TRIAL

AND

REDEMPTION

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With teeth chattering from the bitter cold, Billy trudged along the frozen, urban streets marked by tall, darkened buildings that swayed in surrender to the punishing wind. The frigid chill seeped through his threadbare clothes, numbing his fingers and toes, and paralyzing his mind. Freezing, starving, jobless, homeless; could things get any worse? With his last embers of hope vanishing into the icy landscape like fallen snowflakes, the barren sky was suddenly illuminated by a bright, piercing light. Attracted to the beam like a moth to a candle, Billy approached a two-story, brick building and entered through a large revolving door into a spacious lobby bathed in luminous white light. Once inside, he sighed in welcome relief as a burst of warm, rejuvenating air permeated every pore of his frozen body. A concave-shaped reception counter bearing an encouraging sign, *Welcome Veterans*, beckoned to him. Suddenly, a small, stern-faced man clad in the white lab coat of a staff physician materialized, ghostlike, from behind the counter and spoke in a menacing voice. "You are not welcome here. Get out."

"But I am a veteran." stammered Billy.

"The man replied, "I don't care; get out or I'll have the guards drag you out by your feet."

Reluctantly, Billy turned around and headed back into the arctic unknown. *It's so cold; I'll freeze to death out here.*

Shivering in a violent tremor, Billy suddenly realized his whereabouts as he felt the hard mattress rub against his aching back. It happened again, this dreaded, recurring dream! Jolting

upright, the familiar glare of two red beams emanating from the opposite side of the room met his torpid gaze.

That damn key. Ever since I won it, I've had this nightmare. And those eyes stare back at me like glowing embers every night. They never light up during the day.

Billy recalled the recent events with the strange key. Among the first crop of American soldiers to be deployed in the escalating Vietnam conflict, the eighteen-year-old enjoyed traveling the beautiful country and chatting with the friendly locals in his role as a military adviser to the Army of the Republic of Vietnam. But as the tempo of the war increased and wandering became more perilous, his disillusionment with the conflict grew, especially after witnessing several traumatic incidents, including a brutal attack in a Saigon restaurant by hostile Vietnamese forces. When his tour ended in early 1965, he was more than ready for some R & R back home in Peoria, approximately one hundred and fifty miles south of Chicago. First, however, he and a few army buddies decided to stop in New York City for an extended stay. He had never visited the Big Apple, America's largest city, and was anxious to tour its major attractions.

One evening, during their ritualistic poker game in the cheap Brooklyn hotel room they shared for their New York adventure, one of his colleagues, depleted of cash, placed an ancient-looking key attached to a tarnished brass ring in the pot. When Billy won the round, he grabbed the key with the rest of the winnings and asked.

"Okay, Harry, what am I supposed to do with this thing?"

Harry replied, "I hate to lose that keyring; it was my good luck charm. Look at it closely. The key's shaft is carved in the image of a two-faced, old man, one looking forward and the other

backward. The eyes sparkle, almost like they are seeing right through you. I'm sure it represents Janus, the Roman god of time. Maybe it will bring you luck."

Billy laughed in derision. "Well, I don't know anything about Roman gods, but I could use some good luck." With that, he tucked the small icon into his shirt pocket and proceeded to deal the next hand.

It was later that night when jolted awake from a disturbing dream that had seemed so real—roaming frozen, urban streets in a state of poverty left him trembling in despair—when he noticed one set of eyes on the old icon shining brightly at him, like two ruby red embers. Within a few minutes, the lights subsided, and the icon remained dark until the next night when the pattern repeated itself. Tonight was the fifth night in a row with that same dream and with those same piercing lights greeting him as he woke.

This recurring dream is really bothering me. What does it mean? Could it be a signal from this strange key about my future?

The following morning on his way to a local coffee shop, he decided that he had had enough of the ancient keyring. Glancing around to make sure he wasn't noticed by any passing pedestrian, he grabbed the icon and flung it into the middle of the empty street, hoping his action would cast away his nightmare.

