Salarius PHARMACEUTICALS

SP-3164, a cereblon-binding molecular glue

5th Annual Targeted Protein Degradation Summit
October 26, 2022

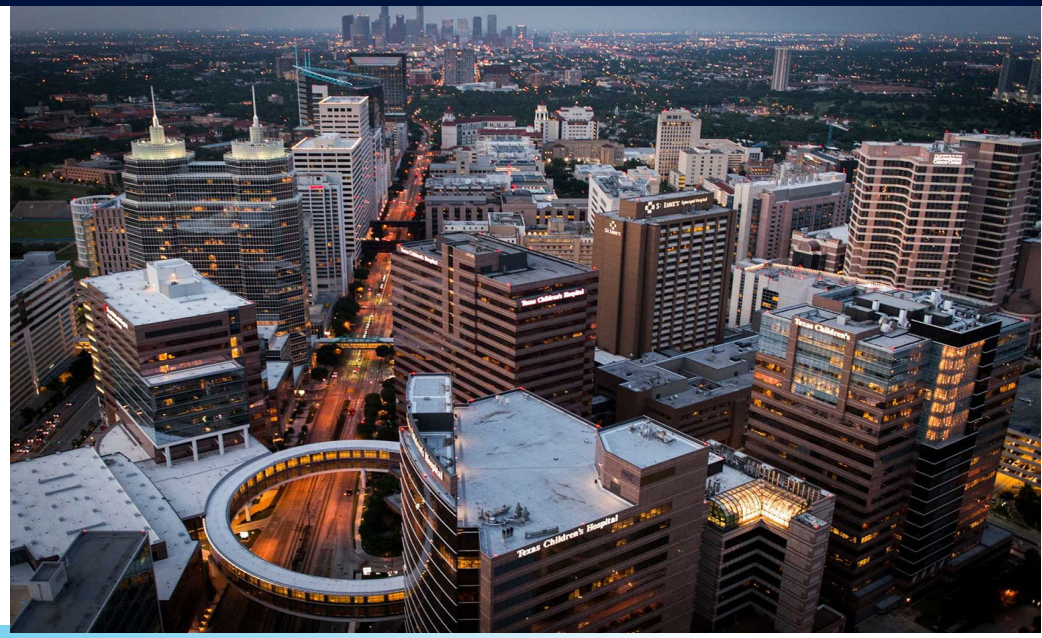
Safe Harbor Statement

This presentation contains “forward-looking statements” within the meaning of the Private Securities Litigation Reform Act of 1995. All statements, other than statements of historical facts, included in this presentation are forward-looking statements. These forward-looking statements may be identified by terms such as “will,” “future,” “believe,” “developing,” “expect,” “may,” “progress,” “potential,” “could,” “look forward,” “might,” “should,” and similar terms or expressions or the negative thereof. Examples of such statements include, but are not limited to, statements relating to the following: the advantages of seclidemstat (SP-2577) as a treatment for Ewing sarcoma, Ewing-related sarcomas, and other cancers and its ability to improve the life of patients; expected cohort readouts from the Company’s clinical trials and expected therapeutic options for SP-2577 and related effects and projected efficacy, including SP-2577’s ability to inhibit LSD1; the future of the company’s Phase 1/2 trial of seclidemstat as a treatment for Ewing sarcoma and FET-rearranged sarcomas following the SUSAR; the advantages of protein degraders including the value of SP-3164 as a cancer treatment; the timing of clinical trials for SP-3164 and expected therapeutic options for SP-3164 and related effects and projected efficacy; impact that the addition of new clinical sites will have on the development of our product candidates; the timing of our IND submissions to the U.S. Food and Drug Administration (FDA) and subsequent timing for initiating clinical trials; interim data related to our clinical trials, including the timing of when such data is available and made public; our growth strategy; whether the company will develop additional undisclosed cancer-fighting assets in the targeted protein degradation space; expanding the scope of our research and focus to high unmet need patient populations; and the commercial or market opportunity and expansion for each therapeutic option, including the availability and value of a pediatric priority review voucher for in-clinic treatments and potential for accelerated approval. We may not actually achieve the plans, carry out the intentions or meet the expectations or objectives disclosed in the forward-looking statements. You should not place undue reliance on these forward-looking statements. These statements are subject to risks and uncertainties which could cause actual results and performance to differ materially from those discussed in the forward-looking statements. These risks and uncertainties include, but are not limited to, the following: Seclidemstat’s impact in Ewing sarcoma and as a potential new and less-toxic treatment; expected dose escalation and dose expansion; the imposition of restrictions imposed by the FDA on the company’s Phase 1/2 trial of seclidemstat as a treatment for Ewing sarcoma and FET-rearranged sarcomas following the SUSAR, including a partial or full clinical hold; our ability to resume enrollment in the clinical trial following its review of the available data surrounding the SUSAR; the adequacy of our capital to support our future operations and our ability to successfully initiate and complete clinical trials and regulatory submissions; the ability of, and need for, us to raise additional capital to meet our business operational needs and to achieve its business objectives and strategy; future clinical trial results and the impact of such results on us; that the results of studies and clinical trials may not be predictive of future clinical trial results; risks related to the drug development and the regulatory approval process; the competitive landscape and other industry-related risks; and other risks described in our filings with the Securities and Exchange Commission, including its Annual Report on Form 10-K for the fiscal year ended December 31, 2021, as revised or supplemented by its Quarterly Reports on Form 10-Q and other documents filed with the SEC. The forward-looking statements contained in this presentation speak only as of the date of this presentation and are based on management’s assumptions and estimates as of such date. We disclaim any intent or obligation to update these forward-looking statements to reflect events or circumstances that exist after the date on which they were made.

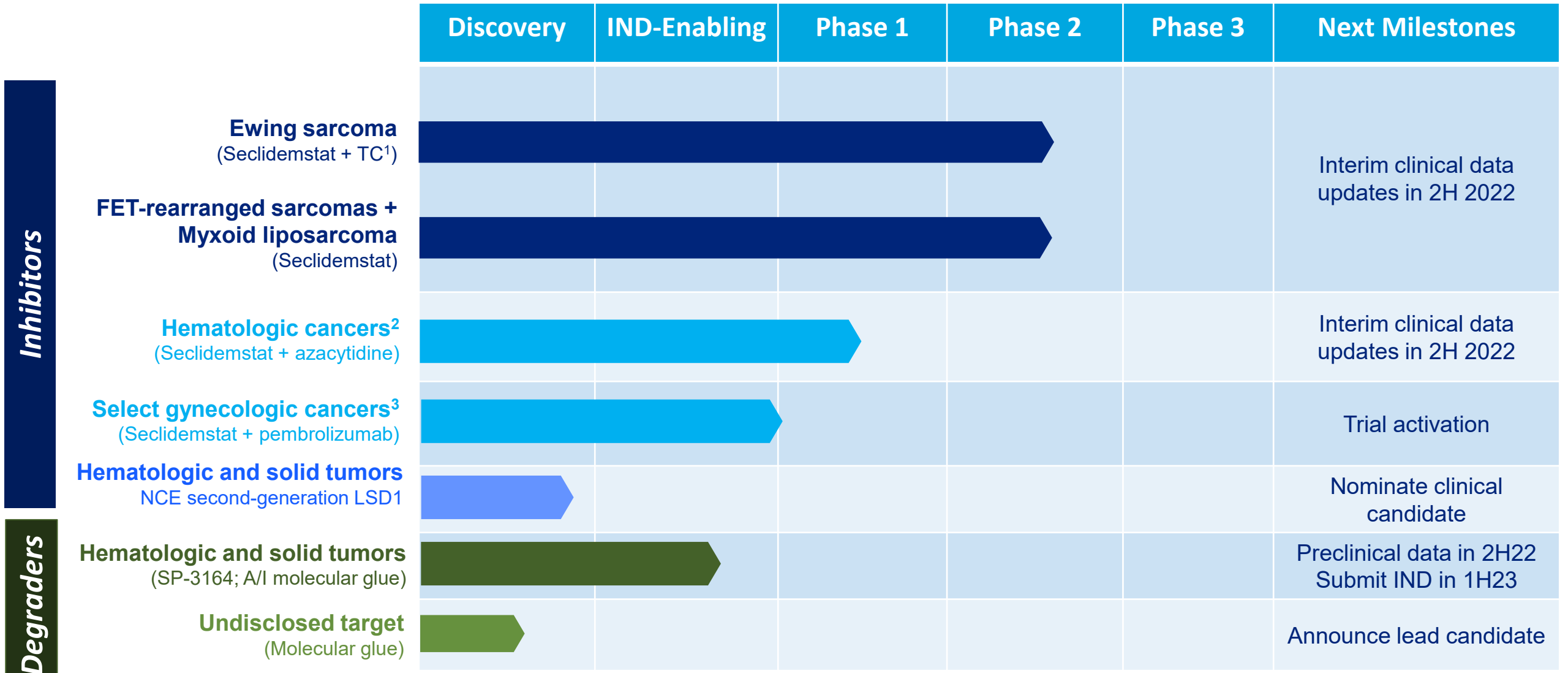
Salarius Pharmaceuticals, Inc.

