

BTK degradation by bexobrutideg suppresses B cell activation and FcεRI-mediated degranulation in preclinical models of chronic spontaneous urticaria

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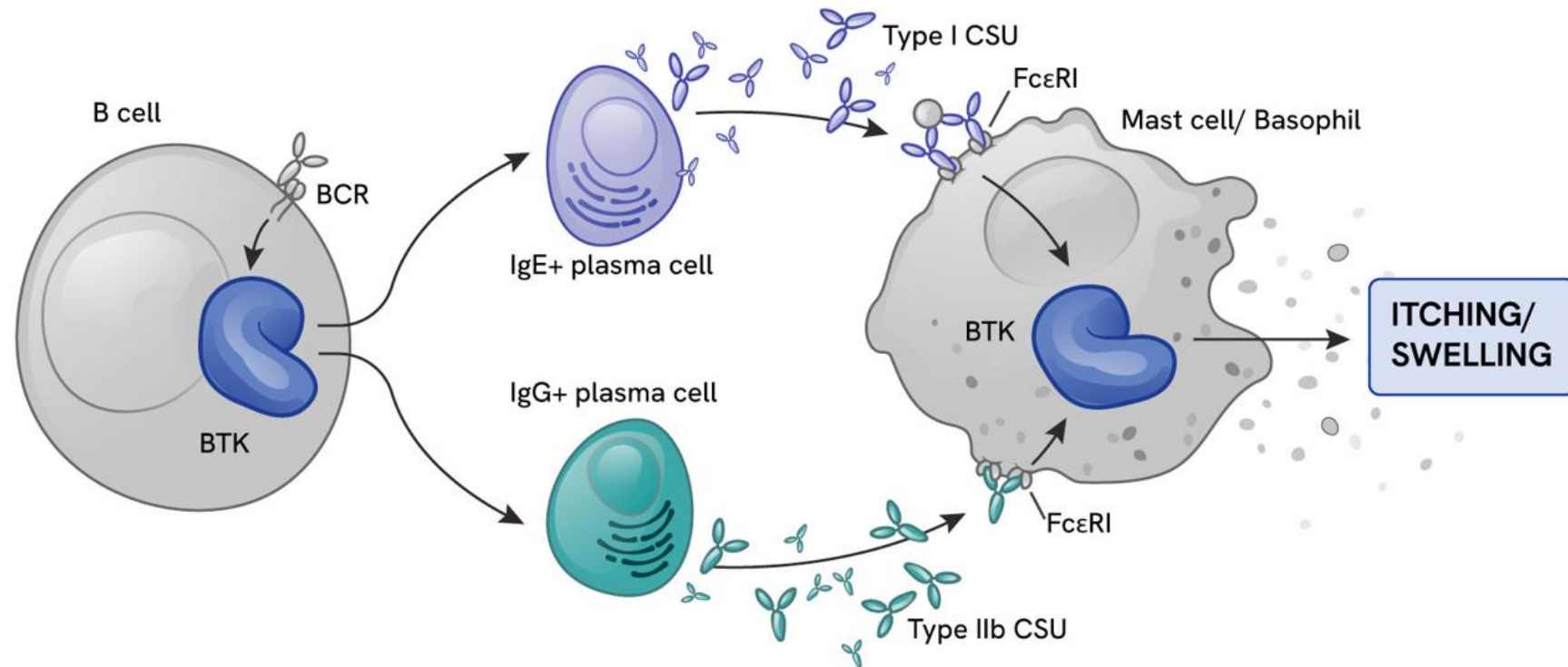
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BTK is a Clinically-Validated Target in Chronic Spontaneous Urticaria (CSU)

B cell activation and mast cell/basophil degranulation are BTK-dependent processes