CHAPTER ONE

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Only the droning buzz of the laboratory machinery disturbed the stillness of the near-empty suite. Centrifuges, freezers, cell incubators, laminar flow hoods, and even the overhead lights contributed their monotonous din to create the steady hum of white noise that provided a background conducive to creative thought and experimentation. The entire lab, indeed, the entire floor, was nearly deserted at this early hour. The quietude provided a stark contrast to the escalating fervor in the mind of the lab's single occupant.

Brian Ellis, a youngish looking thirty-five, was a research director at Capture Pharmaceuticals, a large drug firm located in Evanstown, a North Shore suburb nestled twelve miles north of Chicago. Biomedical research was his passion, ever since the sixth grade when he had completed a school project on Jonas Salk and his development of a vaccine for polio, the most feared childhood disease of the twentieth century. That project earned Brian an A+ and inspired his career choice. Where else but in the realm of medical research could one positively influence so many people's lives just as Jonas Salk had accomplished with his miraculous vaccine?

Brian had overcome some considerable obstacles along the way: the frequent moves necessitated by his father's job as a representative for a large HVAC company; the deaths of both parents, just months apart, from the insidious scourge of cancer when he was eighteen; a debilitating bout with bacterial meningitis during his junior year at the University of Illinois. Through it all, he relentlessly pursued his career goal with a single-minded passion that eventually led to his current position at Capture Pharmaceuticals. That singularity of focus had

always been his greatest asset. Unfortunately for Brian, it also exposed a particular vulnerability, for his obsession promoted a naivete in failing to appreciate developing problems in other areas of his life. The price of this neglect would come to haunt Brian on both a personal and professional level in the coming days.

This morning, Brian was reviewing the results of his latest experiment designed to determine the chemical sequence of a specific gene, which is a small section of DNA that contains the instructions for a particular protein molecule. Examining the fragile gel in front of him, really nothing more than a slab of jelly-like material, he observed a series of stained, blue bands stacked in four columns along the gel's entire length, almost like multiple rungs on a ladder. To an untrained observer, the bands held little meaning, merely resembling a random collection of blue smears. But to a skilled investigator like Brian, they read like a perfectly ordered instruction booklet, for they revealed the exact DNA sequence of the gene's four building blocks, designated A, G, C, and T.

As Brian interpreted his gel results, he could hardly contain his burgeoning excitement. With his heart racing from an overstimulated sympathetic nervous system pulsing burst of adrenaline through his veins, he took a deep breath and pondered the potential impact of his discovery. His experiment had corrected the defective DNA sequence in the hemoglobin gene, the root cause of the insidious red blood cell disorder, sickle cell anemia. If his experimental method applied to different genes, it could offer the promise of cures for several, previously intractable, genetic diseases passed down from one parent to a child. Sickle cell disease, Type1 diabetes, cystic fibrosis, muscular dystrophy; the list was enormous. A new dawn of molecular medicine was possible. This was huge!

Swinging his legs off the metal chair, he stood up to his full six-foot, two-inch height and released his pent-up emotions with a primal shriek of "holy shit!" He could almost imagine the

dark shadows, formed by reflections of the different laboratory instruments on the silent walls of the laboratory, nodding in approval. Jonas Salk, too, would be pleased.

Recovering from the emotional outburst, Brian spent a moment reflecting on his laboratory adventures over the past several weeks. As a release mechanism from the escalating tensions at work and home, he had initiated his own research project as an off-hour diversion, usually late at night. *Hey, the company shouldn't care what I do with my own time.* Perhaps his standing within the research organization had taken a hit recently, but these results would certainly restore his luster. Anyone with even half a brain could recognize the importance of his discovery.

His research centered on gene therapy, the technology that enables changes in the genetic content in cells of an individual affected with an inherited disease. More specifically, he focused on one major problem that limited the wider clinical use of gene therapy, delivering the correct gene to the appropriate target cells without impacting other cells in the body. After an initial series of setbacks, Brian had identified a promising cell delivery vehicle, Tregs, special immune cells with their own internal GPS system that enabled them to target specific organs in the body. Tonight, he had demonstrated that his laboratory modified Tregs could deliver a correct hemoglobin gene sequence to cells that had the sickle cell mutation. Just as importantly, the Tregs failed to incorporate the gene into cells that didn't produce hemoglobin, providing a crucial specificity test of his delivery system. If his genetic honing method, as he referred to it, was adaptable to work *in vivo*, that is in animals, and not just i*n vitro*, as in his cellular experiments, then it could effectively accelerate the clinical applications of gene therapy. *This could be a game-changer!*

CHAPTER TWO

"What, did you spend the night here again?"