- An oncology-focused biopharmaceutical company in Houston, TX
- 15 FTEs plus experienced consultants
  - Seasoned leadership team with Big Pharma and Biotech backgrounds

- Our mission is to develop novel therapies for patients who need them the most
  - Pipeline focused on agents that correct gene dysregulation

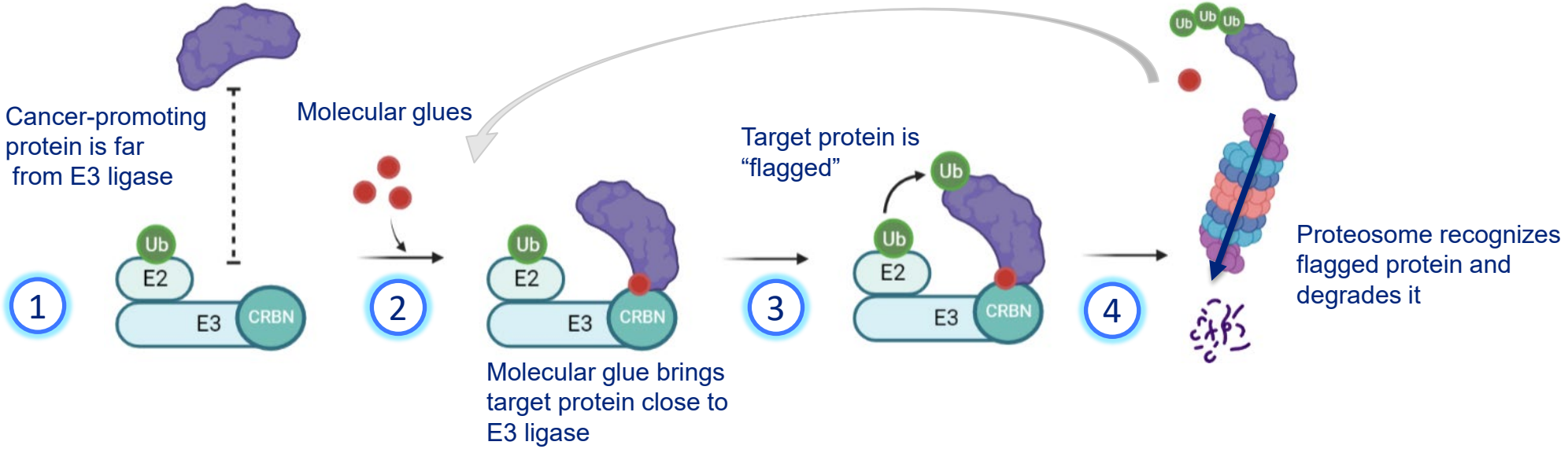


Pipeline Overview

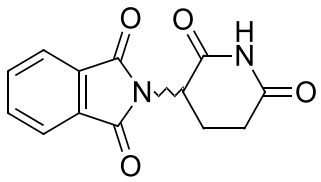


[1] Topotecan and cyclophosphamide [2] Investigator initiated trial active at MD Anderson Cancer Center treating patients with Myelodysplastic Syndromes and Chronic Myelomonocytic Leukemia [3] Investigator initiated trial – Clinical trial agreement not yet finalized.

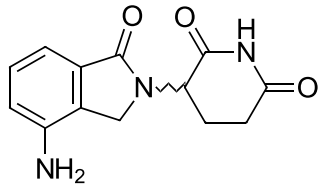
CRBN-Binding Molecular Glues Induce Proteasomal Degradation



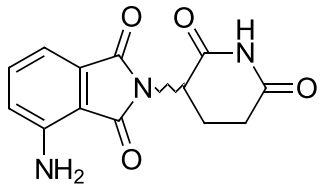
IMiDs® (Immunomodulatory Drugs) – Approved for hematological malignancies



Thalidomide



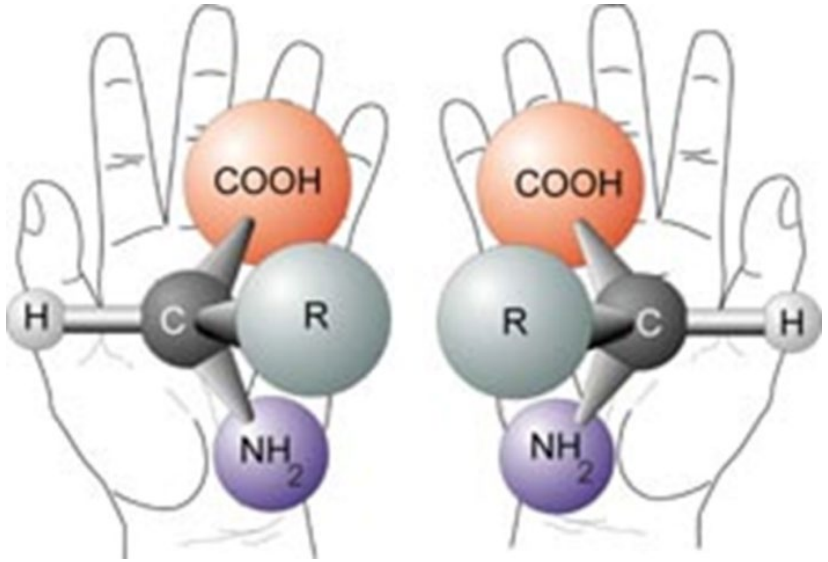
Lenalidomide



Pomalidomide

Chirality Occurs in Nature & Therapeutics

Left- or Right-Handedness Leads to Dramatic Differences



Hands & Chiral Compounds

non-superimposable mirror images (enantiomers)

Turpentine

***S**-Limonene*

Left-handed enantiomer

Orange Peel Oil

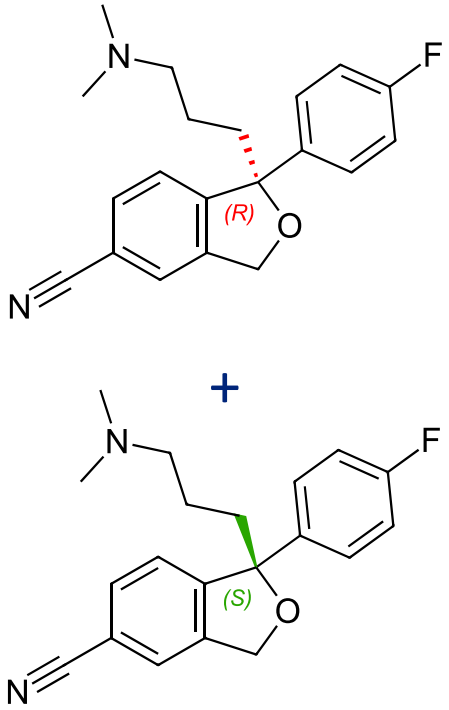
***R**-Limonene*

Right-handed enantiomer

Classic Chiral Switch Example: Celexa® ⇨ Lexapro®

Improved Drug Profile with the Single, Preferred Enantiomer

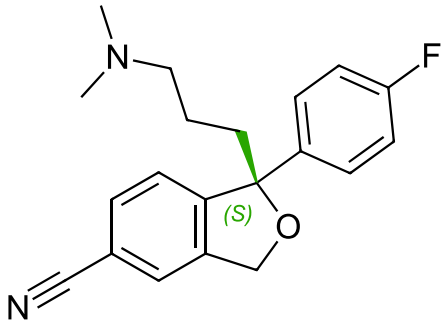
Applied since the 1990s for racemic drugs *with stable chiral centers*



CITALOPRAM
Racemate
Mixture of R & S enantiomers

Chiral Switch

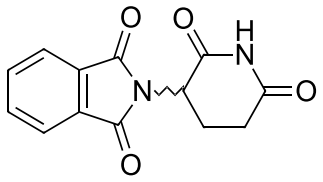
…from a mixture to the Best Drug!



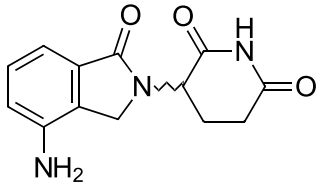
ESCITALOPRAM
S-enantiomer
Better efficacy

Some Racemic Drugs Cannot Undergo Chiral Switching

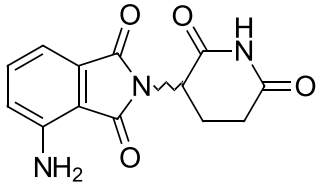
Because Two Enantiomers Interconvert Due to Unstable Chiral Centers



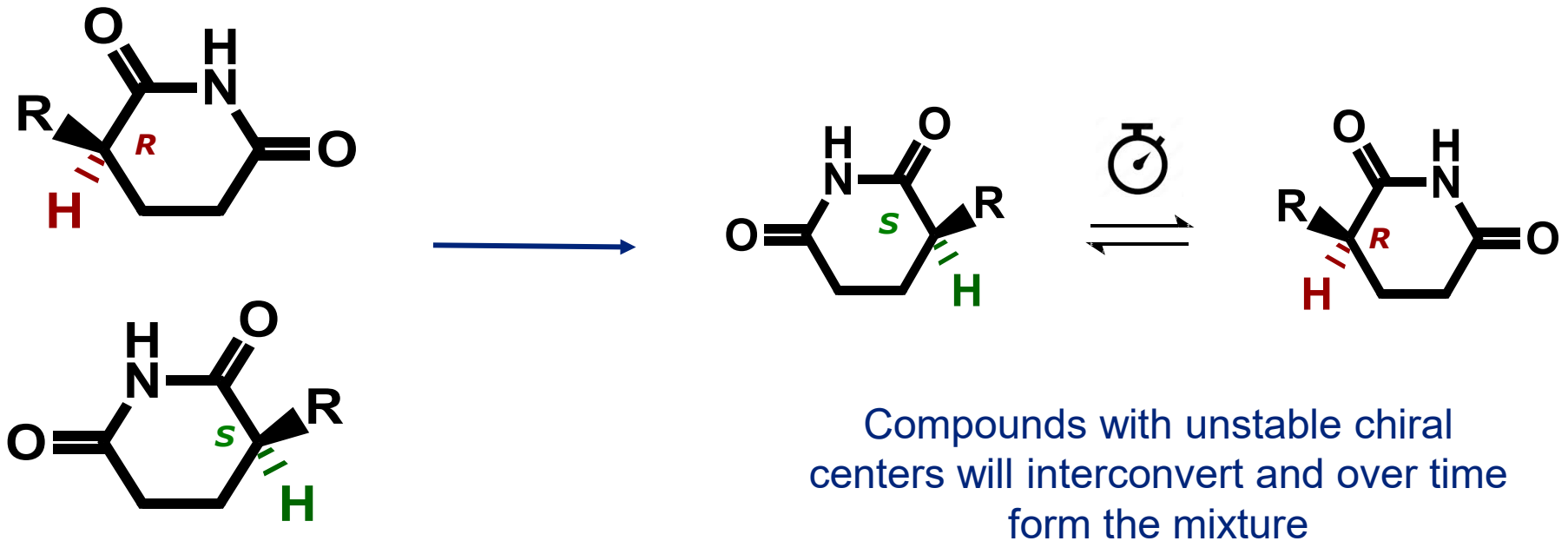
Thalidomide
Racemic



Lenalidomide
Racemic



Pomalidomide
Racemic

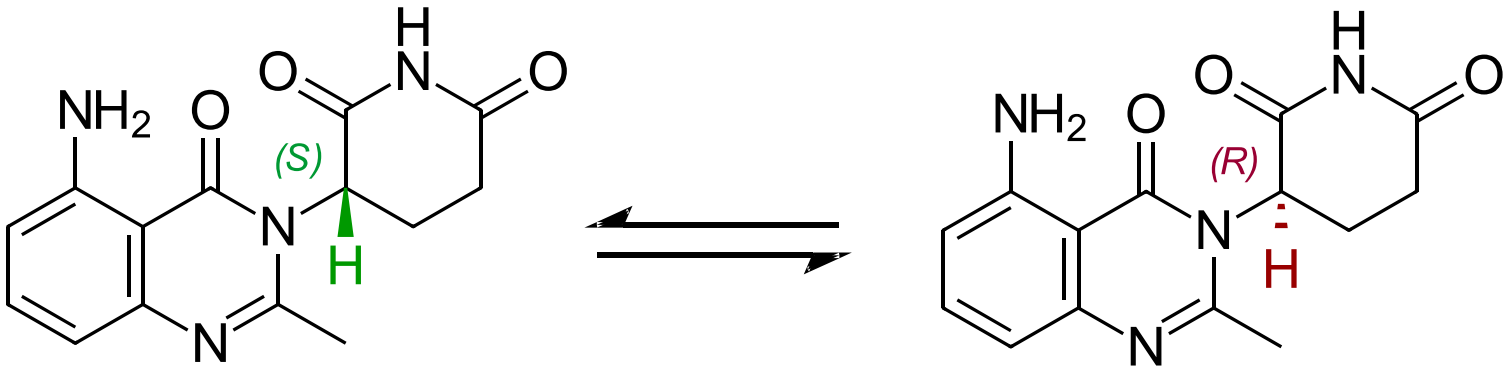


Compounds with unstable chiral centers will interconvert and over time form the mixture

