PROLOGUE

REDEFINING RARE

The value of rare is something I appreciate, something I know intuitively in my life. And the recognition that each of us is infinitely unique—truly rare—is one of those simple, enduring truths that has long spoken to me.

Growing up, I remember secretly thinking of myself as someone who was too different, who didn't quite fit in. An outsider. But over the years I've come to embrace and feel empowered by my rare identity. I've also always been most attracted to those who dare to be rare—who think differently, who don't follow form or fashion but who celebrate the very qualities that set them apart.

The more I've studied rare, the more I've chosen to honor how unique every single human being is—each life is. Not just our faces and fingerprints but our stories and our struggles and our dreams. Yet what I've learned in recent years is that even though most everyone can agree about this universal aspect of rare, it raises one of the greatest challenges in modern medicine: if each of us is fundamentally unique, then why are so many treated with the exact same medicine?

Less than a decade ago, such a thought probably would not have been a concern. Much less something I'd be able to articulate.

Fast-forward. This very provocative question had somehow delivered me to a James Bond, 007–themed conference room at Google headquarters in Silicon Valley, California. I was there to make a presentation to some of the most tech-savvy executives around—and to ask them to turn their supercomputer powers from digital codes to disease cures. Sitting there waiting for them to arrive, I couldn't help but imagine these techies walking in the room as thirty-something hyper-achievers ironically wearing hoodies and lugging backpack laptops.

And so they did—as if in uniform.

I jokingly said, "You know I really feel like I'm in the middle of an episode of *Silicon Valley*," referring to the image of the characters on the TV show and their laid-back lifestyle as "disrupters"—to use their lingo—who are creating the future.

One of the more serious young execs said, "We don't consider that show a sitcom. It's a documentary."

Silence. Then everyone turned to me and waited to hear what I was there to say.

Deep breath.

There have been so many surreal moments on my current journey when I've had to ask myself, *How did I get here, and why did the universe choose me for this path?* This was definitely one of those moments. Not so many years earlier, talking to such brainiacs about Big Data and its use in medical research would have been as likely as me being invited to speak at the Vatican about new cures for an autoimmune disease. And as the universe would have it, both of these impossible moments—and many others—have come true in the course of a lifeline that has taken me from mascara to medicine.

True. The fact is that until February 2008, my professional expertise and success came from making and marketing cosmetics. From lip gloss to moisturizer—these were my tools of the trade for a larger vision. One, in retrospect, that has many parallels to curing a rare disease. I could see the unique beauty in each woman and knew a way to reveal it from the

inside out. I was passionate about helping women feel better about themselves and their lives—and wanted to share what I knew.

Going against the old rules of the cosmetics business, I followed the guidance of my own intuition to create change. That intuitive capacity is sometimes hard to explain; somehow, I understood how to bring the innate beauty in others to the surface. Even so, before I became a makeup artist–turned–cosmetics entrepreneur who challenged the status quo of the beauty world, I was a high school dropout who never dreamed of being able to attend a college class.

Since those early days, I've been amazingly fortunate that my life experiences and challenges have helped make up for my lack of formal education. Besides earning what has amounted to a doctorate in "street smarts," I long ago learned the value of self-education—at every stage of life. Still, I'm the first to admit that my choice to give up mascara for medicine was not made because I was by any means the best candidate for doing so. No, this choice to take a real-life crash course in everything one needs to know to solve a rare autoimmune disease was made out of desperation, anguish, and absolute necessity. My self-taught medical school began the day my beautiful fourteen-year-old daughter, Ali, was diagnosed with a rare, life-threatening, and terrifying "orphan" condition called neuromyelitis optica, or NMO. And when I realized how poorly understood this disease was—and that there were few treatments and no cures—every day became devoted to changing that reality.

The same capacity for harnessing intuition that I used as an entrepreneur has served me well on the journey to curing NMO.

