Salarius PHARMACEUTICALS

Development of the cereblon-binding molecular glue, SP-3164

Molecular Glue Summit
January 26, 2023

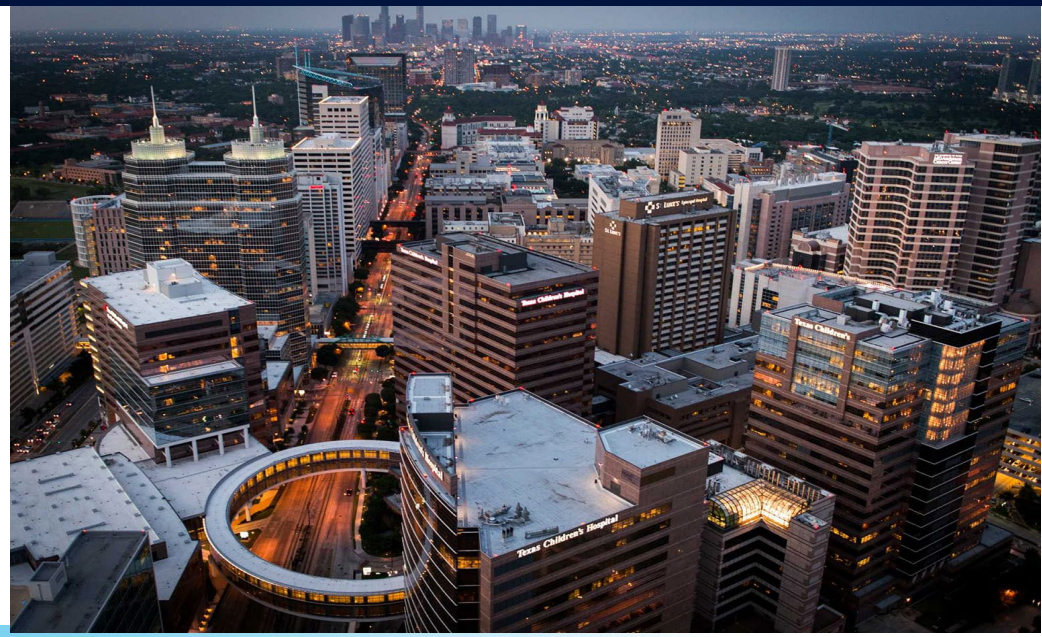
Safe Harbor Statement

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 October 2022 suspected unexpected severe adverse reaction (SUSAR) event and resulting partial clinical hold by the U.S. Food and Drug Administration (FDA); 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 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; resolution of the FDA’s partial clinical hold on the company’s Phase 1/2 trial of seclidemstat as a treatment for Ewing sarcoma and FET-rearranged sarcomas following the SUSAR; 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. You should review additional disclosures we make in our filings with the Securities and Exchange Commission, including our Quarterly Reports on Form 10-Q, Annual Reports on Form 10-K, and Current Reports on Form 8-K. You may access these documents for no charge at http://www.sec.gov. This presentation shall not constitute an offer to sell or the solicitation of an offer to buy, nor shall there be any sale of these securities in any state or other jurisdiction in which such offer, solicitation or sale would be unlawful prior to registration or qualification under the securities laws of any such state or other jurisdiction.