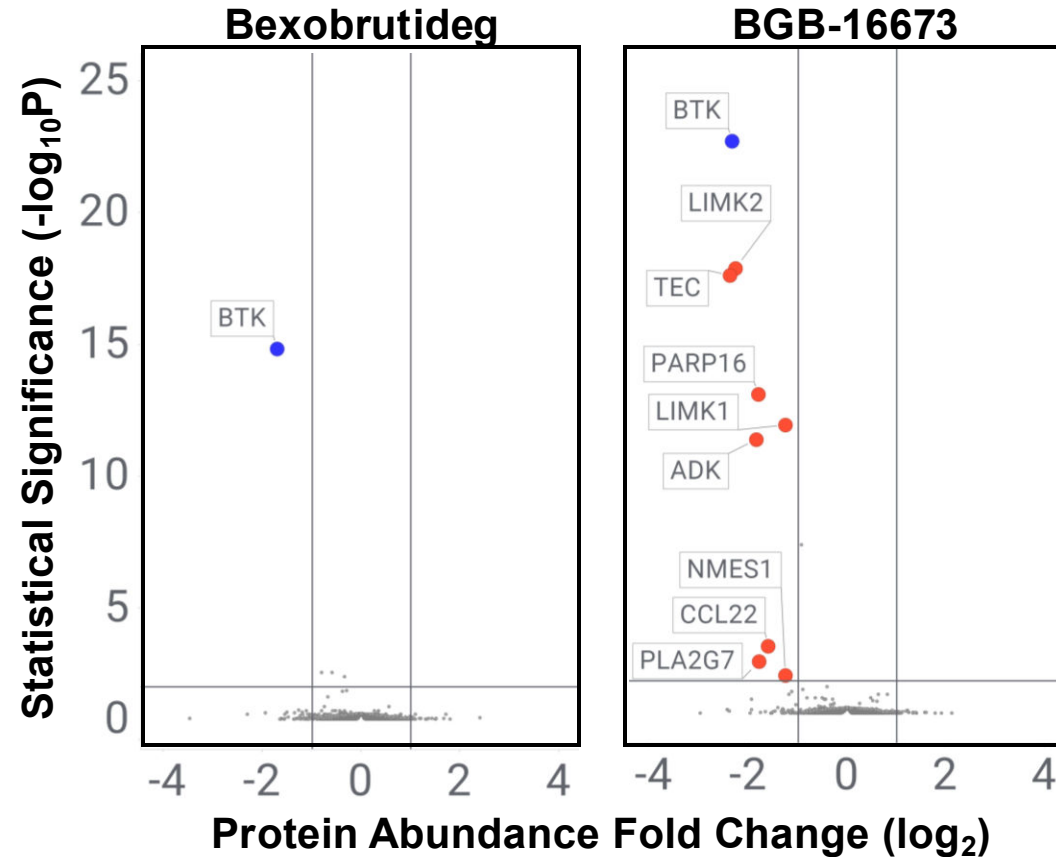
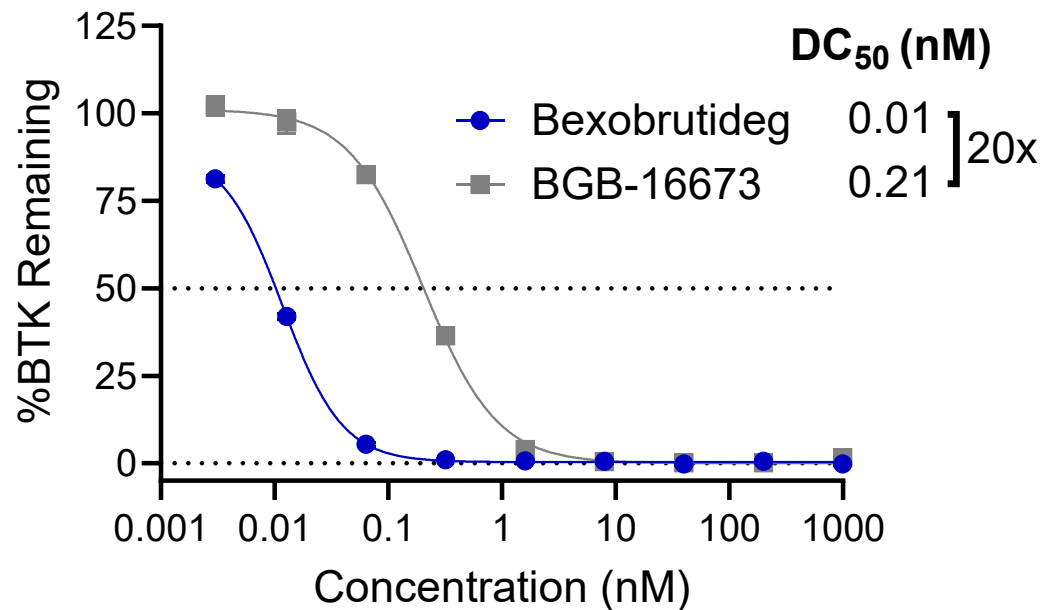


Can targeted degradation of BTK better suppress activation of pathways that contribute to the pathogenesis of CSU?