*Representative chemical structure depicts glutarimide portion of thalidomide analogs

Avadomide, an Extensively Studied CELMoD®

Exists as a Mixture of 2 Enantiomers



S-enantiomer **R-enantiomer**

Avadomide (CC-122)

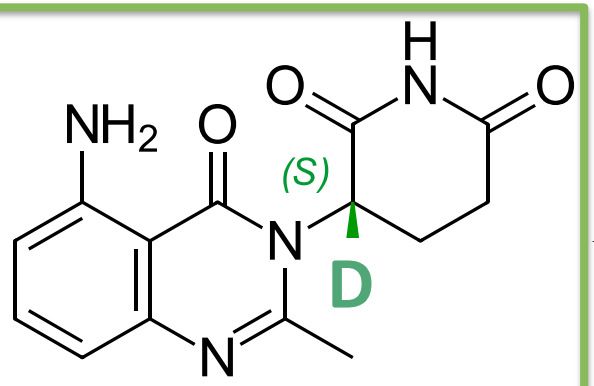
a 1:1 mixture of 2 interconverting enantiomers

✓ Studied in 10 clinical trials in >400 patients

CELMoD – Cereblon E3 Ligase Modulation Drugs, a registered trademark of Celgene / BMS

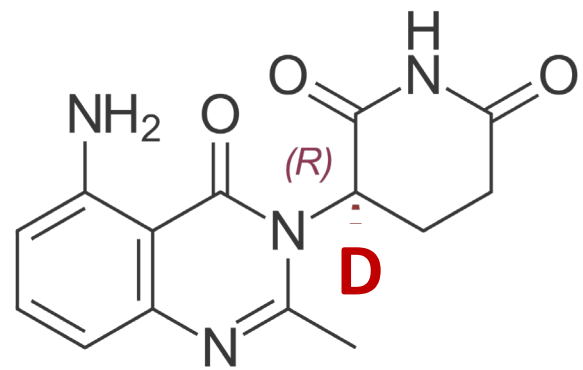
SP-3164: The Deuterium-Stabilized S-Enantiomer of Avadomide

- Stabilization of avadomide enantiomers with deuterium blocks interconversion



SP-3164
Deuterated S-avadomide

- ✓ Cereblon binder
- ✓ Anti-cancer activity
- ✓ Immune stimulation



SP-3165
Deuterated R-avadomide

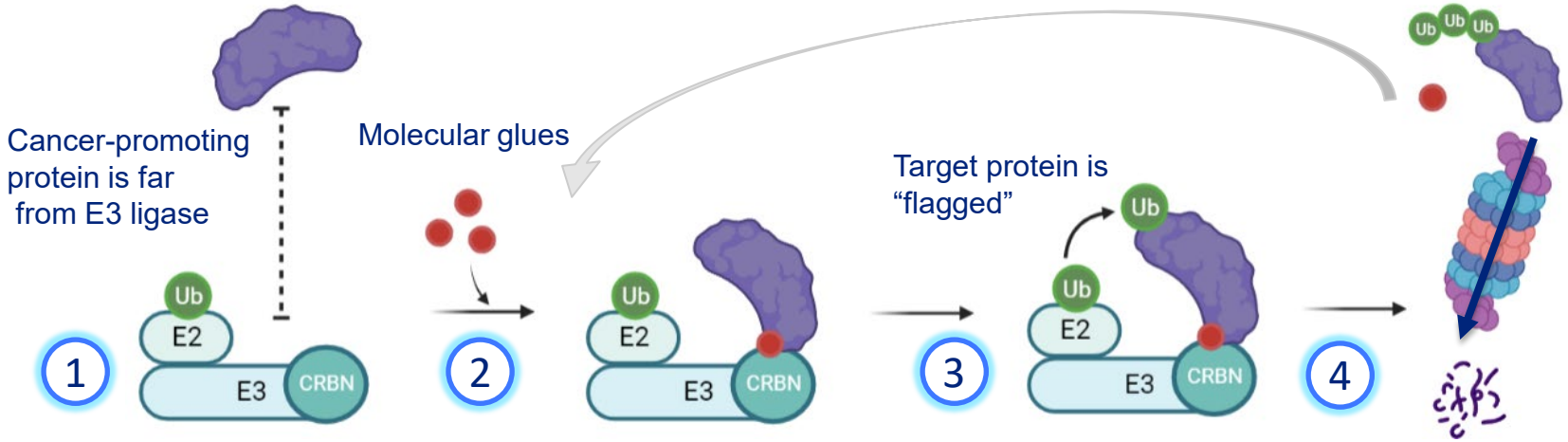
- Does not bind cereblon
- Minimal neosubstrate degradation
- *Potentially* supports tumor growth

- An NCE with its own, issued composition of matter patent
- Potential for **improved efficacy and safety compared to avadomide**

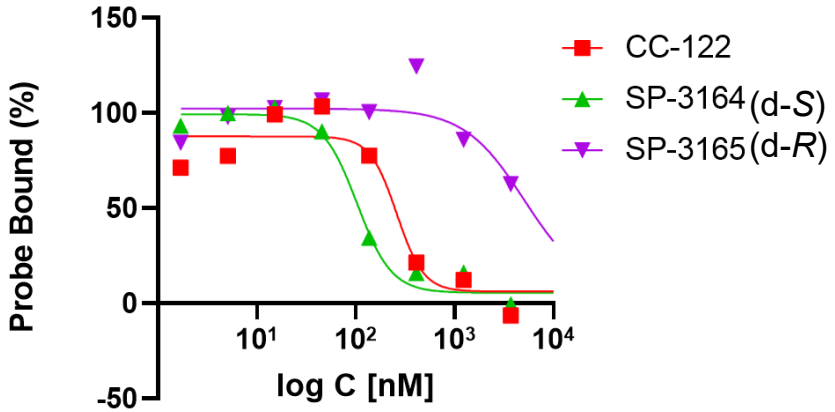
NCE: new chemical entity

SP-3164 Demonstrates Improved Protein Degradation

Characteristics Compared to Avadomide (CC-122)



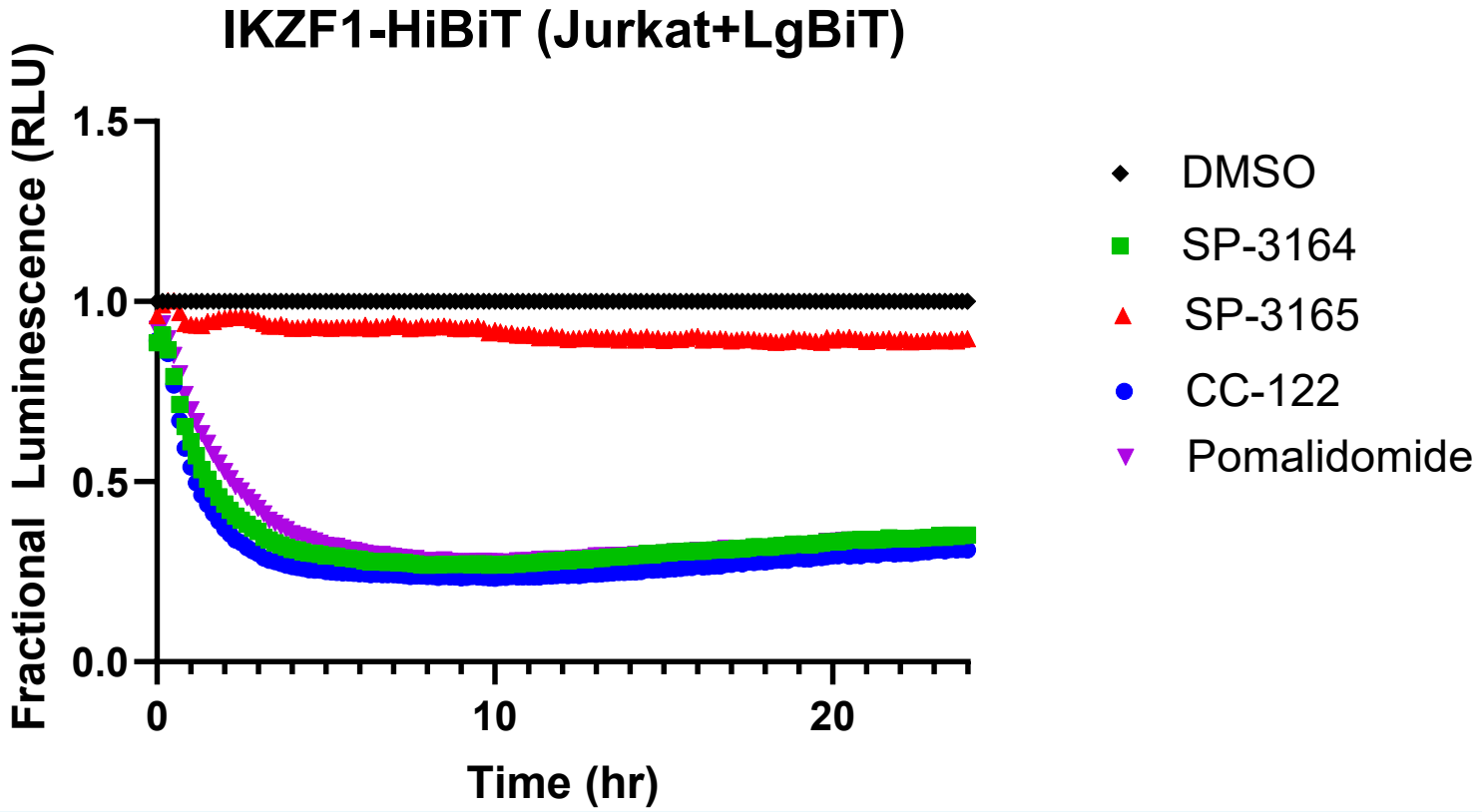
Cereblon Binding



Compound	Kd (nM)
CC-122	330
SP-3164 (d-S)	110
SP-3165 (d-R)	14000

SP-3164 binds more potently to cereblon than the racemate (avadomide, CC-122) while SP-3165 (d-R-enantiomer) does not bind at meaningful concentrations.