We hear the term "rare" so often that it's almost a cliché—until you look at it in a different light. The chance of being struck by lightning in a given year is about 1 in a million. Rare. However, the chance of being struck by lightning in any one lifetime is about 1 in 10,000. Not so rare after all. And even more relatable, everyone understands what lightning is, can read the signs to predict it, and knows to respect it. If only the same were true for rare diseases like NMO.

Then how rare—really—is this rare disease with its misleading, simple three-letter name? Today, based on our work that has taken on this would-be killer, researchers have refined their estimates to suggest that it may impact as many as 500,000 people worldwide. Not so different from the prevalence of lightning strikes; such numbers nearly equal 1 in 10,000. But back in 2008—in those dark and frightening early hours of this journey—I remember hearing that only 2,000 patients in the world had NMO.

Such extreme odds fit into a recurring theme in my life—what I call the Rule of 2%. As far back as I can remember, when faced with the most unlikely of odds for something happening, that is exactly what would happen to me. The awareness crystallized for me several years ago when I was at the dentist and asked what to expect about a procedure and how long it would take to recuperate.

"Most people do fine," he said. "But there's always that 2%." Turns out, he said, a tiny percentage of patients have had unique challenges that could make the process more difficult.

I knew then and there that's where I'd be—in the 2%. Yep, and I told the dentist so.

He laughed.

During the procedure, there were a few surprises, and he had to agree: "You know, you're right. You are one of the 2%."

This may seem like a mundane example, but after that experience and countless like it in my life, I started referring to these rare events as my personal Rule of 2%.

Sometimes the 2% can be bad. But sometimes it can be good—like amazingly good. It's the Rule that wins the lottery . . . that helps you turn crazy pipedream ideas into ways to revolutionize the marketplace . . . and, yes, it was the very Rule that once empowered a scared, insecure but determined teenager (me) to eventually build a cosmetics empire. Somehow my Rule turned a struggling young, then-single mom into a global Good Will Ambassador for Mascara. The Rule of 2% can turn the impossible into the possible, and brings with it the capability of empowering and transforming other lives.

Even so, nothing under the sun could have ever prepared me for the moment when Ali tested positive for a condition so rare that most of the medical community had never heard of it.

At the time, if you Googled "NMO," you would have found little information and even less hope. Most of the content focused on unfortunate accounts of how this disorder could, without warning, bring on blindness, paralysis, and worse. Every parent's darkest nightmare. As if not devastating enough to suddenly find out your beloved child has a life-threatening illness no one can cure—let alone knows much about—it was that much harder to be given the prognosis that our daughter may not live to see her eighteenth birthday.

When my husband and I first heard the doctor speak those words, they were more than shattering. They rearranged the molecules of my mind and soul, ultimately sending me on a mission to lead a cure revolution—even if I didn't know it at the time.

All I knew in those blinding moments was that the Rule of 2% would show me a way forward. How? If 2% had gotten us into this, 2% was going to get us out.

To move toward a solution required me to understand how rare affects everyone.

You might assume, as I once did, that the total number of people afflicted by rare and/or autoimmune illnesses is not very high. Think again.

Dr. Michael Yeaman, a pioneering immunologist and a leading partner in our work to cure NMO—and whose extraordinary vision and voice have guided me on the journey of writing this book—recently put this myth into a global context. Michael has pointed out that the numbers challenge how one defines rare. Given a global population of nearly 7 billion, almost 350 million have a rare disease—and nearly 700 million are estimated to have an autoimmune disease. To give all that perspective, consider this: nearly 10 percent of inhabitants of planet Earth has an autoimmune disease, but only 4 percent uses Twitter. It has been said that if everyone with an autoimmune disease lived in the same land, it would be the third-most-populous country in the world.

No one is immune to disease. Even rare illnesses, taken together, add up to vast numbers of lives impacted and loved ones lost.

Today in the United States alone, more than 30 million people—1 in 10—wake up every morning to the reality of a rare, life-threatening, or debilitating autoimmune condition. There are approximately 7,000 identified rare diseases, almost all of them without cures, and 95 percent have precious few or no treatments.

