can. Most biotechs pioneering new science take years before testing drugs on people; Sirtris's drug reached the clinic less than 18 months after the company's launch.

HOW RESVERATROL MAY SLOW AGING

The Sirtris theory: One key is the compound's effect on cellular power plants, a.k.a. mitochondria.



MEDICINE Resveratrol is a molecule produced by several plants. It is found in trace amounts in the skin of red grapes and is present in red wine.

INTERACTION When the molecule enters the cell, an enzyme called SIRT1 is activated. That, in turn, engenders new mitochondria in muscles and other tissues.

RESULT The presence of new mitochondria boosts the body's metabolic rate, which may mimic the slow-aging effects of a calorie-restriction diet.

For all his mastery at raising money, Westphal isn't your standard-issue CEO. His lead haberdasher is probably Levi Strauss & Co. His cramped, sparsely furnished office, which is shared with Sinclair when the Harvard scientist drops by, is not much bigger than a walk-in closet. And because he doesn't like cluttering his life with things like cars, he often walks five or more miles a day getting to work and meetings. A husky 6-foot 3-inch man with an edgy, no-nonsense air, Westphal doesn't so much ambulate as lunge—his body language suggests a star halfback who has just spotted a football spiraling down about five yards ahead of his pigskin-eager hands. His colleagues are accustomed to his daily barrage of e-mails, which begins around 5:30 A.M. "I must get 50 e-mails a day from him," says Boston hedge fund manager Richard Aldrich, one of Sirtris's founding investors. "He probably overcommunicates." (Westphal says that overcommunication is a nonissue because "nobody reads my e-mails.") In fact, just about the only time anyone can recall the boss giving his BlackBerry a breather was during a few startling minutes last November. It turned out that he had laid it aside for a few minutes to deliver a baby—his own son. In fact, Westphal delivered all three of his children at a Boston hospital under an obstetrician's supervision.

YOU HAVE TO GO BACK TO THE ADVENT OF ANTIBIOTICS IN THE 20TH CENTURY TO FIND SUCH BROAD THERAPEUTIC POTENTIAL.

At first glance, Westphal's frenetic personal style resembles attention deficit disorder. But in his case it's probably better described as bandwidth-coming-out-of-the-ears syndrome. When I interviewed him some months ago at Sirtris, for instance, he couldn't resist assembling a new sound system for his office as we talked. He managed to read the instructions, examine the pieces, and put them together without missing a beat in the conversation.

A few other résumé bullet points: Westphal plays the cello; speaks four languages (his kids speak only German with him and Spanish with his Puerto Rican wife); and has visited two-thirds of the countries on earth. He's also a disarming extrovert who genially crushes competitors into the dust. When Sirtris held a companywide weight-loss contest over last summer and fall, no one was very surprised when Westphal's team won. On the weekend before the final weigh-in, the CEO starved himself and exercised all-out twice a day, pushing so hard that his wife feared he might have a heart attack. "When you get involved with Christoph," says Aldrich, " it's all action, all the time."

It won't come as a surprise that Westphal's powers of concentration appeared early. As a youngster he told his parents, physicians who grew up in Germany and moved to the U.S. in 1967 (young Christoph grew up in the Washington, D.C., area), that he wasn't very interested in following in their professional footsteps. "Of course you'll get an MD," his mother replied. "Then you can decide what you want to do." Rebelling in the way of a good German son, he got a Ph.D. in biology and slogged through an MD on the side—both from Harvard in five years and eight months, nearly a record. After that he worked at a hos-

FORTUNE CHART BY SAMUEL VELASCO—5W INFOGRAPHICS

pital in equatorial Africa, where he delivered scores of babies. Then he decided that what he really wanted to do was start companies that turn basic research into drugs. That led to his furiously productive stint as a venture capitalist.

With the Renaissance man personality and the driving ambition, Westphal seems ready-made for the limelight. But he largely avoided the press until the recent news about resveratrol made that untenable. Recently he granted a few interviews, but his press persona has been low-key, guarded, almost professorial. It's not that he's shy. When a TV news team showed up one day, he put on a white lab coat and safety glasses before going on camera—a nerdy affectation that caused much mirth at Sirtris. Self-satire, he later commented, is part of his campaign "to keep us grounded. We're in trouble if we lose the ability to laugh at ourselves."

