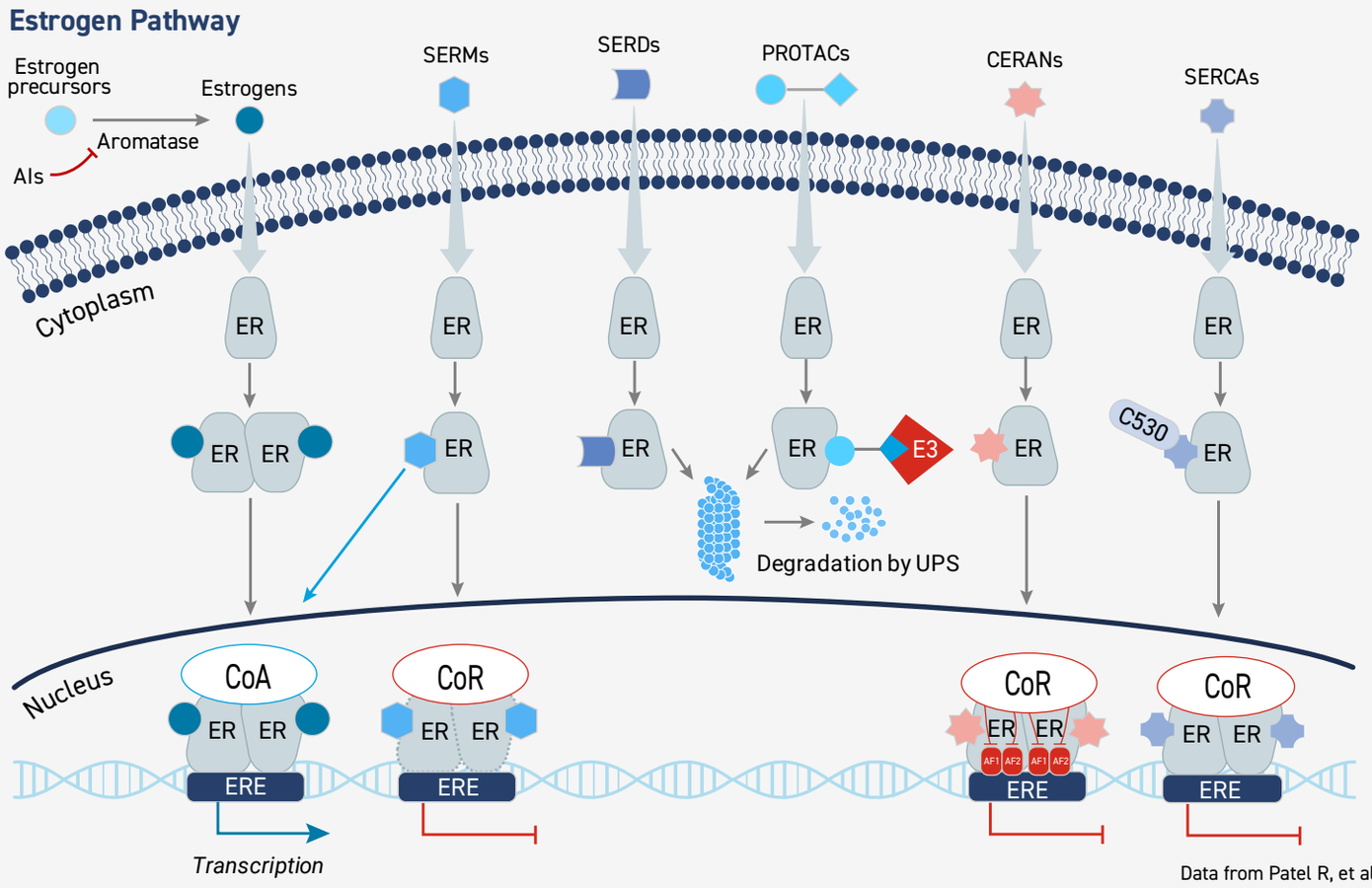
ER+, HER2-, Advanced Breast Cancer

Scientific advancements in ETs seek to maximize antagonizing the estrogen pathway in ER+, HER2-, ABC[1-3]



Data from Patel R, et al.[3]

Next-generation oral ETs are enabling more potent endocrine pathway antagonism while conferring alternative drug-like properties[1-3]

Exposure[1-3]

- Sustained high, dose-dependent exposure supporting oral options

Binding[1-3]

- Potent and highly specific binding to both wildtype and mutated ER
- Maintain activity in AI-resistant and *ESR1*-mutant models

Degradation[1-3]

- SERDs and PROTACs have potent ER degradation and suppression of ER-dependent signaling

Ongoing research is focused on optimizing therapeutic targeting of the ER pathway in ER+, HER2-, ABC[3]

ABC, advanced breast cancer; AI, aromatase inhibitor; CDK4/6i, cyclin dependent kinase 4/6 inhibitor; CERAN, complete estrogen receptor antagonist; CNS, central nervous system; CoA, coactivator; CoR, corepressor; ER, estrogen receptor; ER+, estrogen receptor positive; ERE, estrogen response element; *ESR1*, estrogen receptor 1 gene; ET, endocrine therapy; HER2-, human epidermal growth factor receptor 2 negative; PROTAC, proteolysis targeting chimera; SERCA, selective estrogen receptor covalent antagonist; SERD, selective estrogen receptor degrader; SERM, selective estrogen receptor modulator; UPS, ubiquitin-proteasome system.

1. Lloyd MR, et al. *Ther Adv Med Oncol.* 2022;14:17588359221113694. 2. Mittal A, et al. *Cancers (Basel).* 2023;15(7):2015. 3. Patel R, et al. *NPJ Breast Cancer.* 2023;9(20).