And to add heartache to misfortune, a high percentage of rare patients are young—with otherwise promising but unlived lives ahead of them. Further, autoimmune diseases are even more unfair, striking women much more frequently than men, and often in the prime of life, during child-bearing years and when children need their mothers more than ever. Such are the tragic and daunting realities of rare and autoimmune diseases.

But there is a new hope emerging—catalyzed by the Power of Rare—and not a moment too soon.

This is the extraordinary story that the NMO community has collectively written. From rare patients to equally rare problem solvers who together take on even rarer challenges, it tells of breakthroughs that have revealed NMO to be the *little disease that could*. Indeed, solving this one rare autoimmune disease could unlock doors to solving all other autoimmune diseases—or beyond, to even more common diseases, including cancer. After all, while such diseases may seem very different on their surface, at their core lies a basic identity crisis in the immune system.

This bold and meaningful understanding about the Power of Rare was echoed recently by filmmaker Jesse Dylan of Wondros films, who has collaborated with us on several short films we created to educate the world about NMO. As Jesse reminded me, this thesis has also been considered in the arena of cancer research.

"What people forget," Jesse said, "is that thirty and forty years ago innovations that came in cancer were from the study of rare cancers. In solving one pathway in one disease, you can then extrapolate it to other

pathways. So by focusing like never before on this one condition, NMO, it makes better medicine for everybody."

Medical experts point out similar kinds of breakthroughs. Take for instance the fact that the first medicines to prevent HIV from targeting immune cells were not discovered by studying those who acquired the disease but by studying the rarer individuals who did not, even though they had been exposed.

And NMO takes these concepts further. We know that on the mysterious and miraculous continuum of immune function, too little can make a person vulnerable to cancer or infection, while too much can cause autoimmune disease or worse. Collectively cancer, infection, and autoimmune disease arguably cause more suffering and death than all other conditions combined. By solving NMO, we are learning the secrets of the immune system that control its most basic functions—from why cancer cells or infections elude immunity to why the immune system attacks one's own body in autoimmune disease and everything in between. Imagine the potential these new insights offer for arresting disease at its source—even before it has come to exist at all. That is one Power of Rare.

These realities matter . . . and timing is everything. We are entering a once-in-a-generation window when basic science, clinical medicine, game-changing technology, industry investment, and the Power of Rare are poised together to make quantum leaps in saving and improving lives. In turn, lessons learned and discoveries made by applying the Power of Rare will reveal ideas and resources that can make a world of difference for untold numbers of patients and their loved ones who face rare *and* common diseases.

We need these kinds of solutions more than ever. We are at a crossroads of big challenges and even bigger opportunities. On one hand, we're facing projections of dramatic increases—if not pandemics—of autoimmune disease, as well as cancer and infection. These trends could soon cause unprecedented illness and death around the world—unless we take action *now*. Superbugs are outsmarting antibiotics and threaten to return

civilization to the pre-antibiotic era—unless we do something *today*. The climate crisis connected to global warming is sparking new and dangerous rare diseases—in the face of increasing airborne and waterborne threats—and will continue to do so unless we overcome our fears and act *this moment*.

We are all being called to act because the opportunity to solve or even prevent these crises in new and unifying ways has never been so possible.

Never before in the history of human accomplishments have we had the capability to cure NMO and a slew of other rare and even common diseases—thanks to an unprecedented chance to bring together brave new realities: an advanced understanding of the immune system; the technology to address genetic, molecular, and cellular dysfunctions; a global network of industry and advocacy willing to invest in solutions; and a heroic patient community committed to putting their lives on the line.

Yes, I have learned a lot from my against-all-odds journey with a rare disease—and the amazing speed of life advances we have made in just a few short years. How have these advances been achieved? How has this happened? For starters, by redefining rare—by choosing to see and solve the problem differently, and by gathering a group of dedicated problem solvers to join the mission.