Bexobrutideg Displays Best-in-Class Potency and Selectivity

Selectivity of BTK Degraders by Global Proteomics

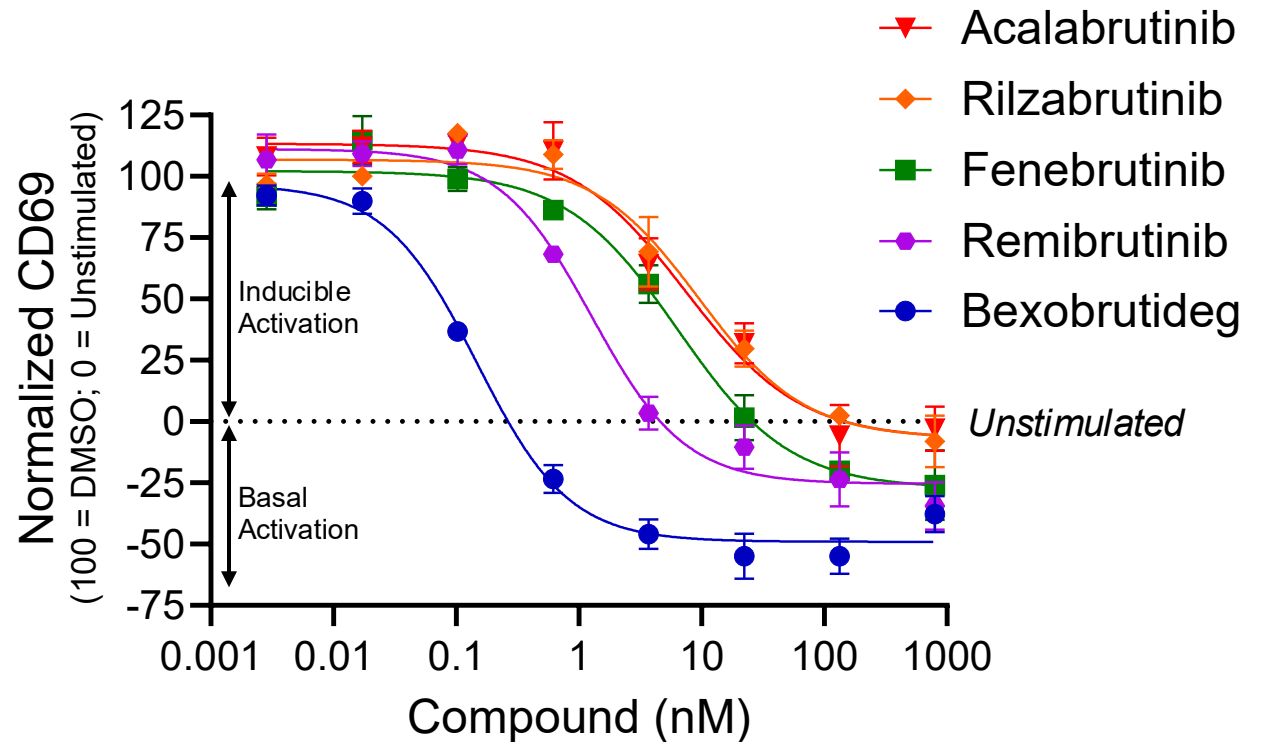
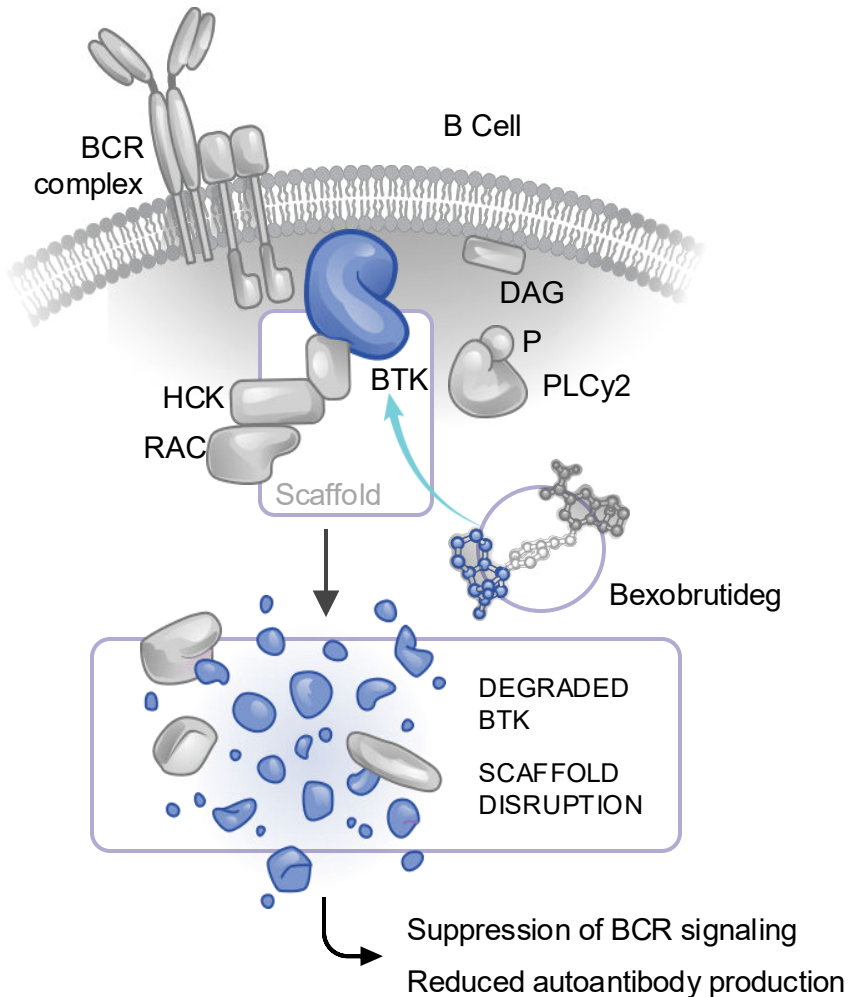
BTK Degradation in Human B Cells