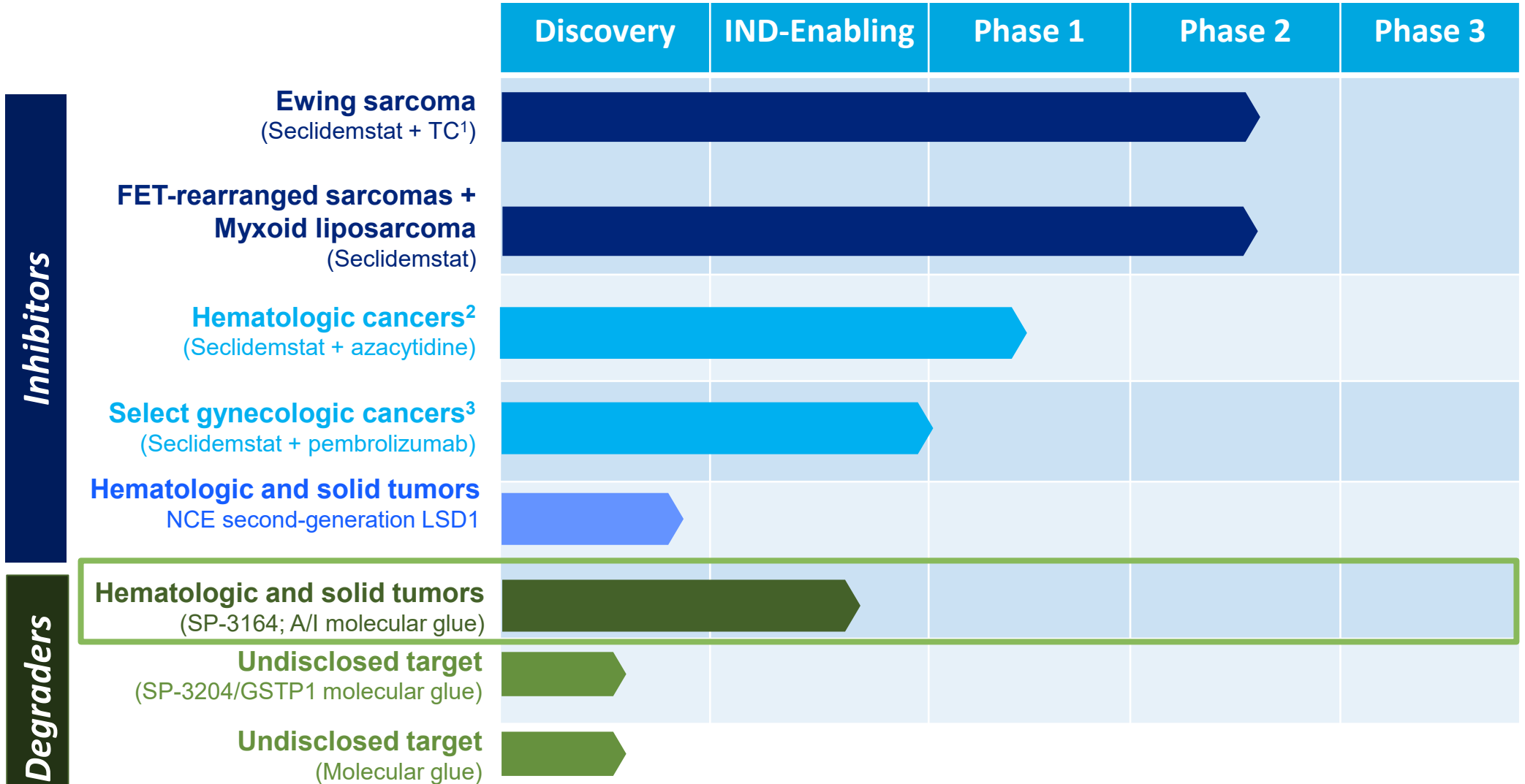
Salarius Pharmaceuticals, Inc.

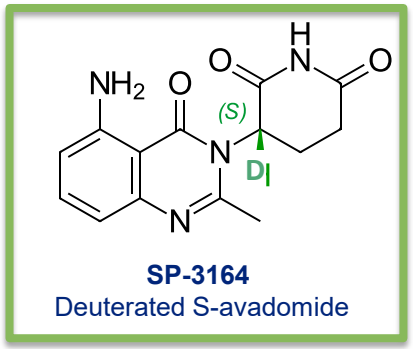
- An oncology-focused biopharmaceutical company in Houston, TX
- 15 FTEs plus experienced consultants
  - Seasoned leadership team with Big Pharma and Biotech backgrounds

