Updated December 3, 2013

Pfizer Inflammation and Immunology (I&I) Fact Sheet

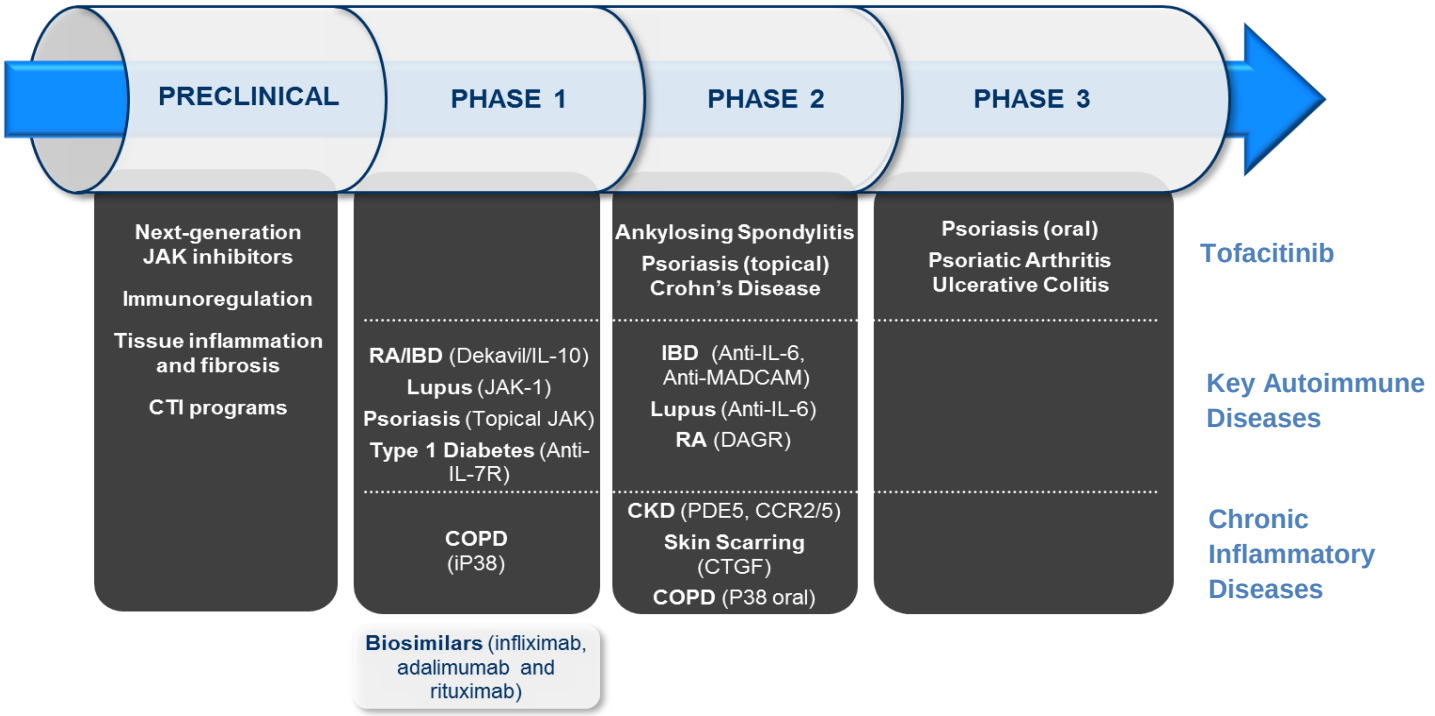
Pfizer is building on our heritage of breakthrough treatments in inflammation with the goal of developing first-in-class or best-in-class therapies to improve the quality of life of people living with inflammatory and autoimmune diseases. We are investigating experimental therapies for rheumatoid arthritis (RA), lupus, psoriasis, chronic kidney disease (CKD), type 1 diabetes, chronic obstructive pulmonary disease (COPD), skin scarring and inflammatory bowel disease (IBD) – including Crohn's disease (CD) and ulcerative colitis (UC) – and others.