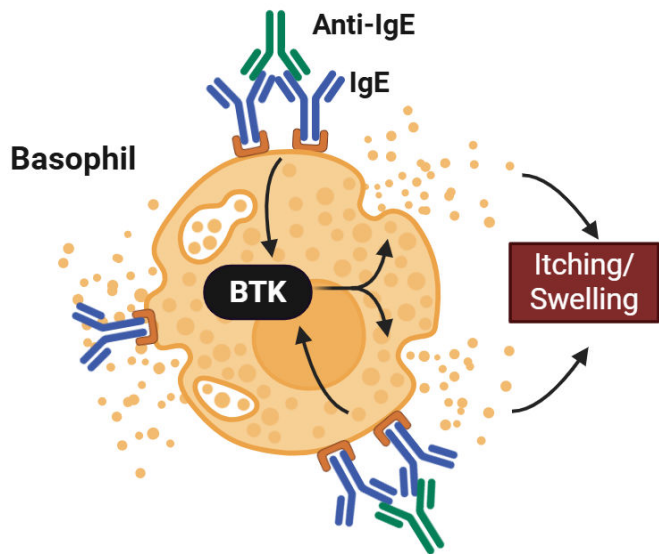
Bexobrutideg Achieves Potent and Deep Suppression of B Cell Activation

Preclinical studies show a BTK scaffold function downstream of particulate antigen stimulation

