FORM 2

THE PATENTS ACT, 1970

(39 of 1970)

&

THE PATENTS RULES, 2003

PROVISIONAL SPECIFICATION

(*See* Section 10 and rule 13)

Title: "BISPECIFIC ANTIBODY FOR TREATMENT OF INFLAMMATORY DISEASE"

Applicant: Mr. VIKAS MEHRA

Dr. BHARAT B. CHATTOO

Address: Genome Research Centre

Department of Microbiology and Biotechnology Centre

Faculty of Science,

M. S. University of Baroda

Vadodara: 390002

Gujarat, India

Nationality: Indian

The following specification describes the invention.

FIELD OF THE INVENTION

The present invention relates to Bispecific Antibodies (bsAbs) that have ability to specifically bind to two different antigens with specificity and affinity. The bsAbs of the present invention are expected to be useful in treating inflammatory diseases particularly psoriasis.

BACKGROUND OF THE INVENTION

Psoriasis is an inflammatory skin condition exhibiting , red, raised, scaly lesions resulting from excessive growth and aberrant differentiation of keratinocytes. Psoriasis affects up to 3% of the world's population, or more than 125 million people. It is a T-cell mediated inflammatory disease, associated with an overexpression of pro-inflammatory cytokines produced by Th1 cells and relative under expression of Th2 cytokines. Studies have revealed that Psoriasis has a major impact on quality of life and is associated with a number of psychological and psychosocial problems.

Cytokines such as Tumour necrosis factor (TNF-α) and Interleukin-17 (IL-17) have found to be in higher serum levels in blood of psoriatic patients. TNF-α is a pro-inflammatory cytokine that amplifies inflammation through several distinct pathways: facilitating entry of inflammatory cells into lesional skin through induction of adhesion molecules on vascular endothelial cells; stimulating keratinocyte production of other pro-inflammatory mediators; and finally activating dermal macrophages and dendritic cells. The efficacy of TNF-α inhibitors in treating psoriasis has been attributed to their inhibition of Th17 T-cells. The interleukin-17 cytokine family consists of six cytokines (interleukins 17A to 17F) and five receptors (interleukins 17RA to 17RE). The interleukin 17A, 17F, and 17A/F heterodimer ligands share a common receptor subunit (interleukin-17RA) for signaling. Studies have revealed that cytokine-targeting strategies aimed at blocking signaling through interleukin-17RA may be beneficial in the treatment of psoriasis.

Recently in 2015, Cosentyx^{TM} (at a dose of 300 mg) was the first and only interleukin-17A (IL-17A) inhibitor to be approved in Europe providing a new and important first-line biologic treatment option for patients with psoriasis. Other biologic treatments for psoriasis, including anti-tumor necrosis factor therapies (anti-TNFs) and Stelara® (ustekinumab) are recommended for second-line systemic therapy in Europe.

Any inflammatory disease is driven by multiple cytokines and therefore one would expect a better efficacy if a single antibody would be able to target more than one cytokine. Therefore, in case of treatment for psoriasis an antibody that is able to target both TNF- α and IL-17R (IL-17 receptor) would be path-breaking. The inventors of the present invention have directed their efforts to fulfil the aforesaid need to provide a better treatment for psoriasis.

BRIEF DESCRIPTION OF THE INVENTION

The present invention is directed towards development of baAb that targets TNF-α and IL-17R for treatment of psoriasis. The genes that are activated, the cellular infiltration, the tissue patterning, the hyperplasia, the clinical features of the disease can be reversed extremely well by blocking both, TNF-α & IL-17R.

The quintessential feature of molecule of the present invention is its scFv (single chain variable fragment) format. The molecules that are approved by the drug regulatory authorities or under clinical trial that are currently known have mAb (monoclonal Antibody) format. An antibody in scFv (single chain variable fragment) format consists of variable regions of heavy (VH) and light (VL) chains of an antibody, which are joined together by a flexible peptide linker.

In one of the embodiment the molecule of present invention has two scFv fragments derived from Human scFv Phage Display Library, one having an affinity for TNF-α

and the other against IL-17R. By using Phage Display Technology a scFv fragment can be displayed on the phage surfaces as functional protein which helps to retain an active antigen-binding domain capability. Therefore, this technology could allow rare clones to be screened and isolated from a large population of phage using any desirable antigen.

In one of the preferred embodiment scFv against human TNF-α and IL-17R have been isolated and the affinities of these binders have been improved. In vitro neutralization potential of these binders was confirmed by cell based assays. The two scFv fragments are linked together by a linker to generate a diabody. This biologic is further expressed in microbial system to get the therapeutic protein.

Since the molecule of the present invention targets two specific cytokines that has well established role in the proliferation of Psoriasis, it will result in synergistic effect. Yet another advantage is that the duration of therapy and the dosage of the biologic may be reduced significantly increasing safety profile of the therapeutic. Further, expressing scFv in microbial system will have a great impact in bringing down the production costs associated with larger biologics. Therefore, the molecule of the present invention may be made available at a highly competitive price.

Dated this the 10th day of September, 2015

Signature: _____

Name: (Meghana Damani)

of Nanavati Associates

Applicant's Agent