

RESEARCH MONOGRAPH . COMPOUND PROFILE

ABT-737

The non-orally bioavailable predecessor of navitoclax; a BH3-mimetic research compound for BCL-2/BCL-XL inhibition studies.

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COMPOUND CLASS	BCL-2 family inhibitor (research)

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ABSTRACT

ABT-737 (CAS 852808-04-9; molecular formula $C_{42}H_{45}ClN_6O_5S_2$; molecular weight 813.43) is a BH3-mimetic BCL-2/BCL-XL/BCL-W inhibitor developed at Abbott. The compound is the structural and pharmacological predecessor to navitoclax; navitoclax was developed by modifications introducing oral bioavailability while preserving the binding profile. Mechanism is identical to navitoclax: high-affinity binding to the BH3 groove of BCL-2 family anti-apoptotic proteins, releasing BAX and BAK to trigger mitochondrial apoptosis. The compound is not orally bioavailable and is administered intraperitoneally in animal studies. Senolytic activity has been demonstrated in multiple mouse models of senescence-associated disease. Used in academic research as a reference BH3 mimetic where oral delivery is unnecessary.

1. Compound Identification

ABT-737 is described as bcl-2 family inhibitor (research). The non-orally bioavailable predecessor of navitoclax; a BH3-mimetic research compound for BCL-2/BCL-XL inhibition studies.

1.1 Class summary

BCL-2 family inhibitor (research)

1.2 Subtitle

The non-orally bioavailable predecessor of navitoclax; a BH3-mimetic research compound for BCL-2/BCL-XL inhibition studies.

2. Abstract

ABT-737 (CAS 852808-04-9; molecular formula $C_{42}H_{45}ClN_6O_5S_2$; molecular weight 813.43) is a BH3-mimetic BCL-2/BCL-XL/BCL-W inhibitor developed at Abbott. The compound is the structural and pharmacological predecessor to navitoclax; navitoclax was developed by modifications introducing oral bioavailability while preserving the binding profile. Mechanism is identical to navitoclax: high-affinity binding to the BH3 groove of BCL-2 family anti-apoptotic proteins, releasing BAX and BAK to trigger mitochondrial apoptosis. The compound is not orally bioavailable and is administered intraperitoneally in animal studies. Senolytic activity has been demonstrated in multiple mouse models of senescence-associated disease. Used in academic research as a reference BH3 mimetic where oral delivery is unnecessary.

3. Mechanism of Action

BH3-mimetic BCL-2 family inhibitor (BCL-2, BCL-XL, BCL-W). Same target profile as navitoclax. Not orally bioavailable.

The mechanistic profile described above represents the consensus position from peer-reviewed literature where available; for compounds with sparse formal characterization, this section reflects vendor-grade reports and structurally-related class pharmacology and should be interpreted with appropriate caution.

4. Pharmacokinetics and Routes of Administration

Pharmacokinetic data are summarized within the abstract for compounds with formal Phase 1 records. Compounds without published human pharmacokinetic studies are noted as such; investigators should treat the absence of data as a research limitation.

5. Reported Research Dose Ranges

Mouse IP studies 25 to 100 mg/kg.

Doses are scaled from clinical use where the compound is approved as a medicine, from Phase 2/3 trials where development advanced, or from rodent dose-response data scaled by allometric assumptions where the compound has no human clinical record. Investigators should treat dose ranges from research-chemical-grade vendors as starting points for their own pharmacokinetic and tolerability characterization rather than validated dosing recommendations.

6. Sourcing and Quality Verification

Investigators should obtain analytical confirmation of identity (mass spectrometry; for peptides, additionally amino acid analysis or N-terminal sequencing) and purity (HPLC area-percent, ideally greater than 95 percent) on every lot. Vendor certificates of analysis vary in quality; third-party analytical confirmation through independent laboratories (e.g., Janoshik Analytical, Anabolic Lab) is the gold standard for research-grade peptides and small molecules.

For compounds with established pharmaceutical-grade marketing in any jurisdiction, sourcing from the marketed product (where legal and accessible) provides the highest quality assurance.

7. Reconstitution and Handling

Peptides should be reconstituted in bacteriostatic water or sterile water for injection in the volume appropriate to the desired concentration; lyophilized peptides should be allowed to come to room temperature before reconstitution to minimize precipitation. Reconstituted peptides should be stored refrigerated and used within the timeframe specified by the manufacturer (typically 14 to 30 days for bacteriostatic water reconstitutions, shorter for sterile water).

Small molecules: storage conditions vary by compound; consult the certificate of analysis for the specific product. Most are stable at room temperature in dry, dark conditions; oxidation-sensitive compounds (e.g., catecholamine precursors) require cool storage and protection from light.

8. Stack Interaction Considerations

Investigators combining this compound with other research substances should consider receptor-level interactions (additive effects at shared targets), enzyme-level interactions (CYP-mediated drug-drug interactions where applicable), and pharmacodynamic interactions (additive sedation, additive serotonergic activity, additive hemodynamic effects).

The stack interaction section in published monographs of well-characterized compounds is necessarily incomplete for any specific combination; investigators should treat novel combinations with elevated caution and titrate gradually.

9. References

1. Oltersdorf T, et al. An inhibitor of Bcl-2 family proteins induces regression of solid tumours. Nature 2005.
2. Yosef R, et al. Directed elimination of senescent cells by inhibition of BCL-W and BCL-XL. Nat Commun 2016.
3. Zhu Y, et al. New agents that target senescent cells: the flavone, fisetin, and the BCL-XL inhibitors, A1331852 and A1155463. Aging 2017.

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