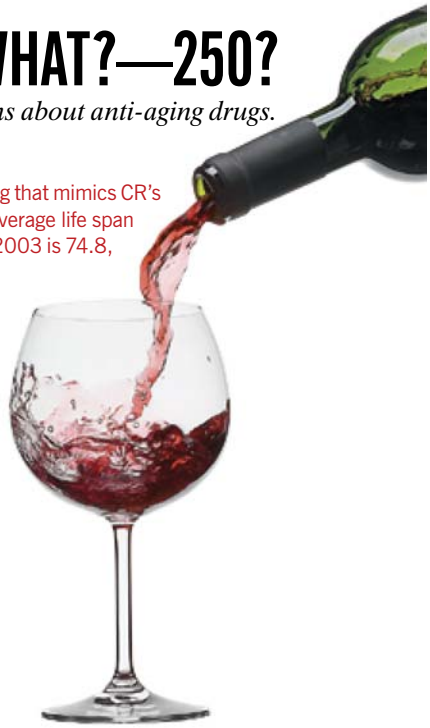
Rather, he's determined to avoid any whiff of "fountain of youth" hype—specifically, of giving the impression that Sirtris is a bunch of flakes chasing miraculous elixirs, which is the kiss of death for a startup trying to raise millions of dollars from hard-nosed money managers. He spends a lot of time explaining that his company is working to cure diseases of aging, not to cure aging itself. There's a difference, especially in the minds of regulators, who view aging as part of the human condition, not an illness warranting treatment. Further, proving that a drug extends life span would require an impossibly long clinical trial. And then there's what Westphal calls the "vortex of inflated expectations," which invariably spins up around scientifically credible anti-aging research. "I don't want to get sucked in," he says.

But Westphal can't afford to steer Sirtris too far from the vortex. After all, it does have to impress those hard-nosed money managers in order to realize its drug-development dreams. And the possibility that its drugs actually will slow aging provides him with a very compelling case to put to potential investors and pharma partners—to wit, aging, when stripped to its dire essence, is simply a process that inexorably increases the risk of killer diseases. So a drug that retards that process should have across-the-board power to postpone such diseases' toll, making it an FDA-approvable blockbuster of unprecedented scope.

So Sirtris's star is hitched to perilously glitzy anti-aging science despite the fact that it isn't pursuing life-extension drugs per se. As a result, Westphal's media stance, like the man himself, is a study in high-speed motion as he alternately approaches and flees the vortex. In an interview last fall he enthused that "studies on long-lived humans indicate there are four key predictors of longevity: low levels of blood glucose and insulin, little weight gain during middle age, and low body temperature. Our drugs positively af-

GREAT! SO I'LL LIVE TO—WHAT?—250?

No. And four more clear answers to obvious questions about anti-aging drugs.



1) How long would these drugs let us live?

One clue comes from studies on calorie restriction, or CR. If a drug that mimics CR's effects gave us the same life span boost that rats get from CR, our average life span might increase to about 110. (Life expectancy for U.S. males born in 2003 is 74.8, and it's 80.1 for U.S. females born that year.)

Still, many experts believe that drugs are on the horizon which could extend average life span by perhaps five to ten years. That may seem unimpressive. But their boost to life expectancy would "far exceed" that from totally eliminating cancer, says S. Jay Olshansky, a University of Illinois expert on the demographics of aging. That's because the risk of many deadly diseases skyrockets as we age, so even if one were vanquished, the others would soon get us, limiting the gain in average life span. In contrast, an anti-aging drug, almost by definition, would retard all major diseases of aging at once.

Drugs that boost life span might also abbreviate late-life disability—we'd stay fairly vigorous until the very end. That sunny view is supported by the fact that very old animals on CR tend to be remarkably lively until shortly before they die. Surprisingly, good health is also often seen in people over 100, whose durability resembles that induced by CR.

2) When will these anti-aging meds arrive?

In 2005 the Rand Corp. consulted medical experts on this question and reported that they believe there's a 50% chance that anti-aging drugs will be available within 20 years. Some researchers on aging, such as Harvard's David Sinclair, believe that medicines like those will come along much sooner—perhaps within a decade. The optimists cite the fact that researchers have discovered dozens of gene mutations over the past 15 years that slow aging in mice, fruit flies, roundworms, and yeast cells. That has revealed many molecular targets in the body that might be tweaked by drugs to mimic the effects of such mutations.

