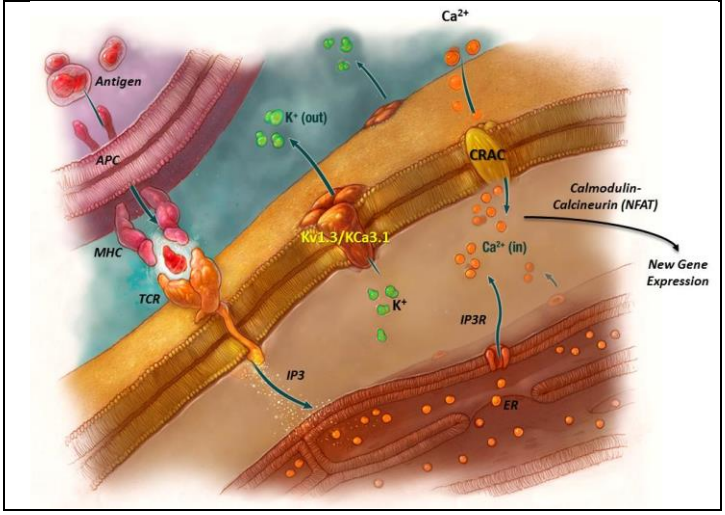
Autoimmune Platform Fact Sheet: Dalazatide, KPI-150, and KPI-190

Mechanism of Action – The Role of the Kv1.3 Channel

Kv1.3 Channel



Dalazatide, KPI-150, and KPI-190, are synthetic peptides that are derived from a molecule originally isolated from a sea anemone. Each of these peptides is a specific and potent inhibitor of the Kv1.3 potassium channel. The Kv1.3 channel is an exceptional target for treating autoimmune diseases and has been an active target of drug development for years. Kv1.3 expression is selectively upregulated on activated effector memory T cells (T_{EM}), which are major mediators of autoimmune disease. Other activated T cells (which are needed for normal immune function) upregulate expression of a different potassium channel, making them insensitive to these novel peptides. This allows these compounds to selectively inhibit the mediators of inflammation in autoimmune disease, while leaving the rest of the immune system intact. This differentiates our compounds from traditional T cell blocking therapies that have a generally immunosuppressive effect.

These Kv1.3 compounds have a novel mechanism of action that is specific to the disease mechanism and doesn't adversely affect the patient's overall immune function.

Demonstrated Proof of Concept in Well Established Models

These peptides, including dalazatide, are novel first-in-class Kv1.3 inhibitors that have demonstrated broad autoimmune activity and safety in numerous *in vivo* models including those for:

- Psoriasis
- Psoriatic Arthritis
- Lupus Nephritis
- Vasculitis
- Multiple Sclerosis
- Uveitis
- Atopic Dermatitis
- Asthma

In each of these models, treatment with dalazatide improved or prevented deterioration in clinical scores, reduced inflammation and improved histological outcomes.

Successful Nonclinical Development Program

The nonclinical development program for dalazatide followed ICH S6 Guidance and included safety pharmacology and toxicology program conducted with chronic toxicology studies of 6 months duration. Dalazatide was well tolerated with no overt toxicity (the no-observed-adverse-effect-level (NOAEL) in chronic studies was at least 17-fold greater than the anticipated maximum therapeutic dose of the drug).

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Proof of Concept Demonstrated in Phase 1 Clinical Trials

Dalazatide has been evaluated in both single and multiple ascending dose safety and tolerability studies and was well tolerated over a range of doses that provide therapeutic levels of the product. A proof-of-concept Phase 1b clinical trial in patients with active plaque psoriasis has also been completed where dalazatide demonstrated:

- Safety and tolerability
- Clinical benefit
- Validation of the PK/PD model
- Establishment of relevant biomarkers of drug activity

Dalazatide

Dalazatide is in initial development in myositis (dermatomyositis and inclusion-body myositis) as well as lupus with a particular focus on dermatological lupus known as cutaneous lupus.

Myositis is an autoimmune disease involving the inflammation of muscle. Diseases such as dermatomyositis (DM) also involve the skin. This disease is associated with skin rash and weakening muscles. The muscle weakness in DM generally begins with muscles of the neck, hip, back, and shoulders. Muscle weakness is frequently progressive and the weakness and pain associated with the disease worsen over time. Vasculitis (inflammation of the blood vessels) is also frequent in patients with DM. There are an estimated 70,000 patients in the US with myositis.

