REVOLO BIOTHERAPEUTICS

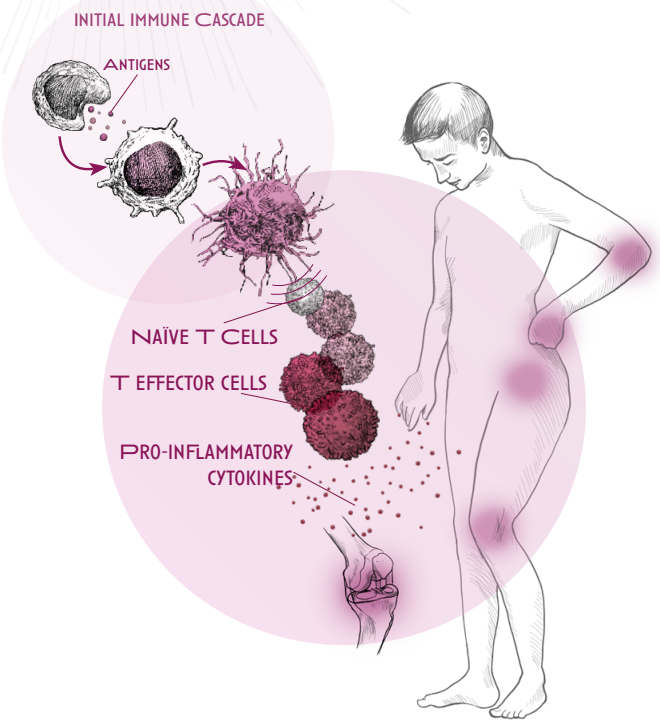
Analyze. Reset. Revolutionize.

RHEUMATOID ARTHRITIS

We aim to revolutionize the treatment landscape for rheumatoid arthritis (RA)

RA is a chronic inflammatory autoimmune disease characterized by swelling, stiffness and pain in the joints, but it can also affect other tissues.

Roughly 1.3 million people in the US have RA[1], making it one of the largest therapeutic areas worldwide.



WHAT DRIVES RA?

RA occurs when the immune system mistakenly attacks its own tissues, affecting the joint lining and causing painful swelling that can lead to joint deformity and bone erosion.

In RA, inflammatory T cells, called T effector cells, infiltrate joint tissues leading to tissue destruction and excessive production of inflammatory molecules (pro-inflammatory cytokines) in the local environment.

T effector cells and an array of inflammatory cytokines play a critical role in initiating and perpetuating the chronic autoimmune response characteristic of RA.

Cytokines including tumor necrosis factor (TNF), IL-6, and IL-1 are key drivers of the complex pathophysiology of RA, contributing to immune system overreaction and persistent inflammation that can exacerbate tissue and bone destruction.

Early disease control is critical to avoid unreversible damage to joints and other tissues.

EXISTING THERAPIES

Options that exist for RA treatment, including steroids, immunosuppressants, and biologics aim to reduce inflammatory cells and certain pro-inflammatory cytokines downstream, leading to **limited response rates** (ie: 25 – 40%)[2], **immune system suppression**, **low rates of sustained disease remission** and an array of side effects resulting in poor patient compliance. In addition, inhibitors of inflammatory pathways such as janus kinase inhibitors (JAKs) have been associated with **severe life-threatening side effects**, limiting clinical applicability.

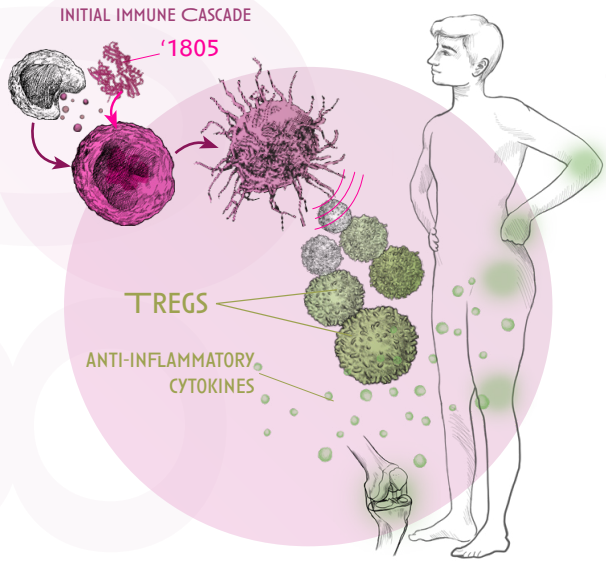
60 to70% of patients in the US fail to achieve remission with available treatments[3] and ~20%do not respond to available therapies.[2]

References: 1. Moawad FJ. Eosinophilic esophagitis: incidence and prevalence. Gastrointest Endosc Clin N Am. 2018;28(1):15-25. 2. de Hair MJH et al. 3. Brown PM, Isaacs JD. Rheumatoid arthritis: from palliation to remission in two decades. Clin Med (Lond).2014;14(suppl 6):s50-s55

‘1805

Resetting the immune system for long-term RA disease remission.

Revolo’s clinical drug candidate ‘1805 is a modified analogue of the endogenous immune regulatory binding protein (BiP).



HOW IS ‘1805 DIFFERENT FROM EXISTING THERAPIES?

‘1805 resets the immune system “upstream” or before the inflammatory cascade.

It increases the number and function of cells that regulate the immune system (T regulatory cells) and restore its balance, preventing proliferation of T effector cells and inflammatory molecules. As a result, ‘1805 avoids chronic inflammation without suppressing the immune system.

Effects are seen up to 8 weeks following a single dose, easing the burdens of frequent therapies for patients.

‘1805 – UNIQUE DISEASE-MODIFYING AND SAFETY PROFILE VERSUS CURRENT THERAPIES

REDUCES BONE LOSS IN ANIMAL MODEL	MAINTAINS LONG-LIVED EFFECT	DEMONSTRATED INCREASE IN T REGULATORY CELLS	REDUCES PRO-INFLAMMATORY CYTOKINES	DEMONSTRATED SAFETY AND TOLERABILITY IN A PHASE 2 STUDY
Single dose of ‘1805 reduced fibrosis, cartilage destruction and cavity erosion, and decreased the number of bone destructive-cells (osteoclasts) in pre-clinical studies[4]	Single dose of ‘1805 sustained long-lived effects ranging from weeks to months[5]	In a Phase 2 study, a single dose of ‘1805 increased T regulatory cells up to 5x and was durable for 12 weeks[5]	Reduces IL-1, IL-6 and TNF and increases anti-inflammatory cytokine IL-10[5]	with rapid onset and sustained RA remission with intravenous administration (total of 24 patients dosed with ‘1805)[5]

PHASE 2 TRIALS

A Phase 2 TRIAL for patients with moderate to severe RA is ongoing.

In another PHASE 2 TRIAL, ’1805 is being evaluated in patients with non-infectious uveitis.

References: 4. TNFa transgenic mouse model study, data on file at Revolo Biotherapeutics. 5. Kirkham et al. 2016. Safety and patient response as indicated by biomarker changes to binding immunoglobulin protein in the phase I/IIA RAGULA clinical trial in rheumatoid arthritis. Rheumatology, 55(11): 1993–2000. 6. Riffo-Vasquez Y, et al. 2020. “Modulation of allergic inflammation in the lung by a peptide derived from Mycobacteria tuberculosis chaperonin 60.1.” Clinical & Experimental Allergy; 50(4), 508–519.

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