Brian peered up from the notes scattered all over his desktop to observe the smiling face of Lois Beaker peeking in through his open office door. *Must be 7:30 a.m.; punctuality is Lois's middle name.* Lois, who led the Inflammatory Diseases Research Team, was Brian's colleague and best friend at work.

Smiling in return, and speaking in a crisp, logical cadence consistent with his scientific training, he answered, "I've got something big this time. My gene honing system specifically corrected the genetic sequence in the hemoglobin beta gene. I'm just finishing the MOI."

An MOI, short for Memorandum of Invention, is a confidential document written by a scientist for use by their company's patent department to establish precedence and to determine whether a patent should be filed on the described invention.

"An MOI sounds like a good idea, but what will Davis think?"

Davis was Dr. Andrew Davis, the recently appointed Head of Research and Development at Capture Pharmaceuticals, the large drug company where Brian, Lois, and their teams of scientists worked.

"Even he can't deny the importance of this discovery," replied Brian. "It could represent a solution to one of the central issues of gene therapy—targeting."

"I'm not so sure he will feel that way," answered Lois. "Remember the meeting from last week."

In a nonchalant tone, he replied. "Don't worry about Davis. Now if you could just sign and date this MOI under the witness line, I'll run it downstairs to Patterson's office."

Pulling out her pen, Lois said. "I think in your excitement, you forgot lawyer hours. Patterson won't be in until his normal ten o'clock start time."

A few hours later, Brain rushed down two flights of stairs to the main floor where the company's executive suites and support offices were located. He knocked loudly on a partially opened door marked in bold lettering, JOHN PATTERSON, Esq.

"Come in, come in already. If you knock any harder, I'm afraid you'll break the door down. What's got you so energized this morning? If it was something in your coffee, I need a cup of that stuff."

John Patterson was a large, almost obese man whose sluggish mannerisms masked a razor-sharp mind and a quick wit. A trained, PhD-level scientist in molecular biology, he had taken advantage of the company's tuition aid program to complete his law degree over five years of night school. Now he served as chief patent attorney for Brian's Division, Cardiovascular Sciences. Brian enjoyed their interactions, usually marked by rigorous scientific discussions coupled with a good measure of sarcastic humor.

Ignoring Patterson's attempt at humor, Brian got right down to business. "Good morning, John. I have an MOI to establish precedence for an invention. This could be big. It outlines a cellular method to specifically target gene therapies to the correct organs."

In an admonishing tone, the lawyer asked. "I hope this invention has to do with CAP-715." He was referring to the experimental cardiovascular drug that was scheduled to begin testing in human subjects in a few months. Patterson's subdued response temporarily dampened Brian's enthusiasm.

"It's bigger than CAP-715," replied Brian. "It could serve as the basis for expanding gene therapy in the clinic."

Patterson gave Brian a long stare before replying. "How is Davis going to react, right after reading the riot act about CAP-715 last week? Remember his words; one hundred percent of everyone's effort must be dedicated to preparing the IND for CAP-715. No exceptions."

IND referred to the Investigation New Drug Application, a regulatory document submitted to the Food and Drug Administration, or FDA, seeking permission to start human clinical trials for an investigational drug or biological product.

"Aren't you in enough hot water with him already after last week's Working Group meeting?" continued the attorney.

Brian recoiled from a sudden sinking feeling in the pit of his stomach as he recalled the public reproach he had received from Davis. When Brian had taken the opportunity to update the CAP-715 Working Group on his gene-honing work, Davis's reaction was harsh.

"If anyone, and that includes you, Ellis, is not dedicating one hundred percent of their time to CAP-715, there will be consequences. I promised the Executive Board that the IND for this compound will be filed before the end of May next year and I'll be damned if we miss that deadline because of some extraneous work on random genetic manipulations."