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



Pipeline Overview

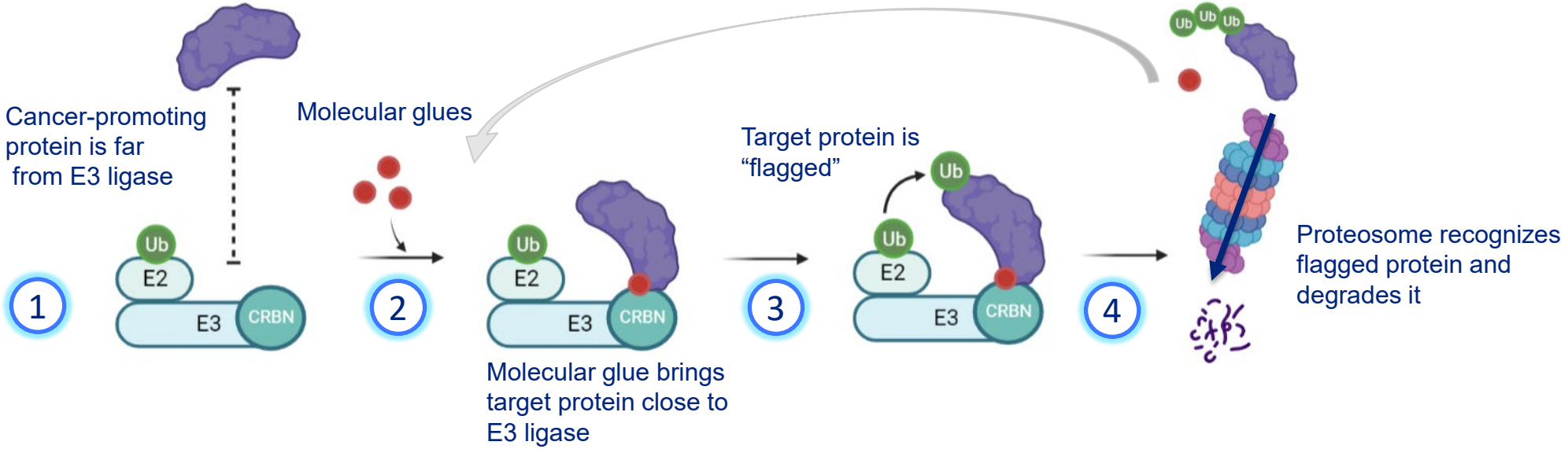




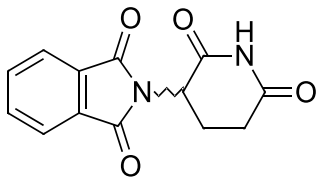
SP-3164
Deuterated S-avadomide

[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.

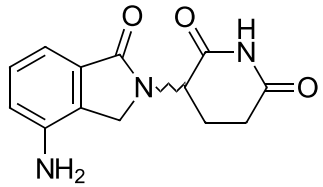
CRBN-Binding Molecular Glues Induce Proteasomal Degradation



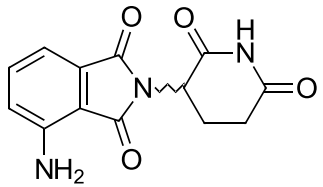
IMiDs® (Immunomodulatory Drugs) – Approved for hematological malignancies