3) Anything besides resveratrol on the horizon?

Several substances have shown tantalizing hints of anti-aging effects in animal and test-tube studies. A diabetes drug called metformin, for example, mimics many of the gene-activity changes that CR does. A metformin-like drug, called phenformin, appears to modestly extend rodent life span. Another compound, called 2DG, has been shown to mimic key effects of CR by blocking glucose metabolism. But all these cause side effects that rule them out as anti-aging drugs.

At this point resveratrol, or drugs that function like it, shows the most promise as an anti-aging medicine. Found to boost life span in diverse animal species, resveratrol appears to be safe to take at modest doses. But whether such doses extend human life span isn't known—and may never be because of the long clinical trials needed to prove it.

4) How large would the market be for these drugs?

Assume that the medicine is priced about the same as low-end cholesterol-lowering drugs—say, $1 a pill. That would make the yearly per capita cost $365. Now multiply that amount times the number of rapidly biodegrading baby-boomers, about 70 million. Ballpark answer: around $25 billion.

DAVIES & STARR

fect these predictors in mice. That's very promising." Then he took pains to caution that "whenever Sirtris is mentioned" in the news, "it should be emphasized that it's going for FDA-approved drugs to treat diseases like diabetes, not anti-aging. No matter how often I say that, folks don't seem to listen."

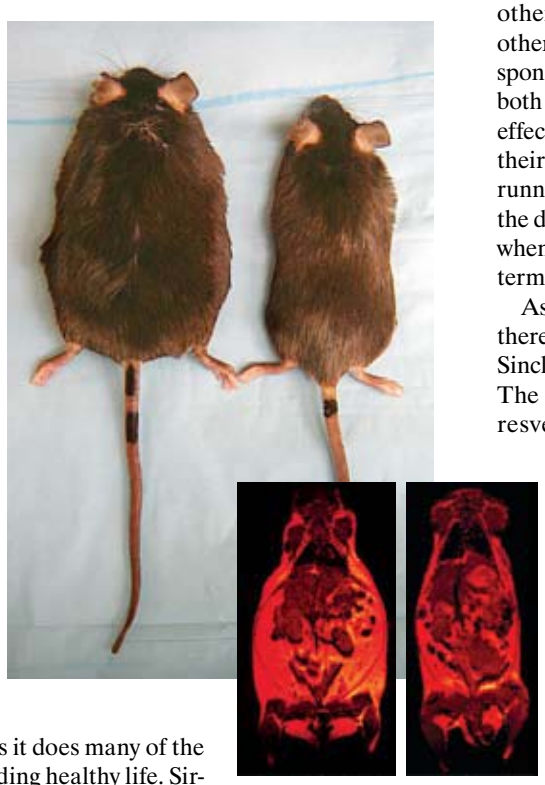
Like most entrepreneurs, Westphal is fixated on the new. Ironically, however, the line of research that led to Sirtris dates from the 1930s, which is when scientists at Cornell University discovered the life-extending effects of calorie restriction, or CR. The researchers found that reducing normal calorie intake by about a third extends animals' life spans by 30% or more, keeping them sleek and vibrant when their normally fed peers look wasted, or are dead. In fact, CR is the only established way to slow aging in everything from guppies to dogs to, many scientists believe, humans. The big drawback, of course, is the not-eating part. CR's stomach-growling regimen requires the self-control of a Mahatma Gandhi. (It also tends to produce the great ascetic's half-starved look.)

And thus the appeal of a substance like resveratrol: Sinclair's research suggests it does many of the wonderful things CR does, including extending healthy life. Sirtris's goal is to develop medicines that function like resveratrol but are far more potent: In principle, people on the medicines could eat heartily while getting the pluses of CR. Further, they wouldn't have to gulp fistfuls of pills. (Heroic doses of resveratrol, comparable to a person's drinking hundreds of glasses of wine a day, were needed to elicit the remarkable effects seen in the high-profile mouse studies.)