This was the case that I presented to the tech gurus in Silicon Valley about why a giant bioinformatics company division should choose to care about a tiny and rare autoimmune disease—for the higher good of making a difference for all.

The truth is that in the universe of rare, people don't always care. If it isn't clear how a disease affects them or their loved ones, most don't connect. Understandable—but unfortunate. And in fairness, it can be hard to see how rare has anything to do with someone not affected by it. This raises another aspect of the work that needs to be done. The reality is that even as the cures of tomorrow require breakthroughs in science and technology today, I believe the concept of a rare disease has a messaging problem—even a marketing problem—that when solved will play a key role in the cure revolution. Caring about rare should matter to us all. And

that's one reason that every time I've been disappointed by how people can shrug off the plight of a patient stigmatized by the label of a rare or orphan disease, I've become even more dedicated to telling my "Power of Rare" story in the cause of life-saving solutions.

My blueprint for building a foundation for a cure rests on the bedrock that we can turn rare causes into rare solutions. But to do so we need to care about each other—to realize that although a rare disease may seem to have nothing to do with you, there is a connection yet to be learned, and a solution yet to be found. It starts and ends with heart—and heart is all about connections. Our approach has not been conventional in this respect. For each of the key players on our revolutionary team, it has always been personal—often because of a loved one diagnosed with a life-threatening condition. This fact gave us courage to do things differently, sometimes even radically. My belief from the start was that if it was going to take a revolution to get all the greatest minds together and cure NMO—then by God or the universe or karma—that is what we would do.

I have learned that sometimes too much time is spent trying to tackle the huge or even insurmountable problems, when life-saving clues and solutions are held in the hands of rare all around us. We can be empowered to observe more closely, think more openly, and act more boldly in this cure revolution.

These can truly be the days of miracle and wonder.

We are entering a new era of personalized and precision medicine. In the coming years, we may no longer lump patients together who have the same superficial diagnosis. We will apply the lessons that are so intuitive: that each one of us—each life—truly is unique. Every disease condition will be both infinitely rare and not rare at all. Every patient will have her or his own distinct diagnosis, treatment, and cure. Yet another reason to redefine rare.

The Power of Rare is a book I was inspired to write and that I wrote to inspire. It is a call to action for a constructive revolution to change medicine from one-size-fits-all to custom-tailored care. If I have learned anything in accomplishing many of the things we were told could not

easily be done—or be done at all—it is simply that heart and intuition can be as powerful as science and data. Combined, they form a blueprint for achieving the cures that one day can conquer all disease.

Beyond facts and figures, beyond the wonders of technology, we desperately need a revolution in caring—so that we can do this together and that no one is left to bear the burden of rare alone.

Hope is not rare. Love, courage, intuition, and the resiliency to keep going, even in the dark—none of these are rare. Strength in numbers, when the numbers would say otherwise, is rare. And the magical irony is that creating a movement to solve illnesses now considered rare will make them even rarer—to the point that they will become the ultimate example of rare: they will disappear.

After I told them my story of bringing together so many diverse and improbable partners, one of the young execs at Google asked me one simple question. "How? How did you bring all of these competitors together and get them to collaborate?"

It occurred to me that *Saving Each Other*, the book I co-authored with Ali about how we overcame those nightmarish early days following her diagnosis, really spoke to the question of *why* I took on the cause. And now the time had come to write about my blueprint that informed *what* we've done and *how* I have led our team—as we continue to push the boundaries of possibilities for cures at every turn.

My sincere hope is that by my sharing the lessons learned along the way—from the challenges faced to the course corrections made and the victories won—you will be inspired to apply the universal elements of our blueprint to your own revolution for change, whatever the highest goals of your mission may be.

And more, I hope that even in these most promising yet turbulent of times, this book will shed a light on your own miraculous possibilities—that it finds a way into your heart and inspires you to recognize your own uncommon gifts for transforming the world we share for the better.

This is *The Power of Rare*.