Thalidomide



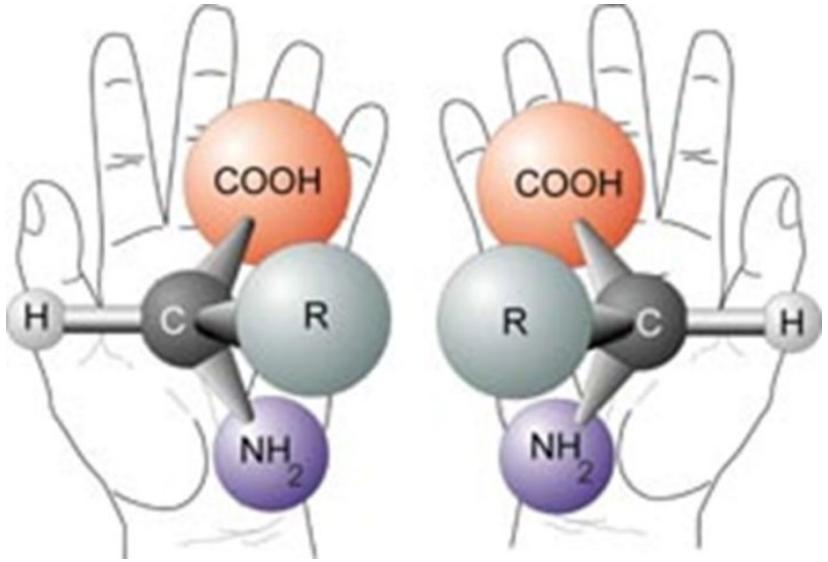
Lenalidomide



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

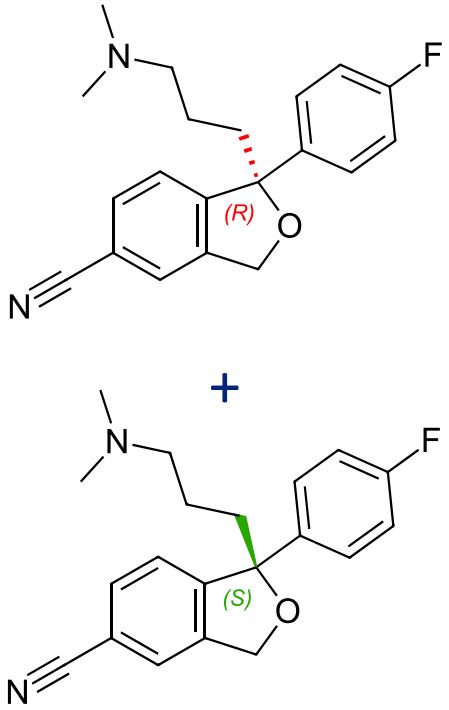
***R**-Limonene*

Right-handed enantiomer

Classic Chiral Switch Example: Celexa® ⇨ Lexapro®

Improved Drug Profile with the Single, Preferred Enantiomer

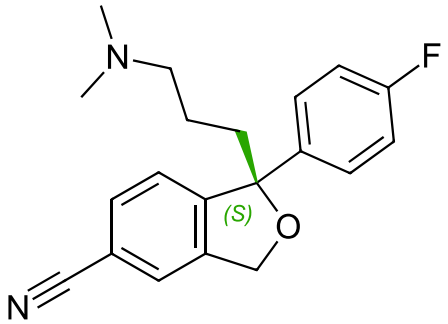
Applied since the 1990s for racemic drugs *with stable chiral centers*



CITALOPRAM
Racemate
Mixture of R & S enantiomers

Chiral Switch

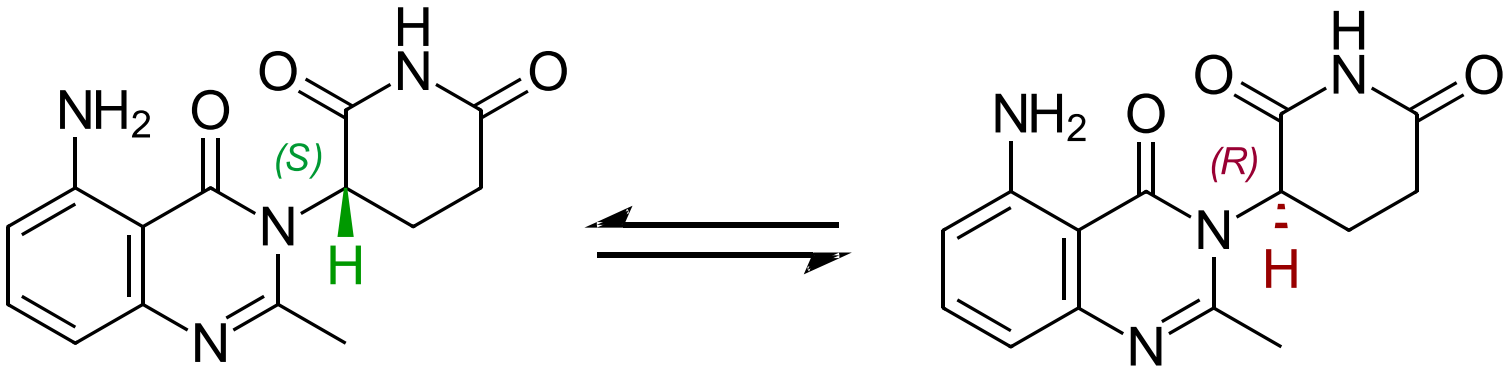
…from a mixture to the Best Drug!