The hubbub about resveratrol began with a 2003 study by Sinclair's group suggesting that the compound can mimic the effects of CR in yeast cells, boosting their life spans by 70%. The following year he and colleagues went on to demonstrate that resveratrol slows aging in roundworms and fruit flies. That made it the first compound to show anti-aging effects in widely divergent species. Then, last spring, scientists in Pisa, Italy, showed that its magic extends beyond creepy-crawlies: Large doses of the compound boosted life span more than 50% in a species of short-lived fish.

"CHRISTOPH'S COMBINATION OF SKILLS IS VERY RARE. I HAVEN'T SEEN HIS EQUIVALENT IN 30 YEARS OF WORKING IN BIOTECH."

This is what happened to the mice that got Jay Leno so jazzed a few months ago: In one of the two mouse studies, conducted by Sinclair's group and the National Institute on Aging, high doses of resveratrol induced a number of CR-like effects, including significantly extending the life spans of mice on fattening diets while warding off diabetes and other ill effects of overeating. In the other study, led by a French team and sponsored by Sirtris, even higher doses both protected mice against deleterious effects of rich diets—including keeping their weight down—and doubled their running endurance. All that is just what the doctor would like to order at a time when bathroom scales are groaning in terminal agony across the globe.



Two mice fed the same high-calorie diet in a Sirtris-sponsored study: The svelte one on the right got high doses of resveratrol. Inset: MRI images highlight the dramatic differences in fat deposits.

As for how resveratrol does its thing, therein lies a raging academic debate, Sinclair being one of the combatants. The dispute stems from the fact that resveratrol is a "dirty" drug, i.e., a blunt instrument that interacts with a complex array of molecules in the body. That makes its main mode of action, and link to CR, hard to pin down. It may be that resveratrol's effects spring from its ability to target many different molecules. Alternatively, it may be that just one of resveratrol's many targets is the really magical one—a kind of master switch that turns on CR-like effects all by itself. Sinclair is in the latter camp: He believes that an enzyme called SIRT1 is resveratrol's key target, and that the compound works its magic mainly by activating that enzyme. (SIRT1 is a member of the sirtuin class of enzymes, hence the company name.)

Sirtris has made a major bet that Sinclair is right about that by designing its novel drugs to activate SIRT1. If it turns out that the enzyme isn't really a master switch for CR-like effects, the company's new medicines may not work. But there's growing evidence that Sinclair is right: Sirtris has already shown that its SIRT1 drugs do nice things like lower blood sugar in overfed mice with diabetes, says Peter Elliott, the company's drug-development chief.

The mouse studies also gave hints that resveratrol induces basic metabolic changes akin to those that CR does. One of the most intriguing was the production of fresh mitochondria, the key components of cells that serve as power generators; they essentially burn sugar in slow motion to release energy. But like coal-burning power plants, mitochondria also pollute. In particular, they spew highly reactive chemicals called free radicals, which damage DNA and other important molecules in cells. Over time the radicals deteriorate the mitochondria themselves, which degrades their efficiency, causing yet heavier production of free radicals. The end result is a cell-degrading

COURTESY SIRTRIS AND NIH

snowball effect that is thought to be a major cause of aging.

Resveratrol's ability to engender new mitochondria is especially exciting because it seems the fresh ones are more efficient than the worn mitochondria they replace, hence are less prone to churn out damaging radicals. CR appears to do the same thing—it's like replacing a smoky old coal burner with a cleaner-burning gas-fired plant. Resveratrol's effect on mitochondria may be enough by itself to account for much of the compound's riveting effects in animal studies. In particular, the effect would seem to account for the abrupt Olympic-caliber running abilities observed in mice.

Again, that is the theory. The mouse studies didn't settle the debate over how resveratrol works, which probably won't happen until researchers with no ties to Sirtris confirm that Sinclair is right. So pursuing the SIRT1 path is a gamble for Sirtris, one of many.

The large, unfathomable risks most biotech startups face make investors' due-diligence process seem like shining a penlight into Carlsbad Caverns. Thus, venture capitalists often look to the stature and track record of the people involved as the best indicator of potential. Says Sirtris board member and co-founder Richard Pops, CEO of Alkermes, a biotech concern in Cambridge: "Pedigree is everything" in early-stage biotech.