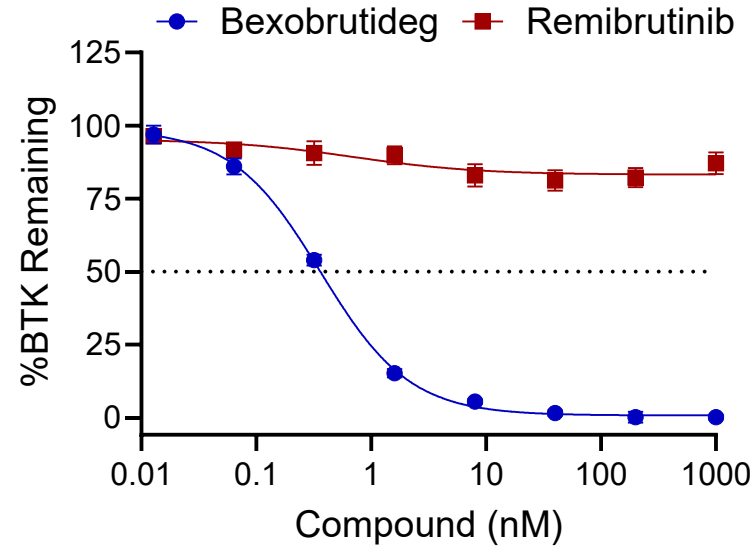
Suppression of B Cell Activation



Bexobrutideg Degrades BTK and Potently Suppresses FcεRI Signaling in Basophils



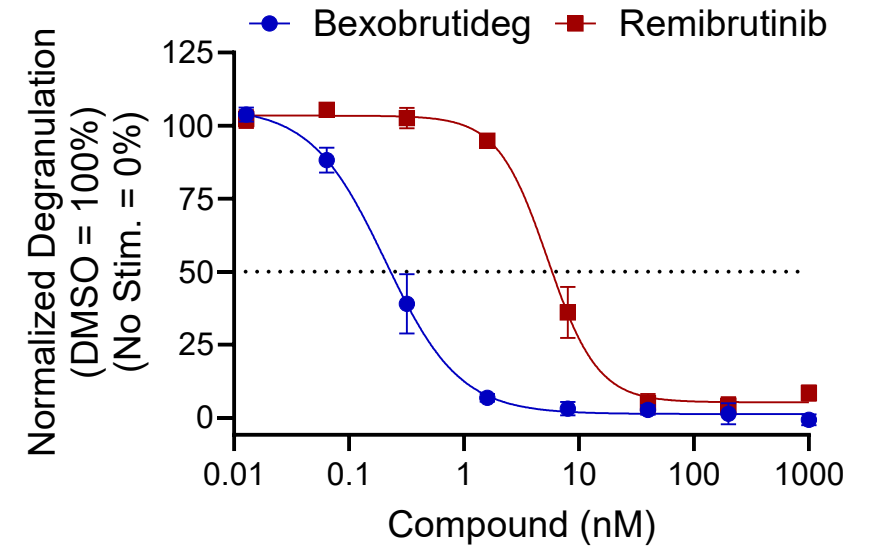
BTK Degradation in Basophils



	DC ₅₀ ± SEM (nM)
Bexobrutideg	0.18 ± 0.002
Remibrutinib	N/A

Assay performed in whole blood

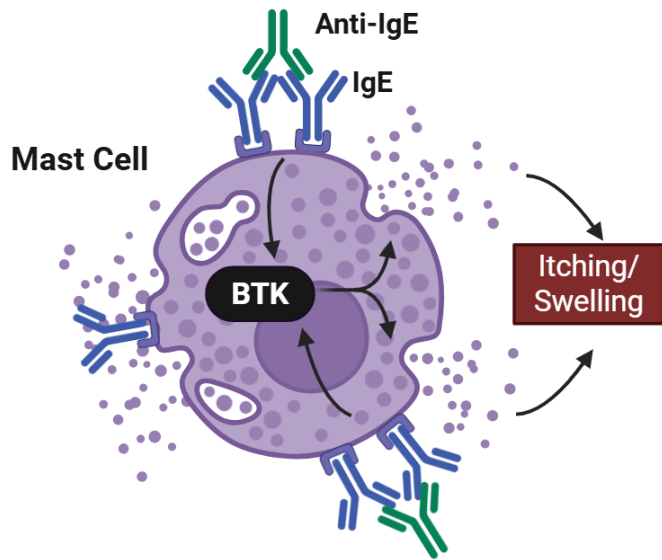
Basophil Degranulation (Anti-IgE Stimulation)



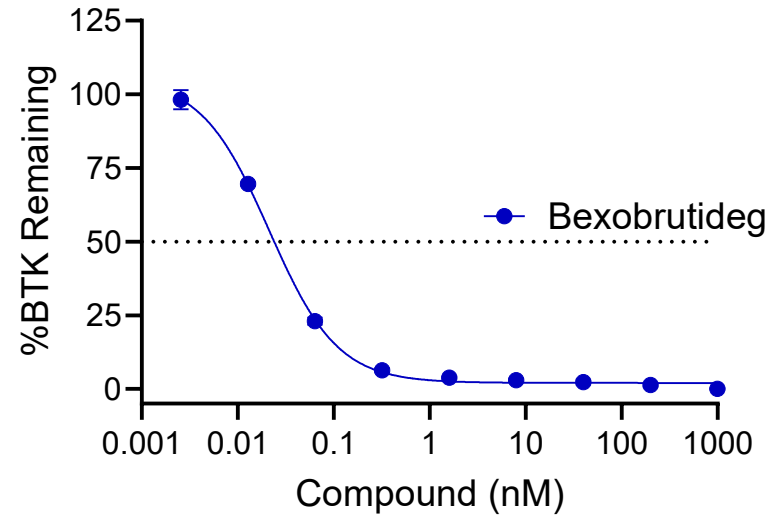
	IC ₅₀ ± SEM (nM)
Bexobrutideg	0.25 ± 0.07
Remibrutinib	6.4 ± 1