ESCITALOPRAM
S-enantiomer
Better efficacy

Avadomide, an Extensively Studied CELMoD®

Exists as a Mixture of 2 Enantiomers



S-enantiomer **R-enantiomer**

Avadomide (CC-122)

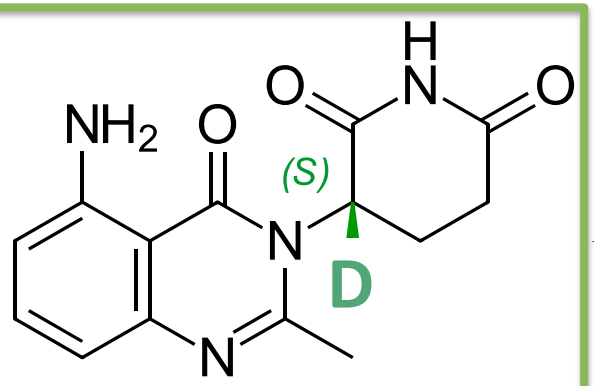
a 1:1 mixture of 2 interconverting enantiomers

✓ Studied in 10 clinical trials in >400 patients

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

Salarius Uses A Deuterium-enabled Chiral Switching Platform To Identify And Develop Novel Drugs

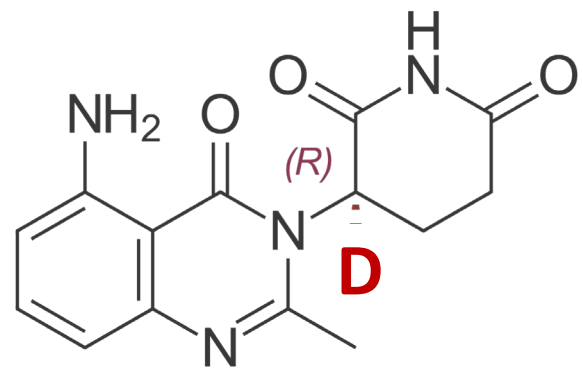
Stabilization of avadomide enantiomers with deuterium blocks interconversion



SP-3164

Deuterated S-avadomide

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



SP-3165

Deuterated R-avadomide

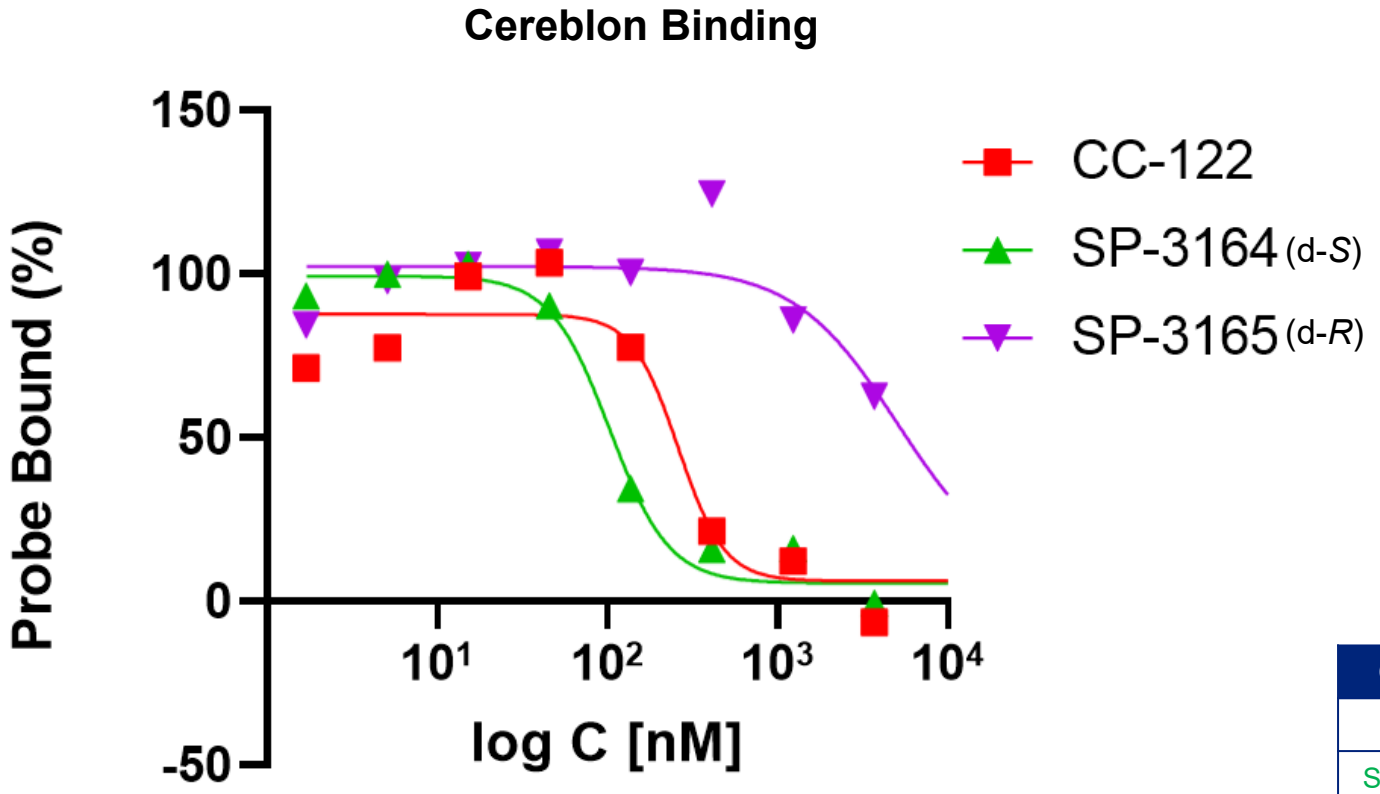
- Does not bind cereblon
- Minimal neosubstrate degradation
- *Potentially* supports tumor growth

