

# E3 ligand-linker conjugate collection: a promising tool for the discovery of protein degraders



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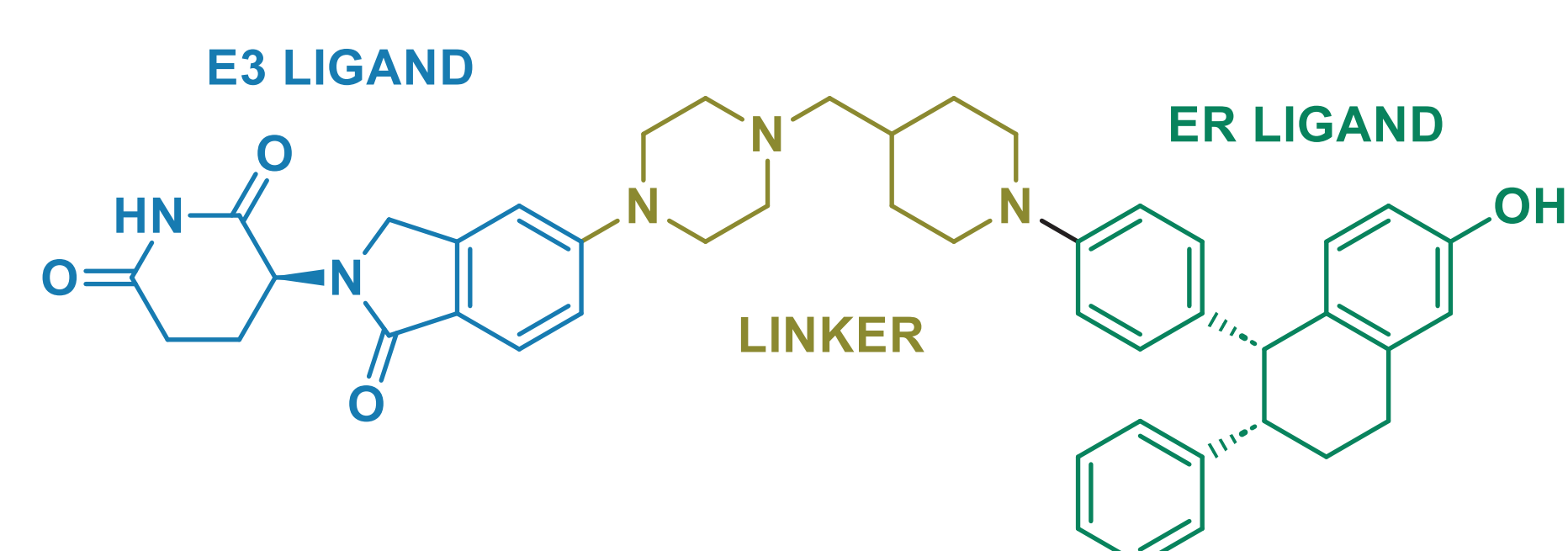
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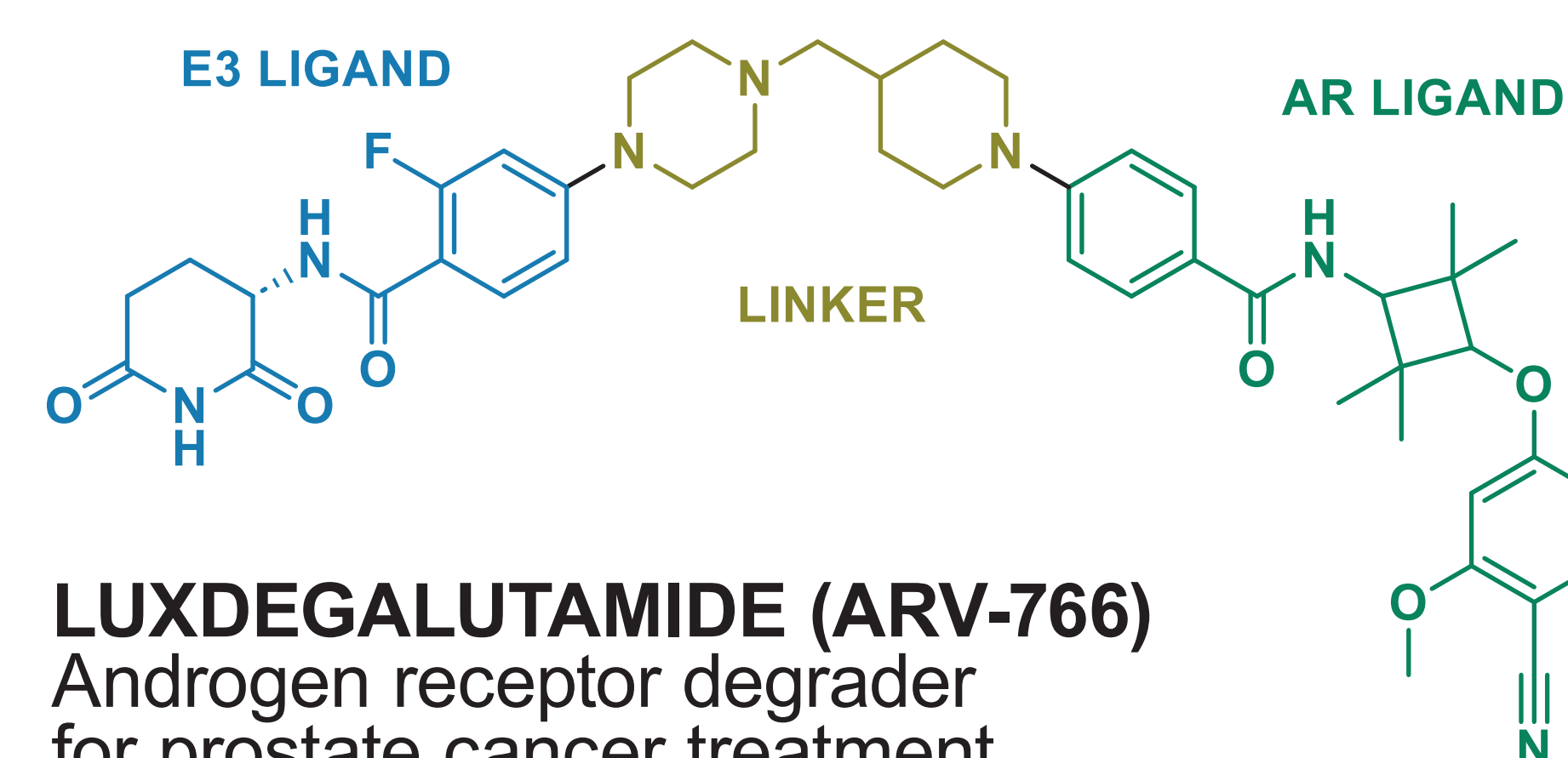
## Background of the project

