Clinical example: *gliadinase* for Celiac Disease
Licensed by UW as KumaMax to PVP Biologics for Celiac Disease Therapy with $35M financing by Takeda in Phase 1 Clinical Trial

**PROBLEM**

- **Gluten** in Wheat, Rye, Barley
- α-Gliadin protein in Gluten
- Unusually Proline-Glutamine (PQ) Rich
- PQ rich peptides from degradation of α-Gliadin
- Resistant to Proteolysis

**Auto-Immune Response**
- Inflammation
- Celiac disease

**SOLUTION**

- Start with Kumamolisin-As:
  - Works in the pH 2-4 range of gut
  - Resistant to digestive proteases

- Use Rosetta Design
  - To modify binding site to target PQ rich peptides

- Re-designed Protein removes PQ rich peptides

*Gordon et al., JACS, 2012.*