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 CRBN binding

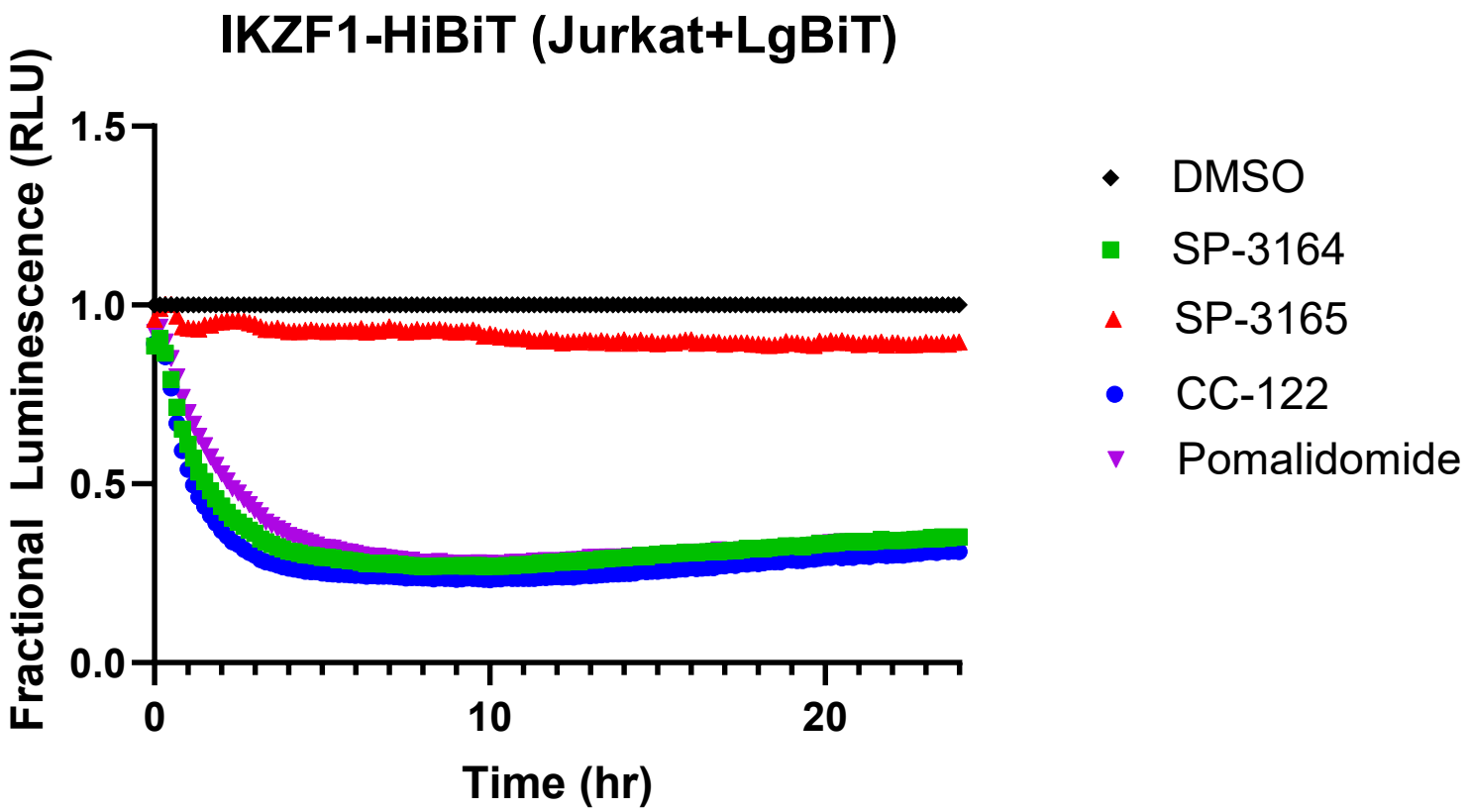
Characteristics Compared to Avadomide (CC-122)