SP-3164 Rapidly Degrades IKZF1 (Ikaros)

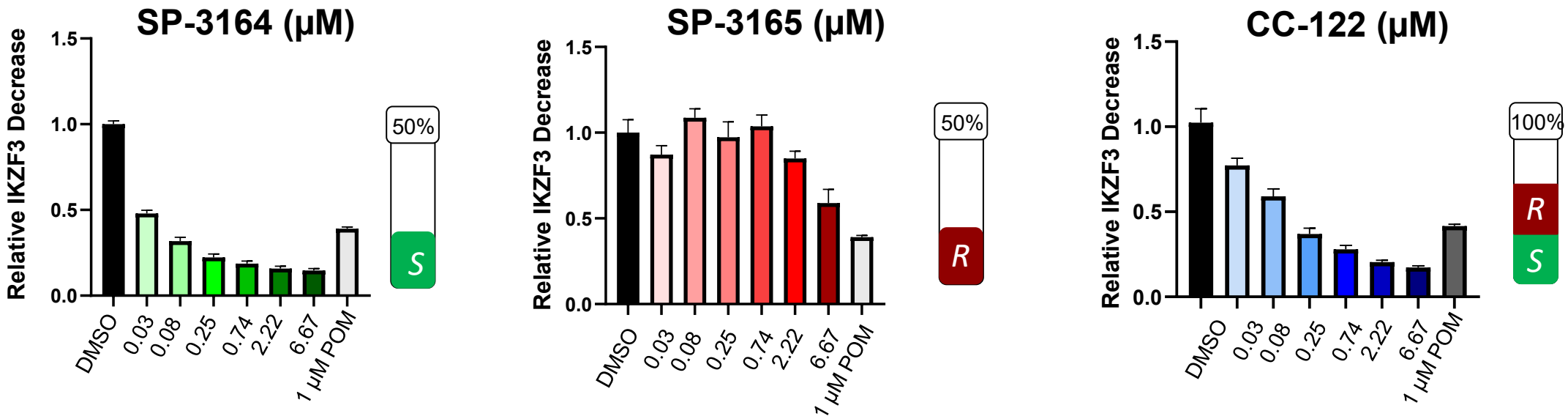


- SP-3164 has a similar Dmax to CC-122 (1 uM)
- SP-3165 does not cause any protein degradation

Performed at Promega

SP-3164 Rapidly Degrades IKZF3 (Aiolos) at Low Concentrations

HiBiT-IKZF3 MM.1S Degradation (2 hours)



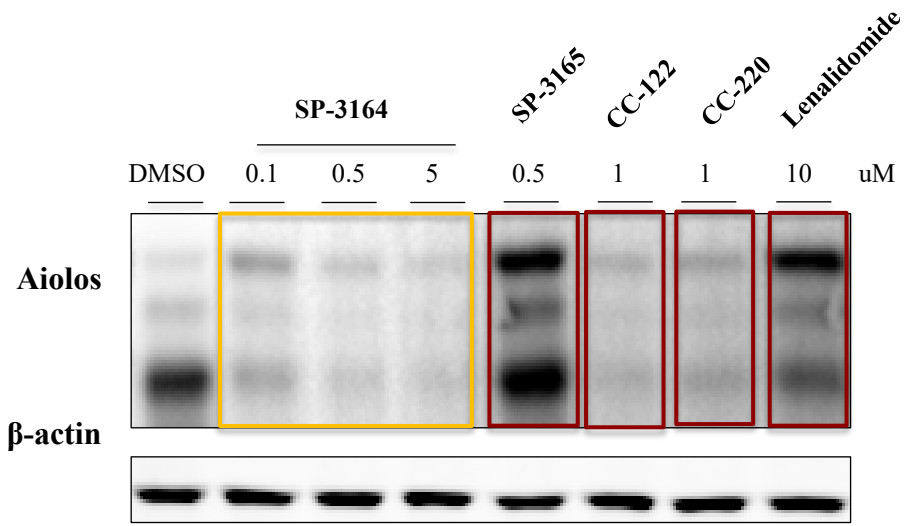
- Treatment with SP-3164 for 2 hrs results in deep and rapid degradation of the target protein, IKZF3.
- SP-3165 does not result in protein degradation except for at high concentrations.
- At comparable concentrations, SP-3164 induced more degradation of IKZF3 compared to CC-122

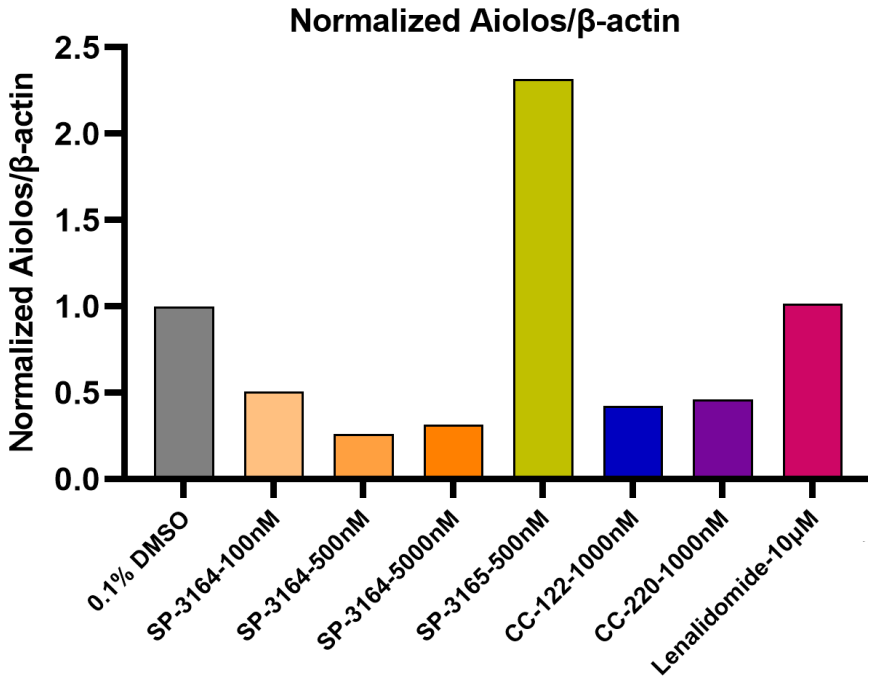
Performed at Promega

SP-3164 Exhibits Dose-Dependent Aiolos Degradation

Compounds studied in WSU-DLCL2 lymphoma cell line (6 hrs)

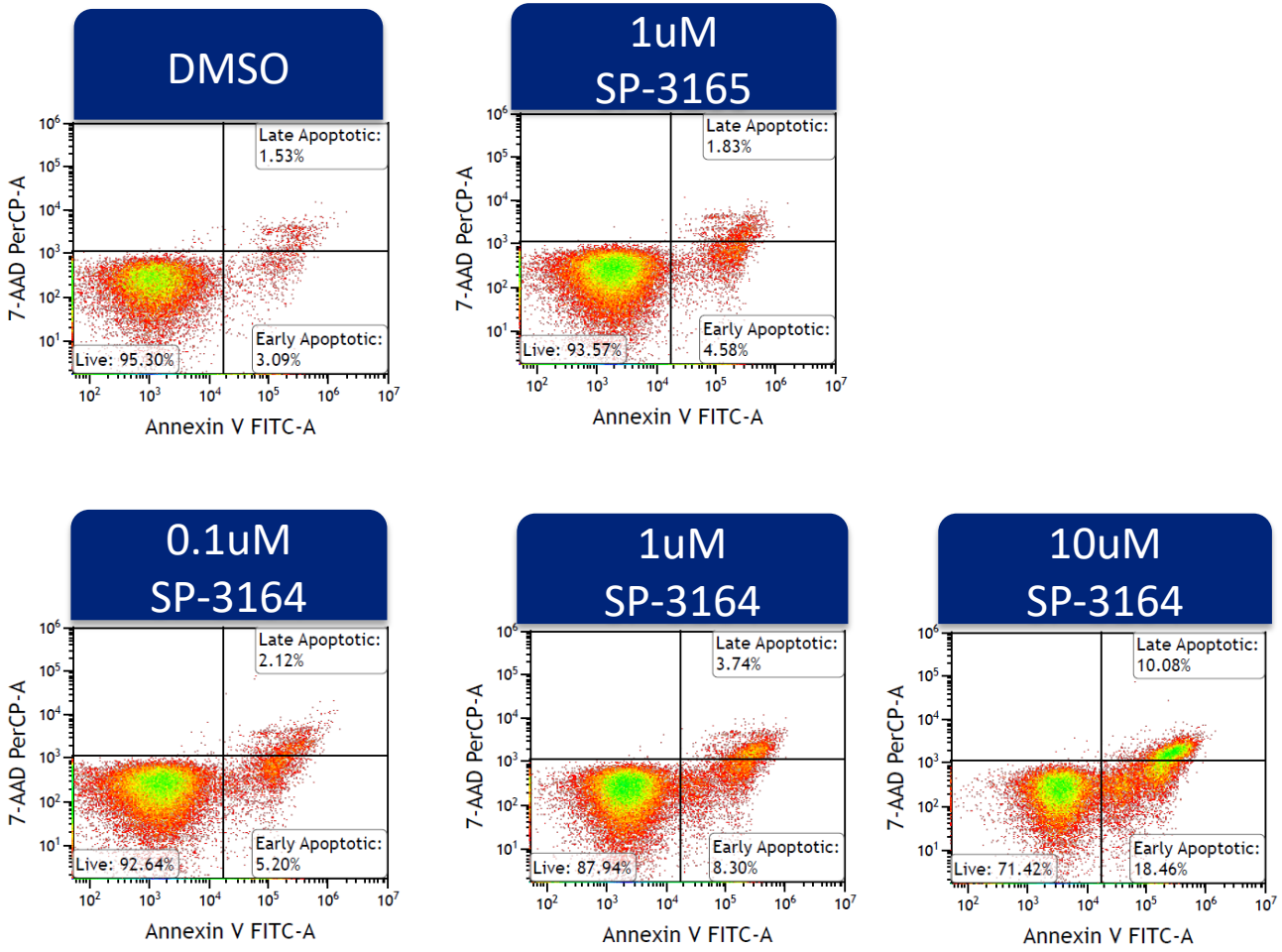
- SP-3164 (100, 500 nM and 5 uM)
- SP-3165 (500 nM)
- CC-122 (1 uM)
- CC-220 (1 uM)
- Len (10 uM)