Pfizer's strategy in Inflammation and Immunology is to:

1. **Continue to evaluate the potential of tofacitinib across autoimmune conditions,** such as psoriasis (topical and oral), IBD, psoriatic arthritis and ankylosing spondylitis.
2. **Advance the treatment of autoimmune diseases in RA and other conditions,** such as lupus and IBD, with fit-for-purpose experimental therapies designed to address immune system defects and restore balance.
3. **Innovate disease-modifying treatments for chronic inflammatory conditions,** such as chronic kidney disease and COPD, diseases where there is a need to find treatments for the underlying cause, not just the symptoms, and skin scarring.
4. **Progress the science around key pathways in inflammation and innovate new technology platforms,** both through our own science and in collaboration with other innovators across the R&D ecosystem.

Collaborations are critical to advancing the science in this field. In fact, 30 percent of our Centers for Therapeutic Innovation (CTI) programs, a groundbreaking partnership model with leading academic medical centers, are in immunology and inflammation. Some key external relationships include:

- University of California, San Francisco (UCSF) on emerging science in immunoregulation
- Alliance for Lupus Research (ALR), in which ALR and CTI co-fund novel translational research projects driven by leading academic medical centers within the CTI network for lupus
- Karo Bio, Philogen, Nodality, to advance key science and experimental therapies



Tofacitinib Clinical Program – Novel Janus Kinase (JAK) Inhibitor

Phase 3:

- Psoriasis (oral), psoriatic arthritis and ulcerative colitis

Phase 2:

- Crohn's disease, psoriasis (topical) and ankylosing spondylitis

Pfizer's Experimental Therapies in Key Autoimmune Diseases

Phase 2:

Anti-IL-6: fully human lgG2 antibody that binds and neutralizes IL-6, a key cytokine in inflammatory disease. This experimental therapy utilizes a novel, broad anti-inflammatory approach and is being studied in diseases with large unmet patient need including **Crohn's disease**, **ulcerative colitis** and **systemic lupus erythematosus (SLE)**

Anti-MAdCAM-1: novel monoclonal antibody that may allow for selective blockage of immune system cell (lymphocyte) recruitment to the inflamed gastrointestinal tract while potentially leaving trafficking to other organs intact. The potential for targeted efficacy and reduced immunosuppressive side effects may have an important impact in **inflammatory bowel disease (IBD)**

DAGR (disassociated agonist of the glucocorticoid receptor): an investigational next-generation steroid being studied in **rheumatoid arthritis**

Phase 1

Dekavil/IL-10: antibody-targeted delivery of interleukin 10 that selectively modulates and promotes anti-inflammatory effects in the target area, potentially sparing unwanted effects on other tissues and restoring immune function. Dekavil is currently under investigation by Philogen, S.P.A. in **rheumatoid arthritis** and preparing to enter the clinic for investigation by Pfizer in **IBD** in 2014

JAK-1: selective JAK-1 inhibitor that is designed to modulate the signaling of multiple cytokine pathways thought to be dysregulated in **lupus**; its specificity may possibly help avoid off-target effects in patients, such as anemia

Topical JAK: new JAK inhibitor being investigated in **psoriasis**. This experimental therapy is specifically designed for local delivery to minimize systemic exposure and offer a new topical alternative

Anti-IL-7R: monoclonal antibody that binds to and inhibits the function of human IL-7R, with the potential to prevent and delay the progression of **type 1 diabetes**, as well as reverse new onset diabetes

Pfizer's Experimental Therapies in Chronic Inflammatory Diseases

Phase 2

PDE5 (phosphodiesterase type 5 inhibitor): novel PDE5 inhibitor with a distinct pharmacokinetic profile with the potential to delay the progression of **diabetic nephropathy** on top of standard of care in patients who are in Stage 3-4 of **chronic kidney disease**