Assay performed in whole blood

Bexobrutideg Degrades BTK and Potently Suppresses FcεRI Signaling in Mast Cells



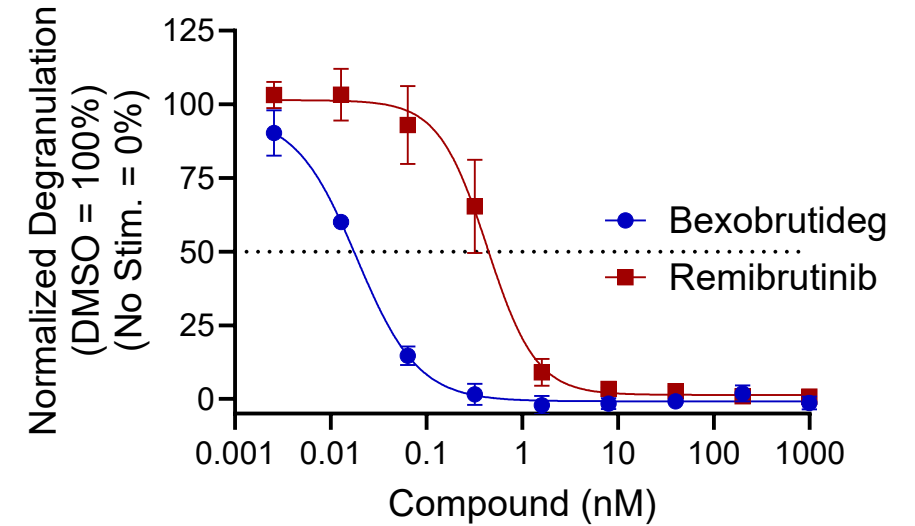
BTK Degradation in Mast Cells



	DC ₅₀ ± SEM (nM)
Bexobrutideg	0.02 ± 0.001

Assay performed in serum-free X-Vivo 15 media with IL-6 and SCF

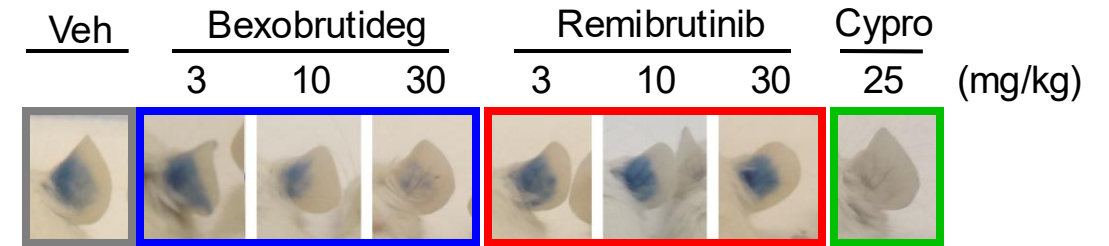
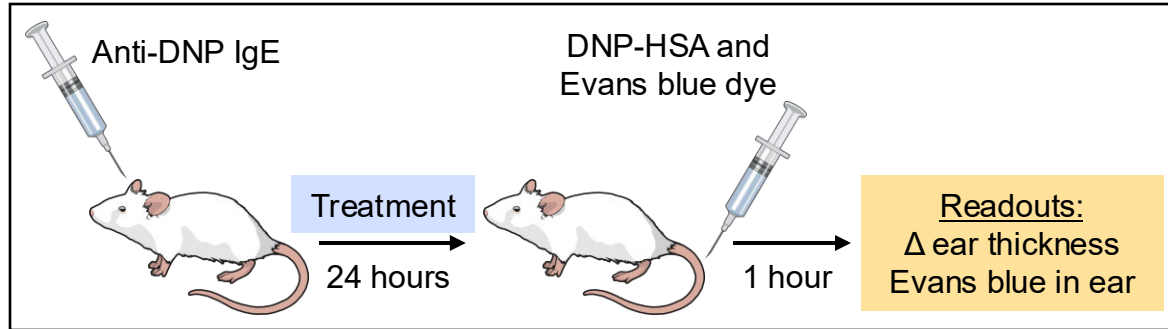
Mast Cell Degranulation (Anti-IgE Stimulation)



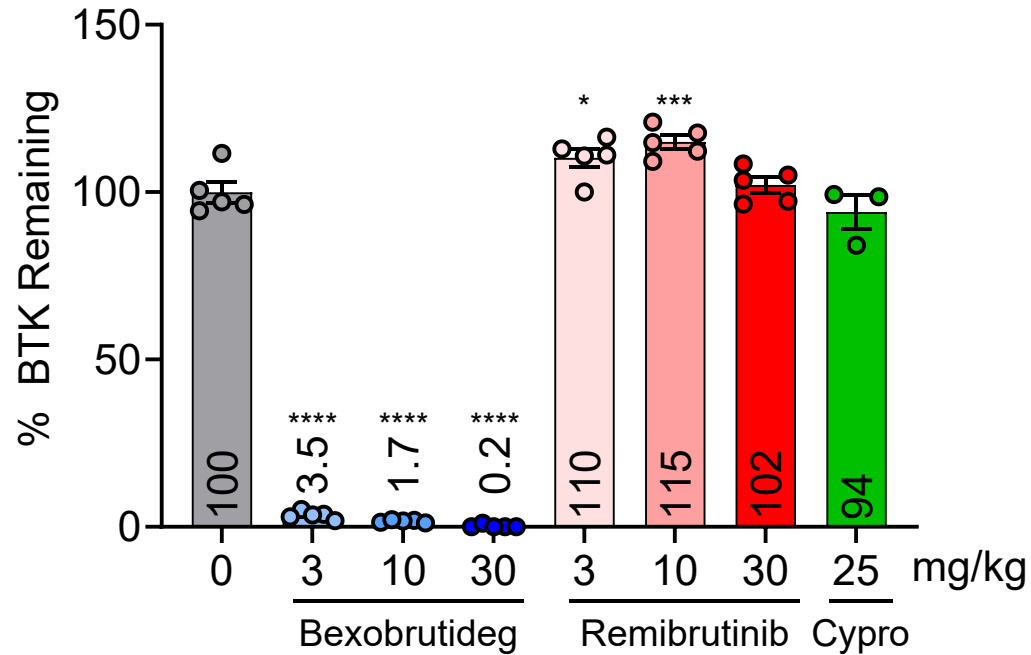
	IC ₅₀ ± SEM (nM)
Bexobrutideg	0.02 ± 0.0002
Remibrutinib	0.44 ± 0.2