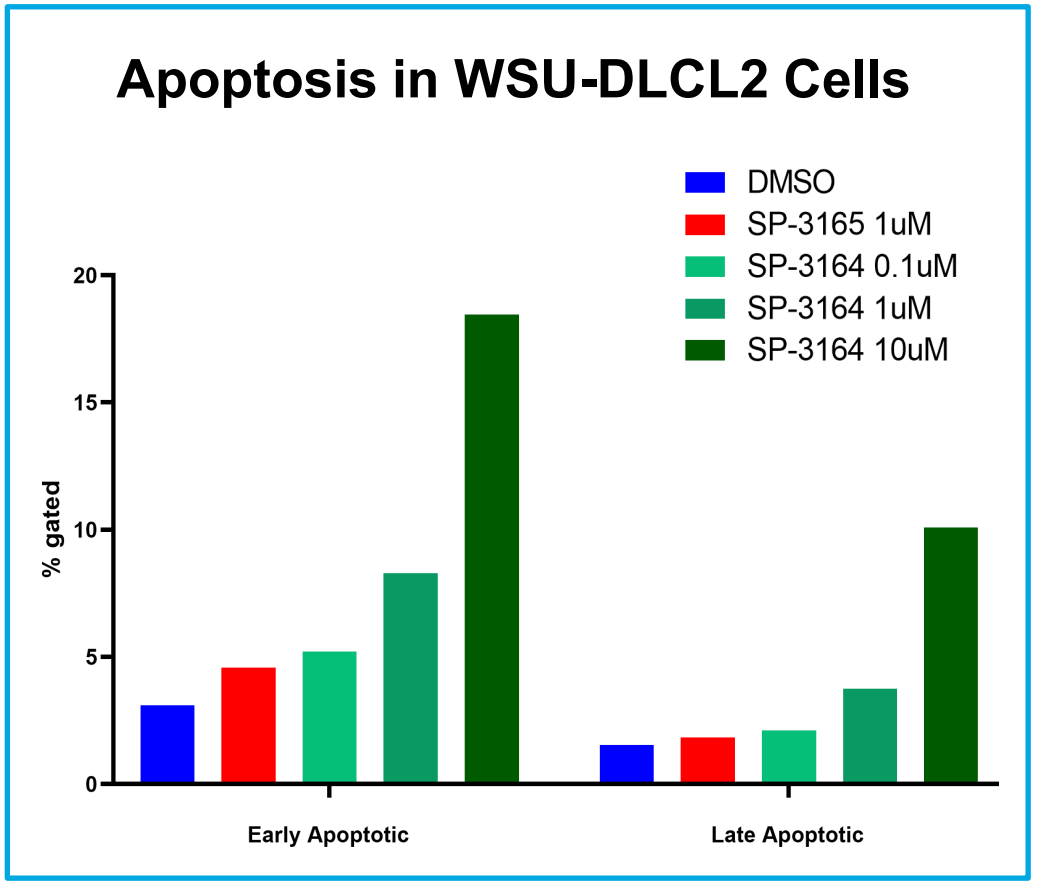




- SP-3164 exhibits dose-dependent Aiolos degradation
- SP-3165 exhibits minimal neosubstrate degradation
- SP-3164 (500 nM) is comparable to CC-122 and CC-220 (1 μM), better than LEN (10 μM)

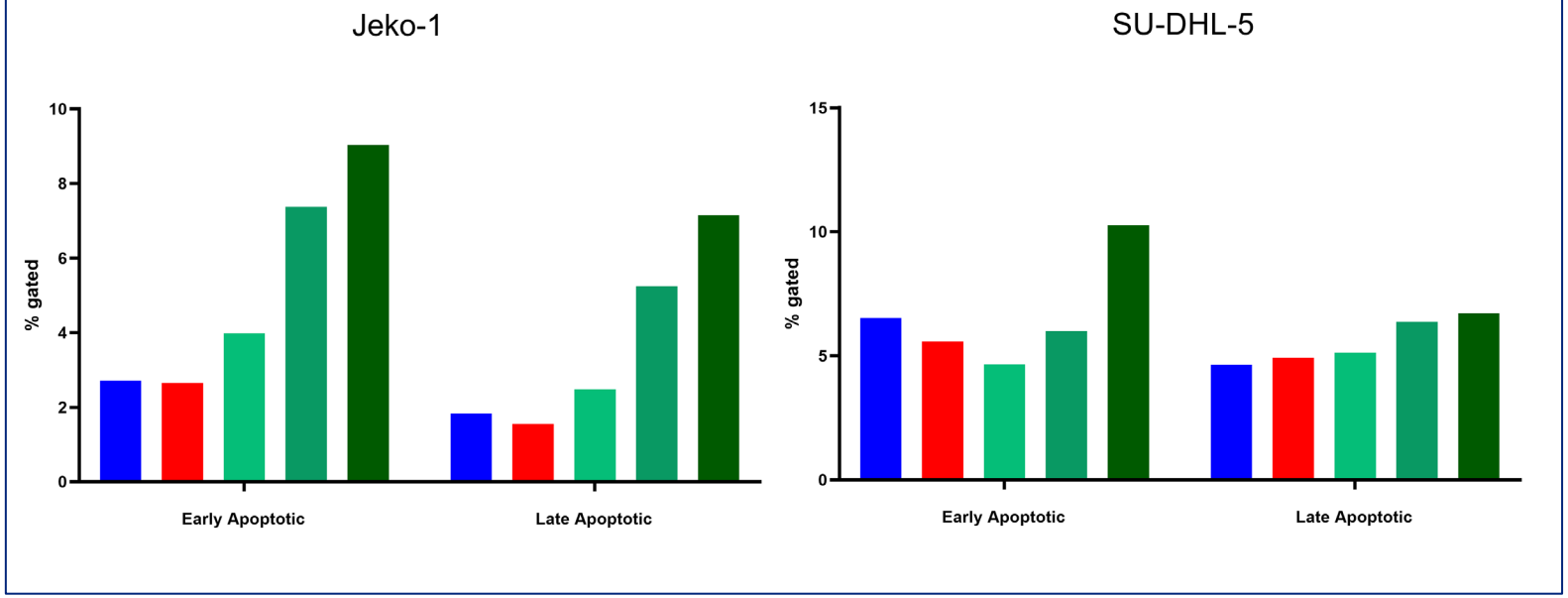
SP-3164 Induces Apoptosis in WSU-DLCL2 (DLBCL) Cells (72h)



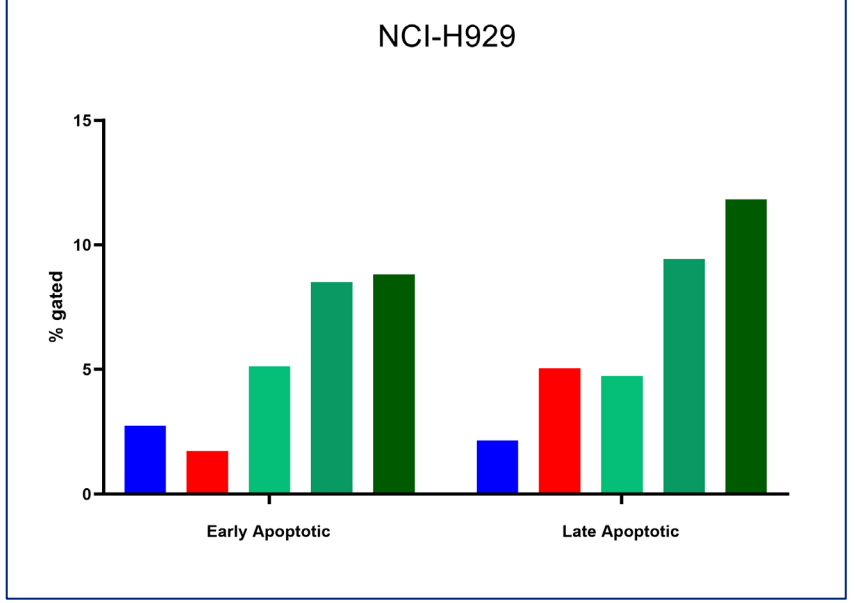


SP-3164 Induces Apoptosis in Lymphomas Cells (72h)