Westphal couldn't agree more. An avid reader of the scientific literature, he had become intrigued by research on sirtuins during his days as a venture capitalist. After Sinclair's high-profile discovery in 2003 that resveratrol extended the life span of yeast, Westphal phoned the Harvard scientist to talk about his findings' commercial potential. The research was highly intriguing, Westphal says, but Sinclair the man was equally important to him. One Sinclair forte instantly stood out: The scientist, a native of Australia with a natural flair for public speaking, has a rare knack for conveying the excitement of the grand quest to nonscientists. "Sirtris has been successful largely because we were able to raise a lot of money and get momentum early on," he says. "That's partly because David [Sinclair] is fantastic at selling the story."

The two didn't hit it off at first. Westphal, then working at Polaris Venture Partners in Waltham, Mass., "came to my office in a somewhat arrogant manner," recalls Sinclair. "He said, 'Tell

The University of Chicago's Kass is skeptical of anti-aging research.

ROGER L. WOLLENBERG—UPI

NASTY, BRUTISH, AND LONG

The case against extreme longevity.

YOU MIGHT THINK the primal desire to elude death would preclude opposition to drugs that may extend healthy life. But "a huge, acrimonious debate about anti-aging research is in the offing that will make the one about embryonic stem cells seem tame," says Daniel Perry, executive director of the Alliance for Aging Research, an advocacy group. "A whole host will come forward to say that it's blasphemy to tinker with God's plan."

In 2001, Leon Kass, a University of Chicago professor soon to chair the Bush administration's Council on Bioethics, issued an anti-anti-aging manifesto. "Let us resist the siren song of the conquest of aging and death," he wrote, for "the finitude of human life is a blessing for every human individual." Life, he argued, would get old if it went on much longer. "How many parents would like to extend the experience [of rearing children] by another ten years?" Besides, if our children "are truly to flower, we must wither and give ground."

The council reflected Kass's views in a 2003 report detailing ways that anti-aging technology may rob life of meaning and wreak social havoc. People might feel less urgency to get important things done before their time was up, making for a "life of lesser engagements and weakened commitments." Anti-aging drugs might make us more selfish and "far less welcoming of children" and the sacrifices they require. They might undermine marriage: "Would people in a world affected by age retardation be more or less inclined to swear lifelong fidelity 'until death do us part,' if their life expectancy at the time of marriage were 80 or 100 more years, rather than, as today, 50?" We'd be overrun with innovation-stifling fogies: "From the small business to the FORTUNE 500 corporation, generational succession might be disrupted, as the rationale for retirement diminished." And "hope, freshness, boldness, and openness" might be in short supply in a society run by oldsters whose "accumulated mistakes and misfortunes" have marked them with "diminished ambition, insensitivity, fatigue, and cynicism."

ATTACKING THE COUNCIL IS TRICKY for anti-aging researchers—they depend on federal research grants. Still, David Sinclair, the prominent Harvard researcher on aging, scored points against Kass in a 2004 debate on NPR. "We're not trying to make people immortal," Sinclair noted, "or even make them live many, many years longer." Instead, most anti-aging researchers plan to treat diseases of aging rather than to extend life span. "What we're doing is basically just another way of getting at the problem of treating diseases. I don't think that will lead to huge changes in society anytime soon."

When patents expire on such meds, Sinclair explained, they may become cheap, over-the-counter drugs like aspirin, enabling millions to have access to them for use as anti-aging drugs. That would lead to longer, healthier lives, in his view. If that's a bad thing, he asked, "should we have stopped treating people with antibiotics" when those drugs began boosting life expectancy during the last century? Kass chose not to answer that.

me more about these molecules you've found.' I told him that first he had to sign a nondisclosure agreement" to keep nonpublic details about Sinclair's work under wraps. "He said, 'I never sign those.' So I told him maybe I can't talk anymore about this. And he said, 'David, if I walk out of this office, I'm not coming back. So I suggest you tell me as much as you can.' "

After that tense beginning, says Sinclair, the conversation turned out to be "like a wonderful game of chess. I wound up telling him more than I normally would have. It soon became apparent that he's one of the smartest people I'd ever met. But it took me months to realize that he's also a nice guy."

They're good friends now, but Sinclair didn't much like Westphal when they first met.

Asked about the episode, Westphal says, "As a venture capitalist, you're in a world where everything is about money. That can really corrupt interactions with people."