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)

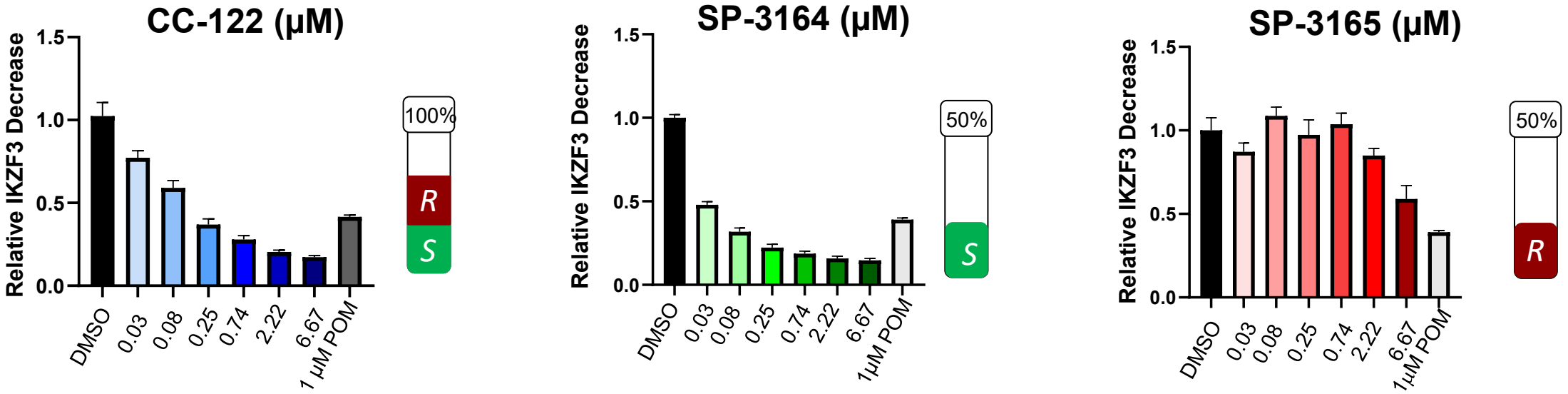


- SP-3164 has a similar Dmax to CC-122 (1 uM)
- SP-3165 does not cause any protein degradation

