

α7nAChR Platform

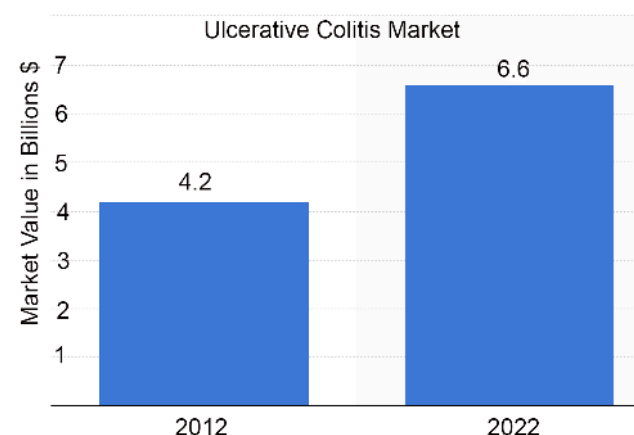
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Decade of research on immune suppression in multiple sclerosis led to realization of the importance of the α7 subunit of nicotinic Acetylcholine Receptor (nAChR)

- α7 nAChR also a central factor in evolutionarily ancient neural circuit to control of inflammation^(1,2)
- Large pharma identified α7 as a pharmaceutical target for Alzheimer's disease and schizophrenia
 - Multiple specific agonists developed
 - All shown to be safe, but did not meet milestones in human clinical trials
 - Strategic goal of 180 LIFE SCIENCES to repurpose drugs for inflammation

- Nicotine binds α7 and is a known immune suppressive
- A subgroup of patients who cease smoking subsequently acquire ulcerative colitis
- Treatment of these patients with α7 agonist has a high probability of therapeutic success (can be viewed as nicotine replacement therapy without issues of addiction)

Significant Unmet Need



Existing Therapies Are Sub-Optimal

Existing Therapy	Issues
Anti-inflammatory drugs (5-aminosalicylates, corticosteroids)	<ul style="list-style-type: none"> × capability to induce remission is quite low × known deleterious side effects of steroids
Immunosuppressants	<ul style="list-style-type: none"> × long-term administration of thiopurine may correlate with an increased risk of developing lymphoma × cyclosporine leads to kidney damage
Infliximab (anti-TNF)	<ul style="list-style-type: none"> × serious adverse events, such as opportunistic infections, including tuberculosis, as well as congestive heart failure in cardiopathic patients

(1) Rothbard JB, Rothbard JJ, Soares L, Fathman CG, and Steinman L. Identification of a common immune regulatory pathway induced by small heat shock proteins, amyloid fibrils, and nicotine. Proc Natl Acad Sci U S A. 2018 115:7081-7086.

(2) Tracey KJ. Reflex control of immunity. Nat Rev Immunol. (2009) 9:418-28

α7nAChR Platform, a Novel Therapeutic Platform for UC

Essential receptor in the neural circuit controlled by the vagus nerve