Lymphomas



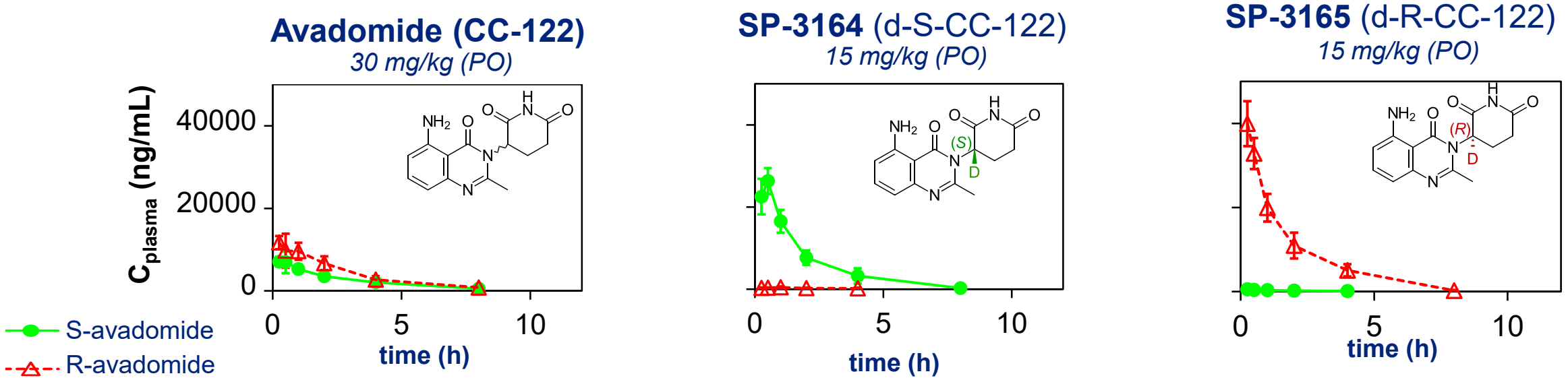
Multiple Myeloma



DMSO
SP-3165 1uM
SP-3164 0.1uM
SP-3164 1uM
SP-3164 10uM

SP-3164 *In Vivo* Pharmacokinetics - Stabilization Demonstrated

Exclusive Exposure to Single Enantiomers in Mice



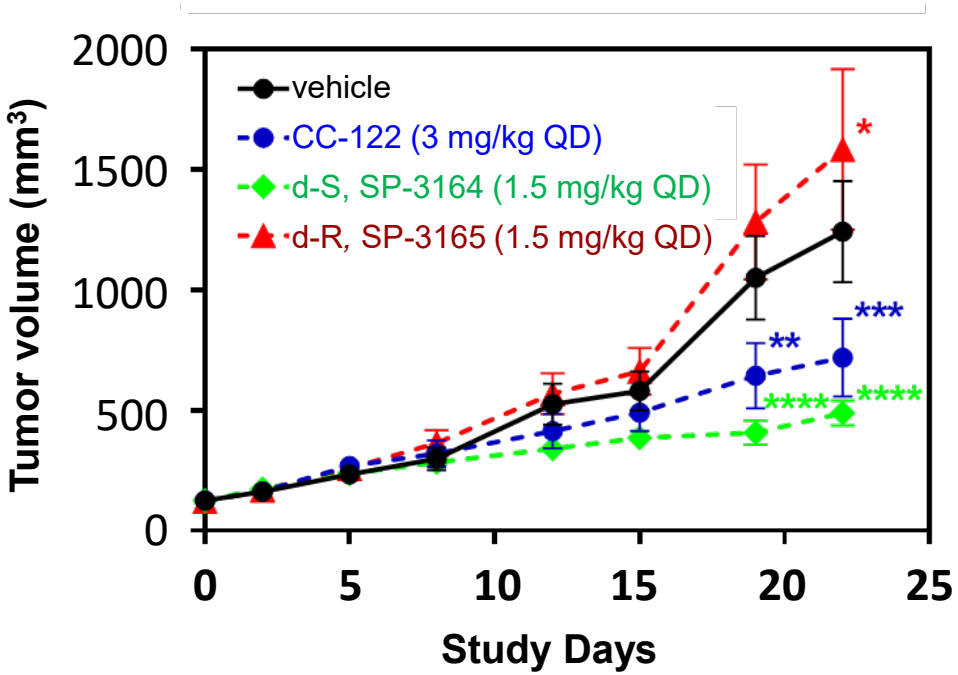
- Avadomide (CC-122): Stereoselective for undesired R-enantiomer after dosing (R>S)
- Little to no interconversion with deuterium-stabilized enantiomers
- Increased C_{max} with single enantiomer vs racemate* → opportunity to lower doses in clinic
- SP-3164 has a shorter T_{max} and $t_{1/2}$ compared to CC-122

PNAS 2015, 112(12): E1471-E1479. Single dose of compound by oral gavage. *Observed with other chiral switches including PXL065 and Nexium®

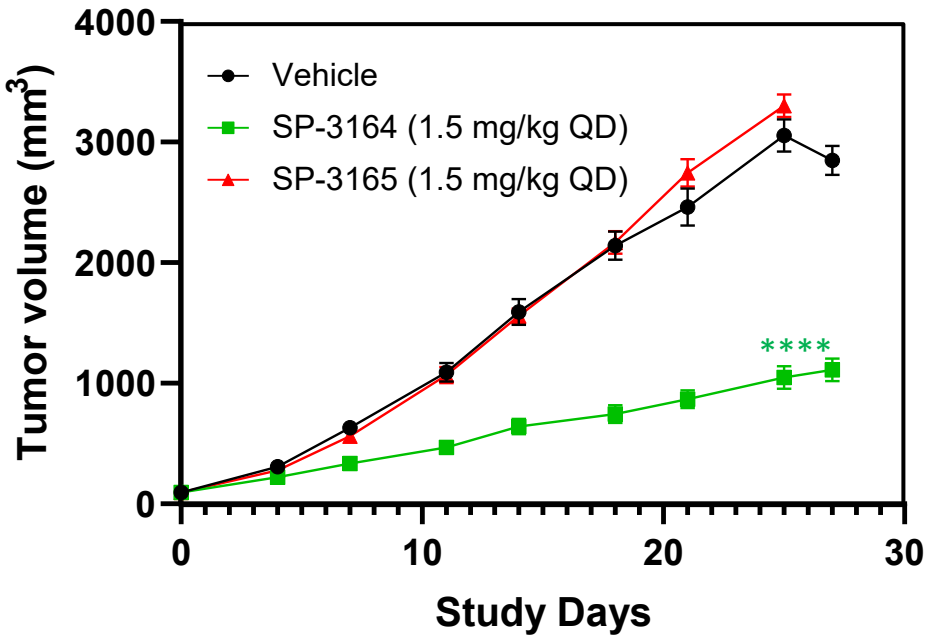
SP-3164 Shows Significant Activity in MM H929 Xenograft Model

R-Enantiomer (SP-3165) is Inactive

NCI-H929 Xenograft Study



NCI-H929 Xenograft Study (repeat)



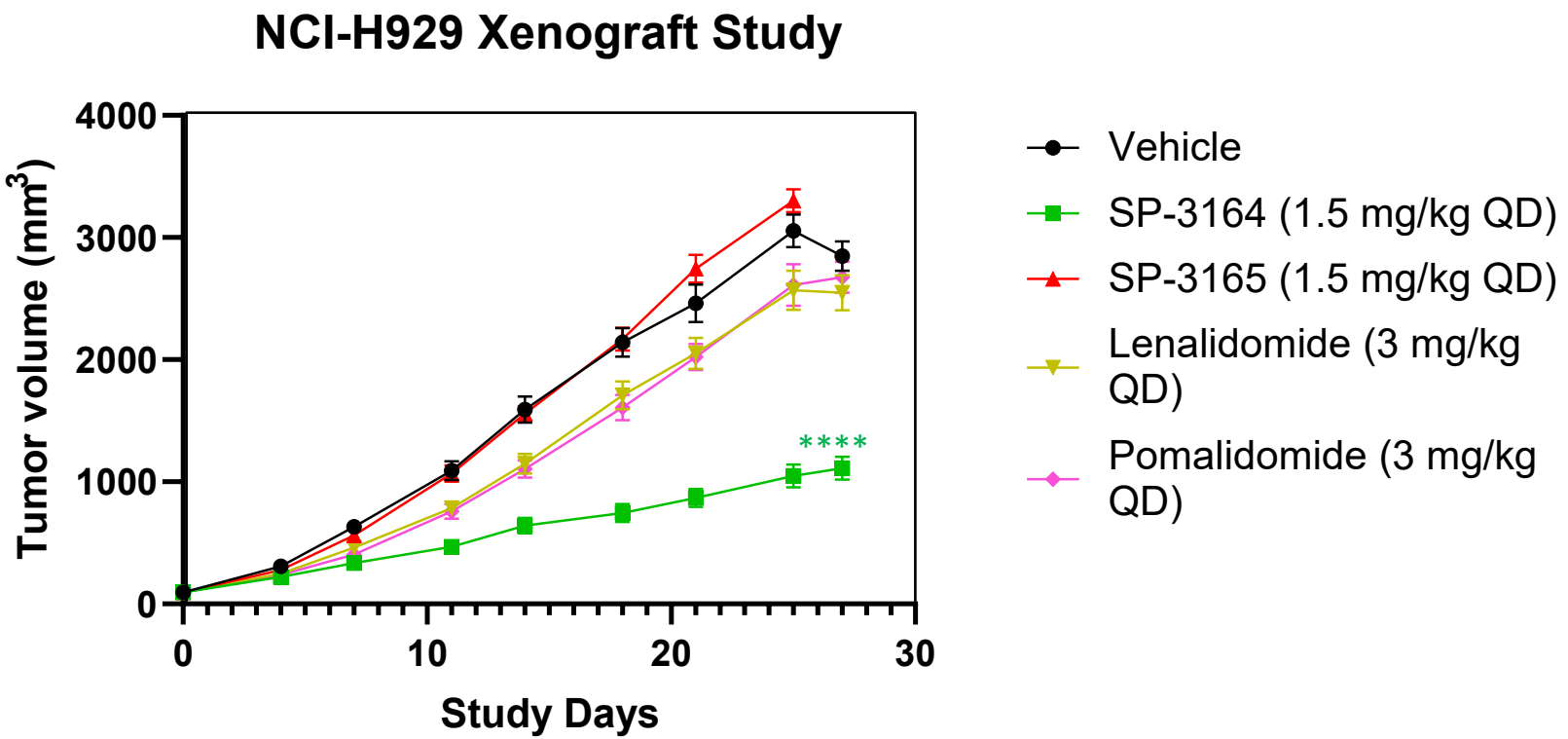
- SP-3164: Significant tumor growth inhibition (TGI) compared to vehicle
- SP-3164: Trended towards more TGI compared to CC-122
- SP-3165: No significant TGI, rather a trend towards supporting tumor growth

Abbreviations: Multiple Myeloma (MM)

Compared to vehicle, *$p < 0.05$; **$p < 0.01$; ***$p < 0.001$; ****$p < 0.0001$

SP-3164 Shows Significant TGI Compared to Other IMiDs®

In MM H929 Xenograft Model



- SP-3164 exhibits significant TGI compared to approved IMiDs for MM[1]
- Future studies will evaluate SP-3164 in IMiD-refractory MM cell lines

1. Revlimid® (lenalidomide) and Pomalyst® (pomalidomide)

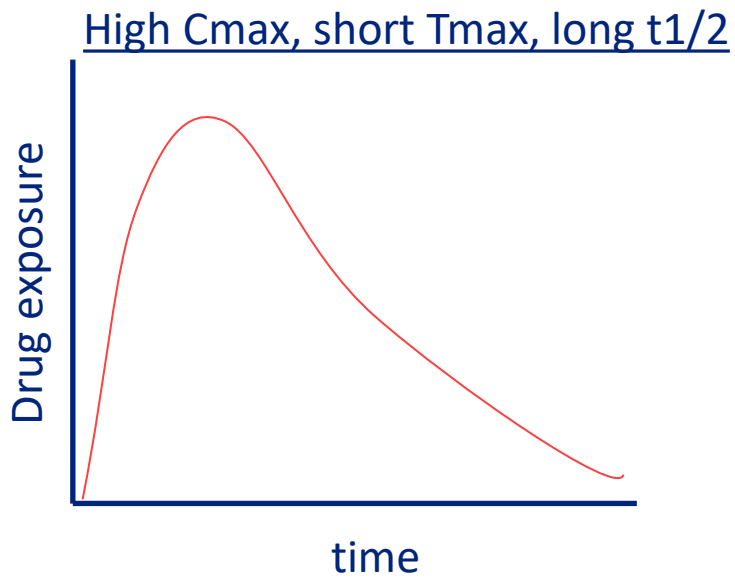
Abbreviations: Tumor Growth Inhibition (TGI), Multiple Myeloma (MM)