CCR 2/5: small molecule dual inhibitor for **diabetic nephropathy**, the leading cause of **chronic kidney disease**. This experimental therapy takes a multi-faceted approach – going beyond the current standard of care – to potentially delay/prevent end-stage renal disease by slowing progression

CTGF (EXC-001): highly selective second generation antisense oligonucleotide inhibitor of connective tissue growth factor (CTGF) to address **hypertrophic scarring** following scar revision surgery; potential to represent a first-in-class therapy, addressing a large unmet patient need

P38: inhibitor that has the potential to be a first-in-class, novel anti-inflammatory therapy for the maintenance treatment of **COPD** and to reduce the occurrence of exacerbations; provides potential alternative, broad-spectrum, anti-inflammatory activity in oral (Phase 2) and inhaled (Phase 1) formulations

Other

Phase 1

Biosimilars: we are currently investigating potential biosimilars of Remicade® (infliximab), Humira® (adalimumab) and Rituxan® (rituximab)

Disease Statistics

Rheumatoid Arthritis (RA)

- RA is a chronic systemic autoimmune disease that can be painful and disabling, making even the most basic movement of the joints a highly uncomfortable experience for patients.
- RA affects approximately 23.7 million people worldwide[i] and 1.5 million people in the United States.[ii] RA can develop at any age, but it usually occurs between the ages of 40 and 70.[iii]

Psoriasis

- Psoriasis is a chronic, systemic inflammatory disease that is estimated to affect 125 million people worldwide, including 7.5 million Americans.[iv]
- Because it is difficult to hide, psoriasis can affect many aspects of day-to-day life including the way people are treated by others, which can sometimes have an impact on a person's overall physical and emotional health.[v]

Psoriatic Arthritis (PsA)

- PsA is a disabling type of systemic, inflammatory disease that affects up to 30 percent of people with psoriasis.[vi]
- In the United States, TNF inhibitors are the only disease-modifying anti-rheumatic drug therapies currently indicated for the treatment of active psoriatic arthritis.[vii]

Ankylosing Spondylitis

- Ankylosing spondylitis is an inflammatory disease that can cause some of the vertebrae in the spine to fuse together, decreasing the spine's flexibility and causing a hunched posture. In some cases, this can be so severe that people can't lift the head up to see forward.
- Currently, there is no cure for ankylosing spondylitis, but treatments can decrease pain and reduce symptoms.[viii]

Lupus

- Lupus continues to be a difficult disease to understand and a mystery to the scientific community. Striking mostly women at the prime of their lives, lupus can affect the joints and potentially every major organ in the body, including the heart, kidneys, skin, lungs, and brain.
- As many as five million people worldwide are suffering from this debilitating disease that has few treatment options.[ix]
- Lupus can lead to a number of debilitating symptoms, including extreme fatigue, painful joints, fever, anemia, swelling, rash, sun-sensitivity, hair loss, mouth and nose ulcers and a number of other conditions that make living a normal life difficult.[x]

Inflammatory Bowel Disease (IBD)

- Ulcerative colitis (UC) and Crohn's disease (CD) are chronic inflammatory diseases of the intestines known as IBD. It is estimated that some 1.4 million Americans suffer from IBD, with approximately 30,000 new cases diagnosed each year.[xi]
- Living with IBD can impact a patient's quality of life in many ways, not just physically, but emotionally as well. The stigma associated with this can be immense. From limiting the foods they can eat, to constant visits to the bathroom, at times enteral feeding, and the need for surgery to remove a portion of a bowel to cause relief, living with IBD is a life-long journey.[xii]

Type 1 Diabetes (T1D)

- As many as three million Americans may have type 1 diabetes (T1D), and each year, more than 15,000 children and 15,000 adults—approximately 80 people per day—are diagnosed with T1D in the U.S.[xiii]
- Neuropathy, or nerve damage, affects more than 60 percent of people with type 1 diabetes. Research shows that people with diabetes are more likely to have high cholesterol and hypertension, both of which cause damage to the cells lining the artery walls.[xiv]