Assay performed in serum-free X-Vivo 15 media with IL-6 and SCF

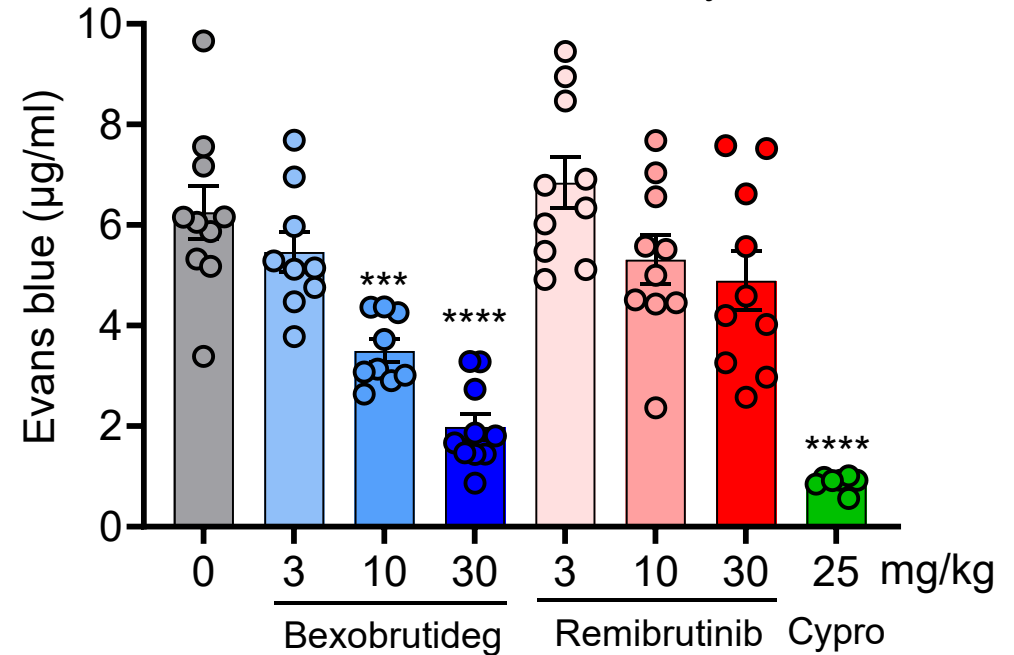
Bexobrutideg Degrades BTK and Suppresses Vascular Permeability in Passive Cutaneous Anaphylaxis Model



Ear Skin BTK Levels



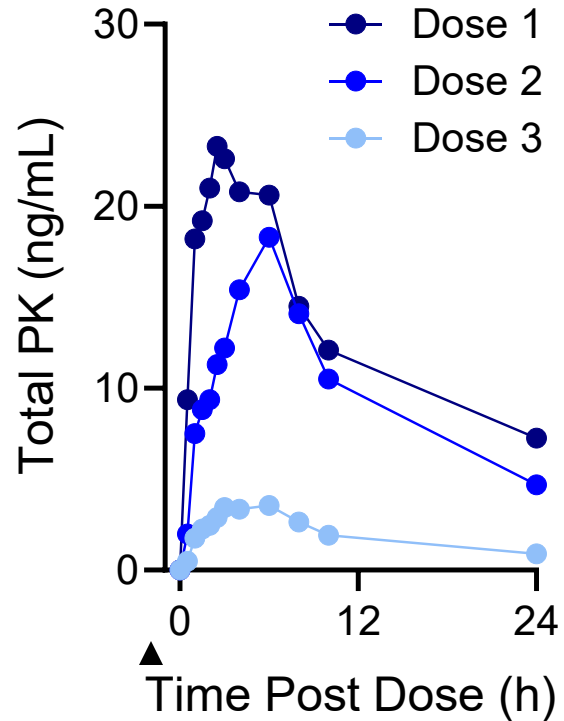
Vascular Permeability



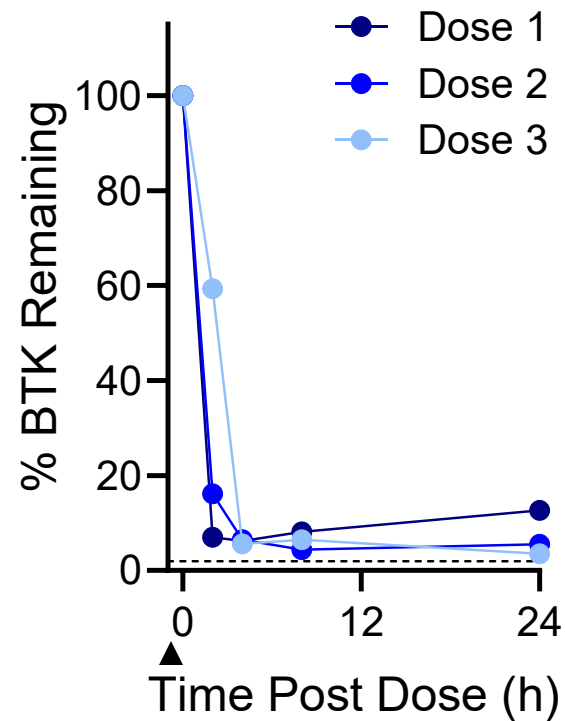
Bexobrutideg was administered orally two times on a QD schedule, remibrutinib was administered orally three times on a BID schedule. Cyproheptadine was administered intraperitoneally two times on a QD schedule. Final dose was administered 4 hours prior to antigen challenge, and dye extravasation was assessed 1 hour after antigen challenge. One animal from bexobrutideg 3 mg/kg group excluded due to excess antigen + Evans blue dosage during IV challenge. Data are represented as mean \pm SEM. * p < 0.05, ** p < 0.01, *** p < 0.001, **** p < 0.0001. One-way ANOVA, Dunnett's multiple comparison test vs. vehicle.