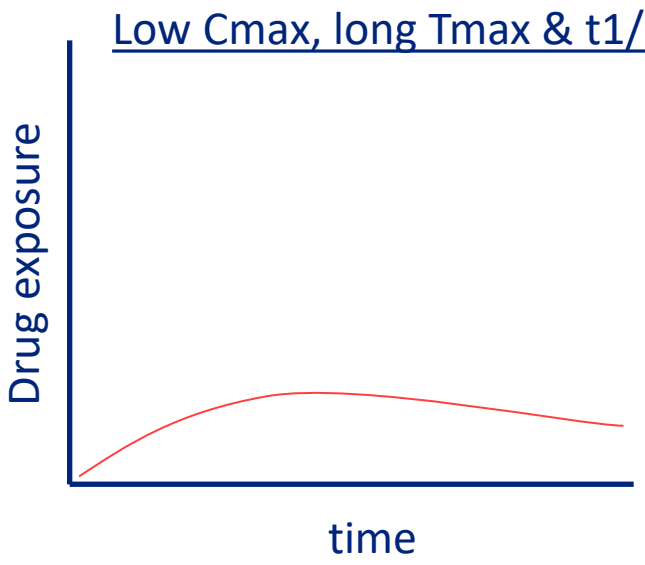
Compared to vehicle, ****$p < 0.0001$

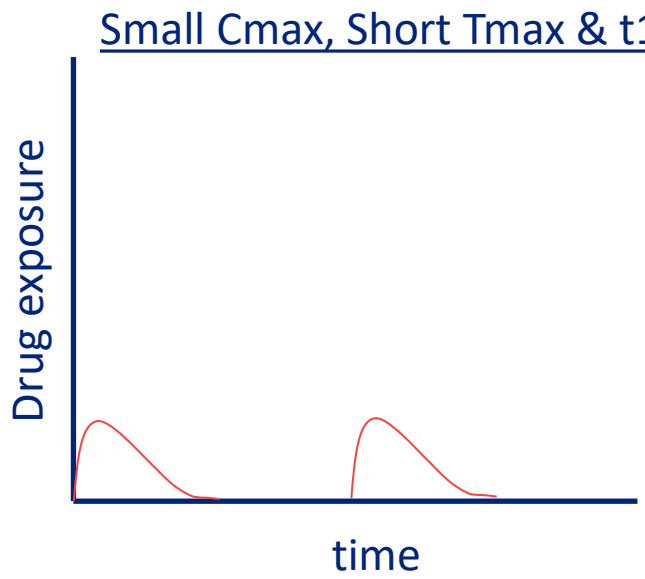
SP-3164: Clinical Dosing Considerations

Identification of Optimal Dose and Schedule to Maximize Effect

- Degrader dosing schedule requires unique considerations
  - Different compared to occupancy-driven inhibitors
  - Take into account compound half-life, sustained PD effect, protein resynthesis, and on-target toxicities
- Preclinical studies may elucidate potential dose schedules to investigate in clinic



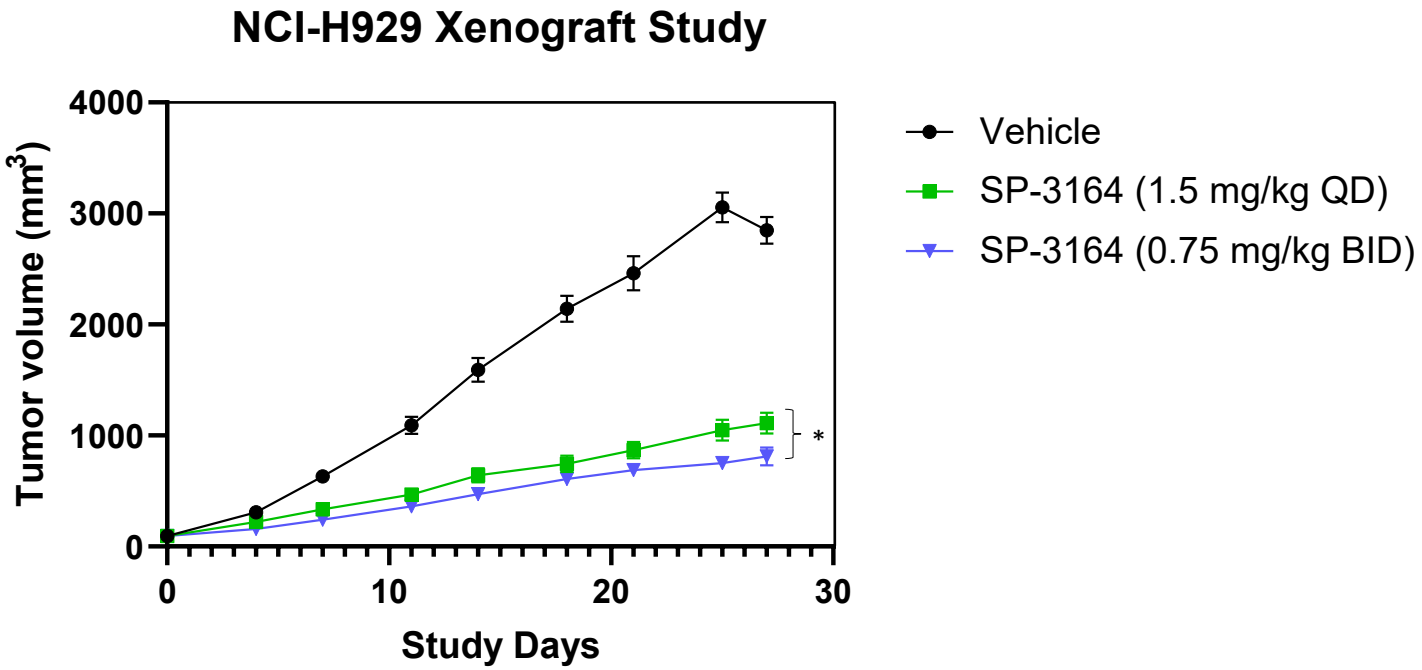




Abbreviations: Pharmacodynamic (PD)

SP-3164: Clinical Dosing Considerations

SP-3164 Dosed BID Has Improved Activity Compared To QD



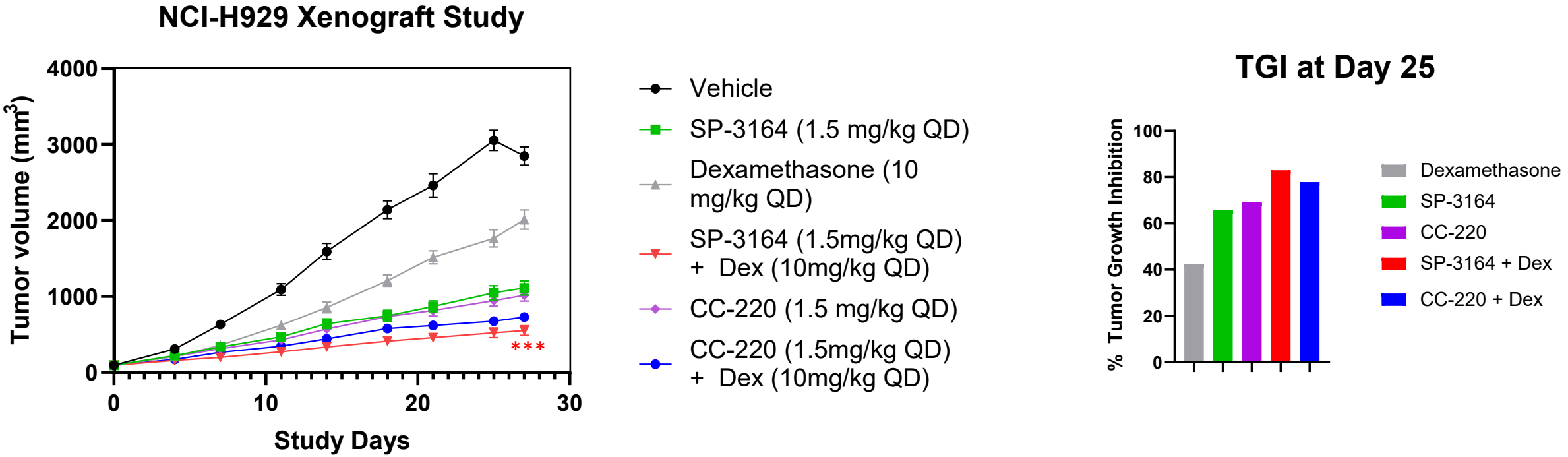
- For equivalent daily exposures (1.5 mg/kg QD and 0.75 mg/kg BID), the BID dose resulted in significantly improved TGI compared to the QD dose
  - ➢ Better to have a lower C_{max}, but increased duration of an effective exposure to SP-3164 than a bolus-like exposure

Abbreviations: Tumor Growth Inhibition (TGI)