Protein degradation is one of the most extensively studied areas in drug discovery, and it is about to deliver several promising compounds to the market (*Vepdegestrant* is in Phase III trials)



### VEPDEGESTRANT (ARV-471)

Estrogen receptor degrader for breast cancer treatment



### LUXDEGALUTAMIDE (ARV-766)

Androgen receptor degrader for prostate cancer treatment

- The key step of this technology involves ubiquitination of the target protein caused by its induced proximity to E3 ligase. To achieve this, a bifunctional molecule consisting of selective ligands for the protein of interest and an E3 ligase connected by an appropriate linker can be used
- To synthesize such conjugates efficiently, collections of E3 ligand-linker conjugates are very convenient since they can be applied to obtain potential degraders of various proteins in a parallel fashion

## E3 ligand collection (building blocks)

Over **500** in-stock building blocks with various synthetic handles:

- Cereblon-related products (a major part of the set);
- VHL ligands and intermediates;
- DCAF-focused ligands.

*We intend to increase uncommon chemotype representation (with further biological validation in progress)*

## Linker collection

Over **6,500** in stock, over **15,000** make-on-demand (MADE):

- Length: 3–20 bonds; 10x10 functional group combinations;
- Various linker types (e.g., spirocyclic, PEG, alkyne, etc.);
- Flexibility/restriction can be fine-tuned.

*A powerful tool for bioconjugate chemistry and design of various bifunctional molecules*

## Contact

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## E3 ligand-linker conjugate collection

- Over **400** representatives in stock
- **6 pre-plated kits:** amines, azides, carboxylic acids, alkynes; cereblon or VHL ligands
  - CRBN Amine kit-1 (96 cpds)
  - CRBN Azide kit-1 (28 cpds)
  - CRBN Amine kit-2 (35 cpds)
  - VHL Amine kit-1 (227 cpds)
  - CRBN Acid kit-1 (40 cpds)
  - VHL Alkyne kit-1 (61 cpds)
- Over **1.2 M** are readily accessible (over 75% synthesis success rate, 4–6 weeks)