Cutaneous Lupus Erythematosus (CLE) occurs in about 2/3 of lupus patients. This skin disease can cause rashes, lesions, and pain. Most of these manifestations occur on sun-exposed areas of the body. The most typical form of acute CLE is a rash that occurs on the face and resembles sunburn. CLE also presents as red scaly skin, which can become discolored. There are an estimated 270,000 patients in the US with lupus and CLE will be present in 70-80% of these patients over the course of the disease.

KPI-150

KPI-150 is a related peptide that also blocks the Kv1.3 channel. KPI is developing this agent as a topical cream for atopic dermatitis, psoriasis, and other dermatological complications associated with inflammatory diseases. Chronically activated T_{EM} cells in atopic dermatitis are the target of KPI-150. A robust safety database has already been established for these compounds.

KPI-190

KPI-190, a topically administered peptide, is being developed as an eye drop for use in several ocular diseases including uveitis and autoimmune dry eye syndrome (DES). Pathogenic T cells have been shown to play a role in autoimmune eye disease as T cell infiltration and cytokine and chemokine production lead to tissue damage in the eye. $Kv1.3^{HIGH}$ autoreactive T_{EM} cells have been identified in uveitis and DES making these conditions a good option for treatment with KPI-190. This compound has demonstrated proof of concept efficacy in models of anterior uveitis, and topically administered KPI-190 has good penetration into the anterior chamber. Uveitis is one of the leading causes of blindness in the US and remains a significant unmet need. DES affects over 13 million people a year in the US.

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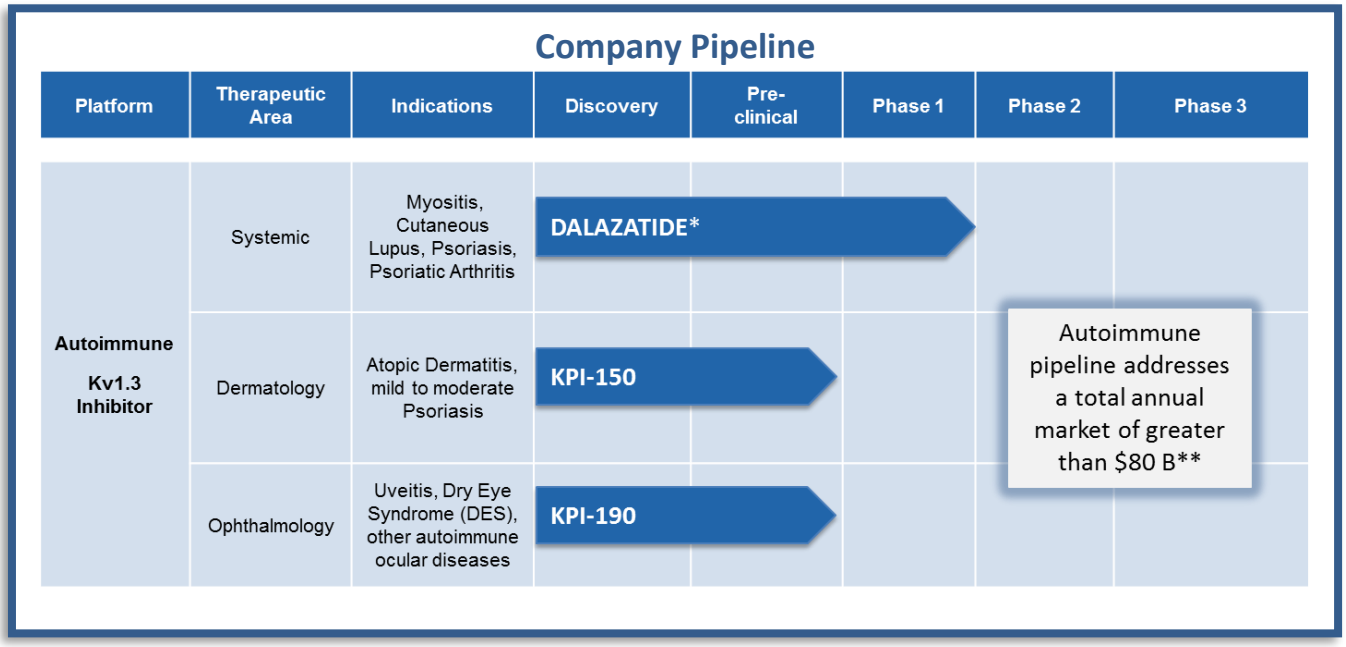
SUMMARY

KPI is developing three first-in-class drugs across our scientific platform. These programs include dalazatide for systemic autoimmune diseases such as lupus, KPI-150 for atopic dermatitis, KPI-190 for ocular diseases.



Please visit our website at KPITherapeutics.com for more information