* $p \leq 0.05$

SP-3164 Shows Enhanced TGI In Combo With Dexamethasone

Comparable activity to CC-220

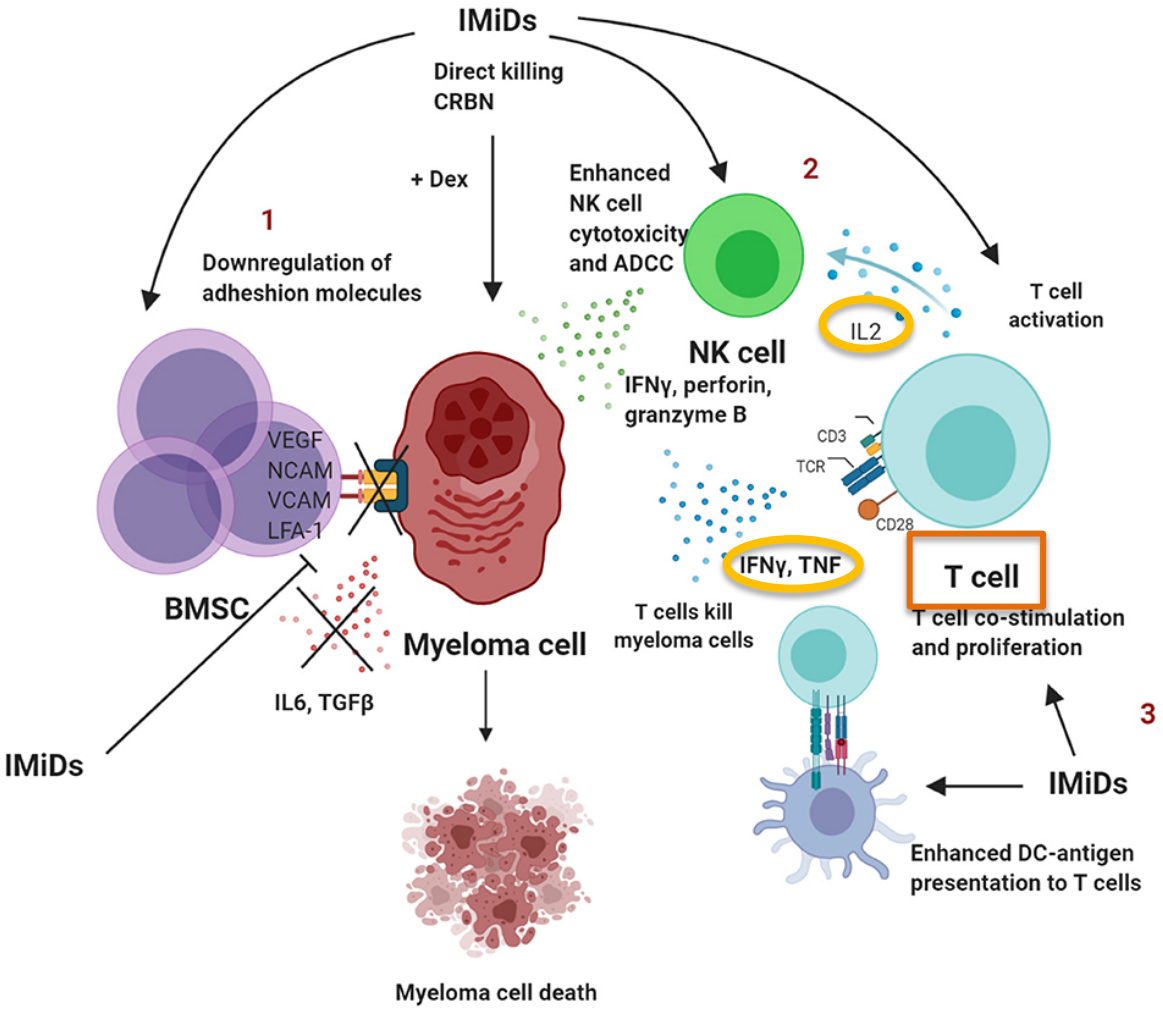


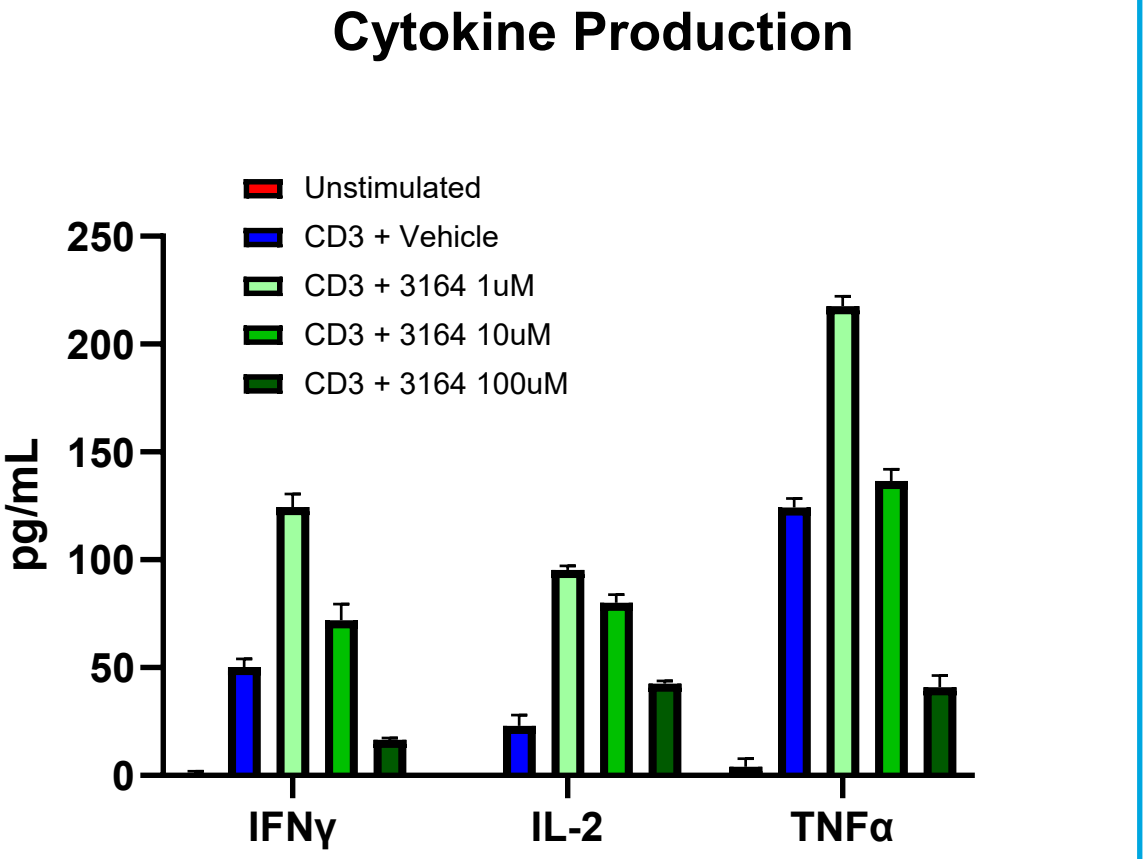
- Combo SP-3164 + dexamethasone (Dex) showed increased TGI vs either agent alone.
  - Compared favorably to CC-220 (iberdomide) + Dex
- Future studies with combos of SP-3164 and MM standard-of-care (SOC) agents

Abbreviations: Tumor Growth Inhibition (TGI)

Compared to single agent SP-3164; ***$p < 0.001$

SP-3164 Exhibits Immune Modulation Effects





D'Souza, C. et al. Frontiers in Immunology 12 (2021)

Conclusions and Future Directions

Conclusions

- Selecting for preferred enantiomers is a proven method for successful drug development
- We successfully developed SP-3164 to be the stabilized, active S-enantiomer of CC-122, a widely studied molecular glue with clinical activity/safety data. SP-3164 demonstrates:
  - ✓ Potent cereblon binding, efficient degradation of neosubstrates, induction of apoptosis
  - ✓ Minimal to no interconversion to the R-enantiomer in *in vivo* studies; differential PK could lead to dosing advantages
  - ✓ Significant TGI in *in vivo* studies; improvement over approved IMiDs and comparable to CC-220 (Ph3)
- Elimination of the R-enantiomer may lead to improved activity and safety, as demonstrated by SP-3165's lack of anticancer activity and its potential role in supporting of tumor growth.

Future Directions

- Explore SP-3164 in other heme malignancies; *presenting at ASH 2022*
- Continue assessing PK/PD effects to better understand clinical dosing
- Continue exploring immuno-oncology effects and potential combinations for SP-3164

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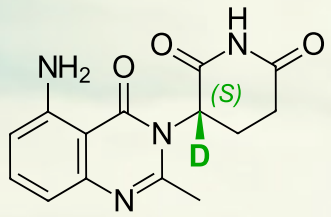
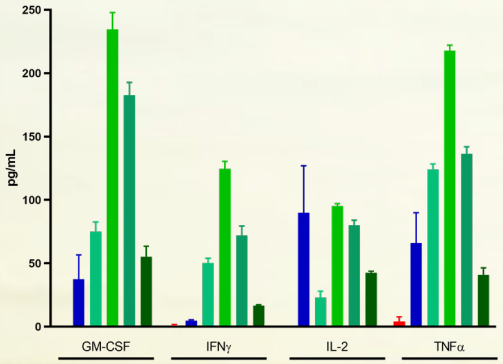
* Employees of DeuteRx, a collaboration partner with Salarius

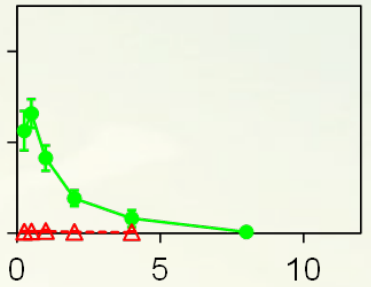


SP-3164



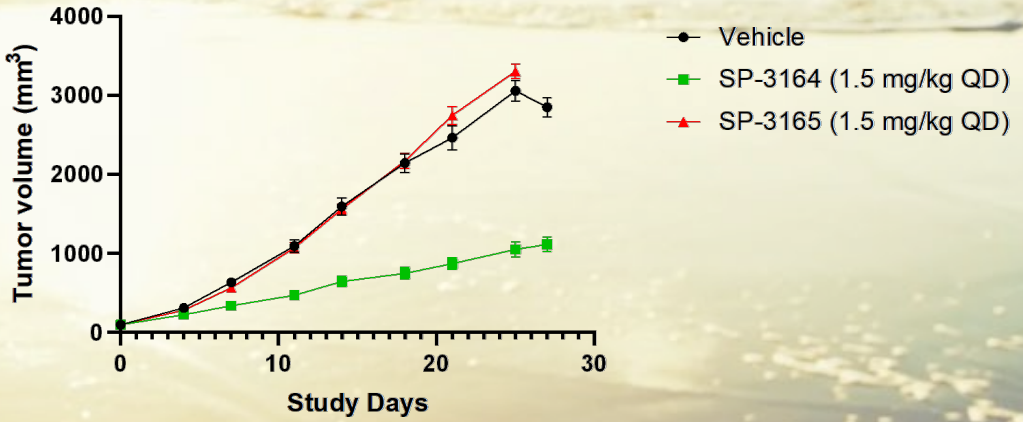
SP-3164 (d-S-CC-122)

15 mg/kg (PO)



Thank you!

NCI-H929 Xenograft Study



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