

Comments on Application # CLIN2-16063

A phase 1/2 study to evaluate a bi-specific CD19/CD20-directed CAR T-cell, in refractory lupus nephritis (LN) and systemic lupus erythematosus (SLE)

Thank you for the opportunity to provide my unique perspective regarding ImmPACT Bio's grant application to support their clinical development of the first bispecific CD19/CD20 CAR T therapy being investigated for the treatment of refractory lupus nephritis (LN) and systemic lupus erythematosus (SLE).

I submit the following comments as both the leader of Lupus and Allied Diseases Association, Inc., (LADA), a national patient-led organization and as an individual who has lived with the debilitating effects of lupus since childhood, to urge CIRM to approve and support ImmPACT Bio's grant application. As a patient advocate who has had a front row seat to lupus drug development and research for decades, I understand the critical need for pioneering treatments for lupus nephritis and lupus.

Lupus is an extremely complex, chronic inflammatory autoimmune disease affecting virtually any organ system of the body with limited treatment options. It is highly individualized, extremely volatile, difficult to diagnose, potentially fatal, presently incurable, totally capricious, painfully limiting, life altering, dream stealing, career ending, and financially, emotionally, and physically devastating.

Lupus is an unpredictable condition in which symptoms come and go and complications can arise suddenly. It is a costly multi-system disease as patients must regularly see several specialists, and can affect virtually any part of the body including vital organs, making it the prototypical autoimmune disease. Since there are approximately 100 autoimmune conditions, the benefits of lupus research could be far reaching.

Like many others with lupus, I struggle to manage the life altering effects of 8 different autoimmune disorders and several co-morbid conditions. I presently take 48 medications a day and have unique allergies and sensitivities to both active and inactive ingredients in drugs, requiring careful monitoring by my healthcare providers. Please understand *no one size fits all* products exist for complex individuals like me, our response to treatments is unique, divergent, and at times adverse.

I have endured decades of destruction and disfigurements from harmful treatments and I used to weigh 220 lbs. My entire digestive tract is impaired and it takes 5 different drugs to allow me to eat each day. I haven't eaten fruits or vegetables in 24 years now and suffer from constant colicky abdominal pain. Maintaining adequate nutrition is a constant battle. The veins in my arms are inaccessible due to scarring from decades of lab draws, so I am on my second infusa-port for bloodwork and infusions, I have kidney disease and I am blind in my right eye.

At times, I could barely think, walk or raise my arms above my head and have spent months in bone gnawing, soul wrenching pain going from physician to physician begging for help. Believe me, it is a desperate place to be. My life has been filled with missed opportunities, pain, limitations and loss. It takes a tremendous amount of self-motivation to manage my medical care, maintain my dignity, and attempt to have any quality of life.

For every two steps I take forward, I take one backward. It feels like I am constantly climbing a mountain, struggling to reach the peak and place my feet on solid ground, but as soon as I am close to the summit I lose my foothold plummeting backward into the unknown abyss; desperately grasping for anything substantial to grab onto. Not only does this drain one physically but the emotional toll is devastating. Dreams and goals are always being reassessed and some days it is a victory just to get out of bed, shower and put on clean pajamas.

Lupus disproportionately affects women of color in the United States; it is 2 to 3 times more common among African-Americans, Hispanics and Latinos, Asians, and Native Americans. Minority women tend to develop lupus at a younger age, experience more serious complications, and have higher mortality rates—up to 3 times the incidence and mortality of Caucasians. 90% of those affected are women, but men and children are also diagnosed with lupus. 80% of those diagnosed are between the ages of 15-44 during their child-bearing years or prime of life.

Fatigue is the most prevalent and incapacitating symptom, resulting in decreased physical and mental function, and for many of us it is the most disabling symptom. Nearly 40% of individuals with lupus are disabled and rely on government-sponsored health plans such as Medicare and Medicaid. Lupus profoundly affects a person's ability to be a parent and capacity to pursue their education and career goals, as well as those of their care partner's. The societal and economic impacts of lupus are staggering. Developing more effective and safer lupus therapies has the potential to reduce socioeconomic and health disparities in our community.

All of us at LADA know firsthand the daily impacts of lupus as well as the challenges that our physicians face in making the best treatment decisions for us. It is extremely difficult to be diagnosed correctly, much less have access to a specialist that has the time to work with us to find the right treatment. Due to the heterogeneity of lupus, no two patients are alike and treatment is highly individualized, effectively treating people with lupus is like balancing on a pinhead. Therefore, a treatment that works in one person may not work in another.

Physicians who manage individuals with this complex condition need an armamentarium of therapies to effectively treat them. Often clinicians are left with a try and fail approach in seeking the most optimal treatment while patients become sicker, organ damage accrues, and both patient and physician become more frustrated.