Chronic Kidney Disease (CKD)

- Chronic kidney disease (CKD) includes conditions that damage the kidneys and decrease their ability to keep someone healthy – more than 26 million American adults have CKD and millions of others are at increased risk.[xv]
- Currently, in the U.S., eight million patients are living with stage 3 or higher CKD, many of which will experience a rapid progression in disease, which could lead to the need for dialysis or transplant.[xvi]

Chronic Obstructive Pulmonary Disease (COPD)

- An estimated 65 million people worldwide suffer from moderate to severe chronic obstructive pulmonary disease (COPD), and the disease claims more than three million lives each year. COPD is the fifth-leading cause of death worldwide and its prevalence is rapidly increasing.
- Total deaths from COPD are projected to increase by more than 30 percent in the next 10 years, unless urgent action is taken to reduce the underlying risk factors.[xvii]

Skin Scarring

- Each year in the developed world, 100 million patients acquire scars, some of which cause considerable problems, as a result of 55 million elective operations and 25 million operations after trauma.[xviii]

###

[i] World Health Organization, "The Global Burden of Disease, 2004 Update." Accessed 18 November 2013. Available at http://www.who.int/healthinfo/global_burden_disease/GBD_report_2004update_full.pdf.
[ii] Centers for Disease Control. Arthritis-related statistics. Accessed 18 November 2013. Available at: http://www.cdc.gov/arthritis/data_statistics/arthritis_related_stats.htm
[iii] Lee DM, Weinblatt ME. Rheumatoid arthritis. Lancet. 2001; 358:903-911. Available at: http://www.nhs.uk/conditions/Rheumatoid-arthritis/Pages/Introduction.aspx
[iv] National Psoriasis Foundation. Statistics. Accessed 18 November 2013. Available at https://www.psoriasis.org/learn_statistics.
[v] http://www.psoriasis.com/living-with-psoriasis.aspx
[vi] Pfizer November 13 Pipeline Tracker.
[vii] Goodman, A. Psoriatic Arthritis Improved With Ustekinumab. Medscape, November 2012. Accessed 18 November 2013. Available at: http://www.medscape.com/viewarticle/774565.
[viii] Mayo Clinic. Ankylosing Spondylitis. Definition. Accessed 18 November 2013. Available at: http://www.mayoclinic.com/health/ankylosing-spondylitis/DS00483.
[ix] Lupus Foundation of America. Statistics on Lupus. Accessed 18 November 2013. Available at: http://www.lupus.org/about/statistics-on-lupus
[x] Lupus Foundation of America. Accessed 18 November 2013. Available at: http://www.lupus.org/answers/entry/common-symptoms-of-lupus
[xi] Crohn's and Colitis Foundation of America. Managing Irritable Bowel Disease as a Young Adult. August 2010.
[xii] Crohn's and Colitis Foundation of America. Emotional Factors. Accessed 18 November 2013. Available at: http://www.ccfa.org/assets/pdfs/emotional.pdf.
[xiii] Type 1 Diabetes, 2010; Prime Group for JDRF, Mar. 2011
[xiv] Juvenile Diabetic Research Fund. Accessed 18 November 2013. Available at: http://jdrf.org/life-with-t1d/type-1-diabetes-information/diabetes-complications/
[xv] National Kidney Foundation. About Chronic Kidney Disease. Accessed 18 November 2013. Available at: http://www.kidney.org/kidneydisease/aboutckd.cfm.
[xvi] National Kidney Foundation. American Journal of Kidney Diseases. Annual Data Report. Accessed 18 November 2013. Available at: http://www.kidney.org/news/keep/pdf/adr2008/KEEP_2008_ADR.pdf.
[xvii] World Health Organization. Burden of COPD. Accessed 18 November 2013. Available at http://www.who.int/respiratory/copd/burden/en/index.html.
[xviii] Sund B. New developments in wound care. London: PJB Publications; 2000. pp. 1–255. . (Clinica Report CBS 836.)