Since combining forces with Sinclair, Westphal has organized what is arguably the most pedigree-rich scientific advisory board in biotech, including MIT's Sharp; Robert Langer, one of medicine's most prolific inventors, also of MIT; Harvard gene-cloning pioneer Thomas Maniatis; and Thomas Salzmann, formerly executive vice president of Merck's research arm. The group now numbers 27, among them many of the world's leading experts on sirtuins. Westphal also assembled an impressive list of directors—they include Alkermes's Pops; Aldrich, the Boston hedge fund manager and biotech veteran; and Paul Schimmel, a prominent scientist at the Scripps Research Institute in La Jolla, Calif., who has co-founded half-a-dozen biotech concerns. Westphal's right arm at Sirtris is chief operating officer Garen Bohlin, 59, formerly a senior executive at the Genetics Institute, a biotech now owned by Wyeth.

The Sirtris team wasted very little time reaching its first milestone, which was to develop "high throughput" screening tests that enabled it to quickly analyze nearly 500,000 compounds for resveratrol-like activity. The rapid-fire winnowing led to several potent molecules that promise to replicate resveratrol's health benefits at doses hundreds of times smaller than are required with the natural substance. These two standard steps in drug development often take several years; Sirtris completed them in a little over a year.

Meanwhile, hoping to get an early indication of efficacy against disease, the company formulated a resveratrol-based drug, dubbed 501, to begin the tests in diabetic patients. Westphal cautions that the drug is likely to be a product for only a few indications—Sirtris's more potent medicines will probably have much broader applications. Still, in animal tests, 501's proprietary formulation gets more than ten times as much resveratrol into the bloodstream as do dietary supplements containing equal amounts of it, says the company. The 501 trial's results should be available this year—if Sirtris decides to disclose them. So far the drug has shown only mild side effects. The main one has been occasional nausea among people taking it on an empty stomach. One reason for that could be that the orally administered liquid drug tastes awful; Sirtris hopes a new cherry-flavored version will go down easier.

Of all the decisions Westphal has made—reject the hype but not too much; which medicine flavors are least nauseating—the biggest may prove to be simply speed. Sirtris's rapid push into clinical trials, the costliest stage of drug development, is likely to force it to raise more money soon. One option: license drug rights to big pharma concerns. But those who reach into pharma's deep pockets tend to get entangled in its bureaucratic strings. Major decisions on developing a drug, for instance, must go through layers of managers. Further, if Sirtris licenses rights to its drugs, it might hand over compounds to a pharma partner before their full value has been assessed and factored into the deal—the possibility that the drugs could treat many diseases of aging is still too tentative to put a pricetag on. Despite the controversy over how resveratrol works, there's no telling how many diseases it can treat. And resveratrol's ability to boost mitochondria, those cellular power plants, indicates Sirtris's medicines will be highly versatile. In fact, the list of disorders thought to involve malfunctioning mitochondria includes adult-onset diabetes, heart disease, stroke, cancer, and Alzheimer's and Parkinson's diseases—all diseases of aging.

"If I had $500 million today," says Westphal, "I'd be tempted to take our drugs into the clinic against two or three devastating neurological conditions and other metabolic diseases besides diabetes. That would be incredibly risky. But sometimes I think, 'This is the kind of company that could gather enormous resources' " based on its extraordinary promise. " 'It would be a real shame if we didn't go for it and try to address these huge medical problems.' "

At some point Sirtris will probably go public, raising the money Westphal would need to pursue this vision. In fact, the excitement about resveratrol may well allow Sirtris to make an initial public offering at an earlier stage of development than is feasible for most biotechs. Westphal declines to comment on that. When asked about it, though, he suddenly reverts to vortex-avoidance mode: "Part of my job is to calm people down," he says. "You have to remember, most things in biotech don't work."

Sobering words—especially for us hopeful resveratrol watchers of a certain age. But here's an antidote: Pour a glass of pinot noir, and while imbibing, step back and regard the big picture. Humanity has dreamed for millennia of medicines that extend life span. Sirtris may not fulfill the dream. But the company's very existence shows that the quest for compounds that slow aging has been transformed from sorcery into the fairly routine process of pharmaceutical development. Thus, the dream is likely to be realized within, at most, a few decades. The question now is when, not if. F

FEEDBACK *fortunemail_letters@fortunemail.com*