Bexobrutideg Demonstrates Deep BTK Degradation in PBMCs and Skin of Healthy Volunteers

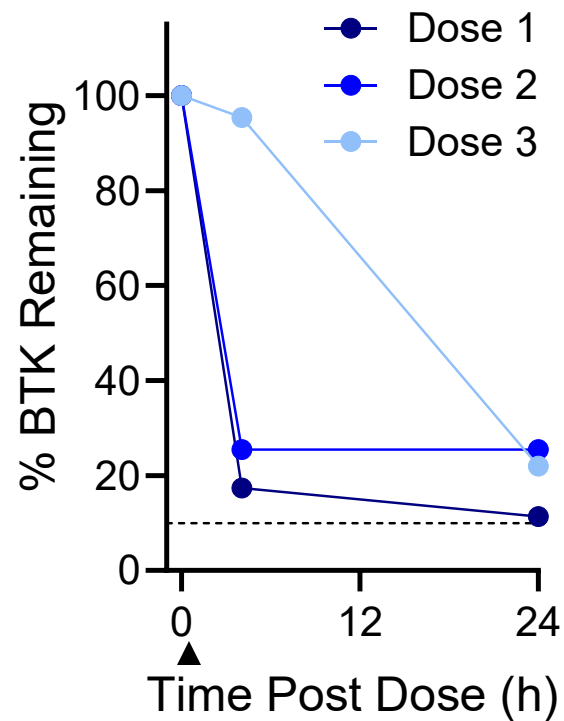
SAD Plasma PK



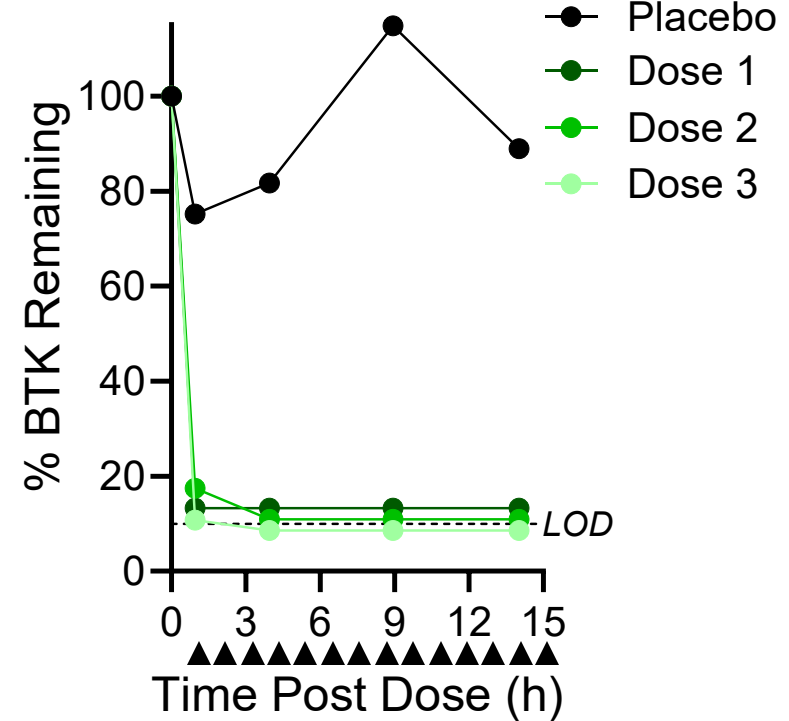
SAD BTK Degradation in PBMCs



SAD BTK Degradation in Skin



MAD BTK Degradation in Skin



Bexobrutideg was safe and well tolerated at all doses tested^a

▲
Dose

Data as of 07 May 2026

¹⁰ SAD, single ascending dose; MAD, multiple ascending dose; LC-MS, liquid chromatography–mass spectrometry; PBMCs, peripheral blood mononuclear cells. BTK was quantified by LC-MS, DNA-normalized, and expressed as % remaining relative to average baseline. Dashed lines indicate the approximate effective limit of detection after DNA normalization. Values below the assay lower limit were imputed as one-half the lower limit. Arrows indicate dose administration. ^aData not shown (NCT06717269)

Bexobrutideg: A Great Mechanistic Fit for CSU

Preclinical

- **Bexobrutideg** is a potent, selective BTK degrader
- Bexobrutideg demonstrates superior immune modulation vs. BTK inhibitors by providing deep **target coverage** and removing BTK **scaffold functions**
- Bexobrutideg achieves **strong efficacy** in CIA and PCA models

Translational

- **Bexobrutideg** achieves high plasma exposure and robust BTK degradation in PBMCs and skin

Clinical Safety

- **Bexobrutideg** is safe and well tolerated in healthy volunteers

Path Forward In CSU

- **Bexobrutideg** exhibits a safety, exposure, and PD profile that can **potentially confer advantages** over BTK inhibitors in CSU