Due to the heterogeneity of both lupus and the patient population, unpredictable relapsing and remitting course of the symptoms, lack of validated biomarkers, clinical endpoints and outcome measures, uniform control group, and existence of background medications—usually steroids and immunosuppressants that ablate the immune system, it has been challenging to develop new treatments in lupus. Lupus is a disease of great unmet need.

We have been eagerly awaiting more efficacious and safer groundbreaking treatments that target the offending molecule or cell that disrupts our immune system and in a perfect world, people like me would take one pill a day for treatment instead of forty-eight. We desperately need safer, more innovative treatments that address the pathogenesis of diseases, while impacting what matters most to patients—reducing symptoms and improving daily functioning and quality of life.

In addition, clinical research trials have not been traditionally designed to measure what is most important to those who are participating such as improved daily quality of life, reduction in current drug regimen, side effect tolerability, steroid sparing, and co-morbid conditions. Patients are also concerned with potential cosmetic side effects such as hair loss, rashes, weight gain, gastrointestinal problems; things that may be socially challenging to young people in the prime of their life.

Most of us living with lupus desperately cling to the belief that there will be more effective treatments and a cure during our lifetime. Like so many others, this disease cut me down in the prime of my life and drastically impacted my future. It has stolen precious time from me, as well as the opportunities to have a successful career, financial security, or that of being a Mother, just to name a few.

Existing treatments for lupus are absolutely inadequate; many are toxic and cause detrimental side effects with long-term use, and since there are only 5 drugs currently approved for SLE, and 2 for lupus nephritis, many therapies being used are not approved such as cancer treatments and transplant drugs. For decades the “go to” drug for treating lupus has been corticosteroids.

Here at LADA, we call it, “the drug you love to hate.” It saves your life and fights inflammation quickly, especially in an acute situation, but this comes at a high price with horrific side effects such as glaucoma, cataracts, hypertension, diabetes, atherosclerosis, bone thinning, infection susceptibility, elevated cholesterol, obesity, manic feelings, and an appetite equal to that of 4 growing teenage boys.

Other treatments include immunosuppressives that ablate the entire immune system and antimalarials, which can cause retinal toxicity. Chemotherapy drugs can cause infertility and miscarriages. We catch numerous infections and some of us even end up with cancer. And here’s my favorite—we take drugs to treat the side effects of other medications which is just ludicrous. Many therapies are merely band-aids treating the symptoms and never getting to the root of the problem.

The lupus community has eagerly awaited the arrival of safer, newer, more efficacious drugs and all of us here at LADA are excited that several novel treatments have finally been approved, but not every person with lupus responds to them. Since there are a multitude of treatments for lupus nephritis and lupus currently in the development pipeline, ImmPACT Bio's groundbreaking therapy has the potential to be an important step in this critical juncture of lupus drug discovery, development, and delivery.

In closing, we passionately urge you to consider supporting ImmPACT Bio's grant application and stand with people with lupus and their loved ones by helping to advance Car T therapy. People living with diseases of unmet need such as lupus who currently have only limited or no effective therapies, need access to an array of novel, promising treatments that will give them a better quality of life. There are millions of people who could benefit from innovative drugs now, and many more in the future who have not yet been diagnosed.

For anyone struggling to live with lupus or to love someone with lupus, what motivates us to face another day is our hope that research advancements lie just around the corner that will

improve our lives. Because of this, we believe wholeheartedly that CIRM's funding of ImmPACT Bio's clinical trial has the potential to be a catalyst in advancing innovative treatments for people with lupus nephritis and lupus, and we are thrilled with the prospects this holds for our entire community. Your support would put us one step closer to ensuring that the next generation of people with lupus are given the chance at a better quality of life and the opportunity to pursue their goals and achieve their dreams.

The Lupus and Allied Diseases Association, Inc. (LADA) was founded in 1978 and is a national non-profit organization dedicated to enhancing quality of life by engaging and empowering individuals impacted by lupus and diseases of unmet need to become proactive in their care. As a passion-driven charity led by people with lupus and their loved ones, we work to ensure that the patient stakeholder is included as an equal participant in the healthcare, regulatory and public policy arenas, and across the research continuum.

It is our goal to improve access to care and quality of life by fostering collaboration among stakeholders, promoting unity in the community, and wielding the patient and care partner voice as a catalyst to advance innovative advocacy, education, awareness and research initiatives that will identify causes, advance better diagnostics, and discover superior treatments, and cures.

Thank you for the opportunity to provide our exclusive patient viewpoints and for recognizing the value of including people living with the disease in the process.

Please contact me at 315-264-9101 or kathleen@ladainc.org if you have any questions or require additional information.

Respectfully Submitted-

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