Performed at Promega

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

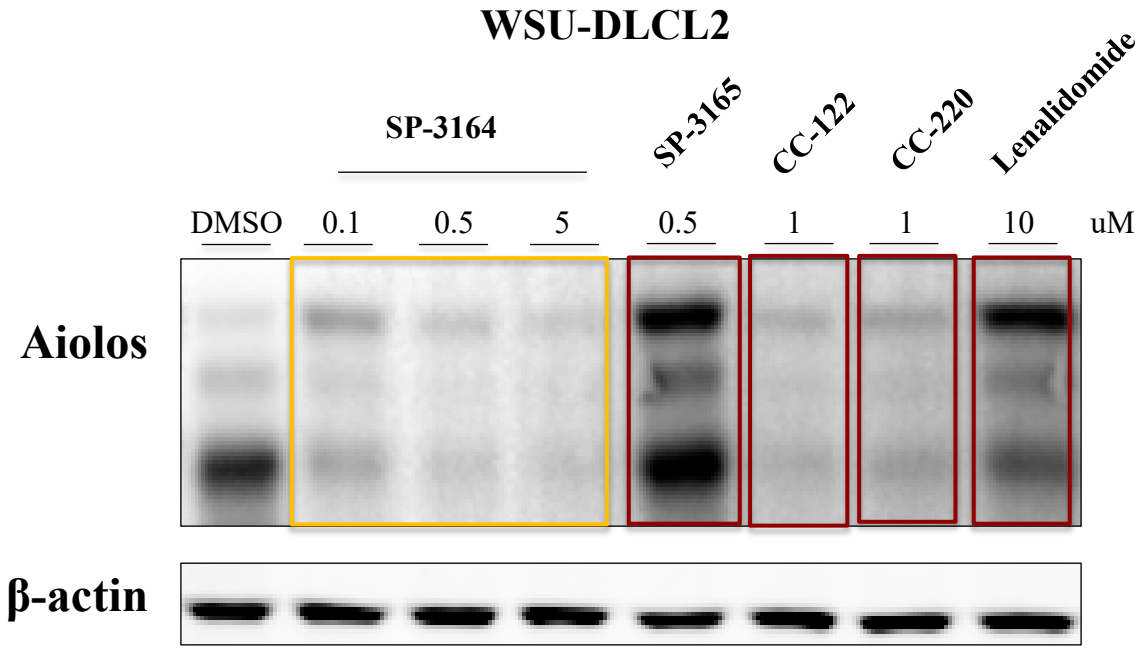
HiBiT-IKZF3 MM.1S Degradation (2 hours)

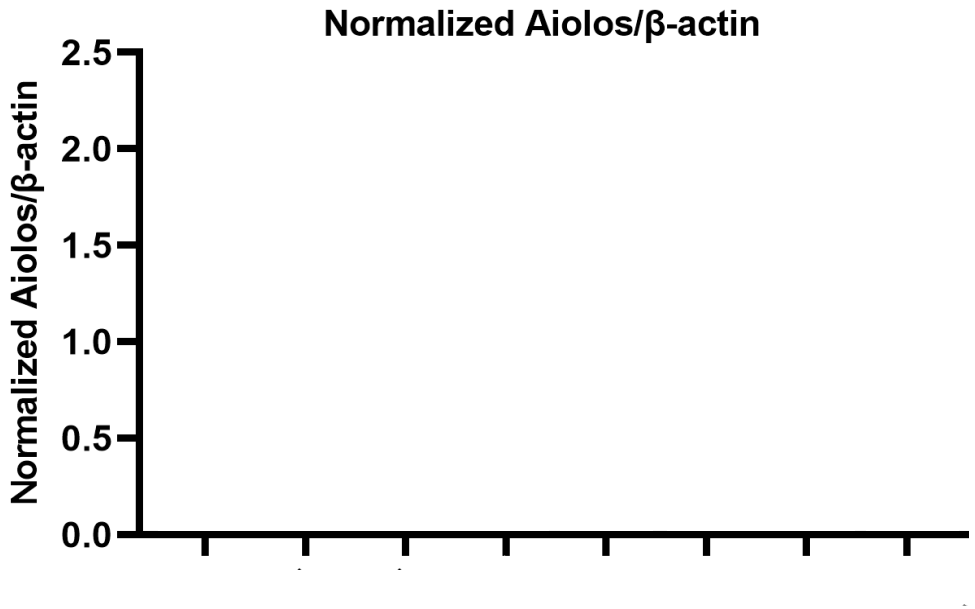


- Treatment with SP-3164 for 2 hrs results in deep and rapid degradation of the target protein, IKZF3.
- At comparable concentrations, SP-3164 induced more degradation of IKZF3 compared to CC-122
- SP-3165 does not result in protein degradation except for at high concentrations.

Performed at Promega

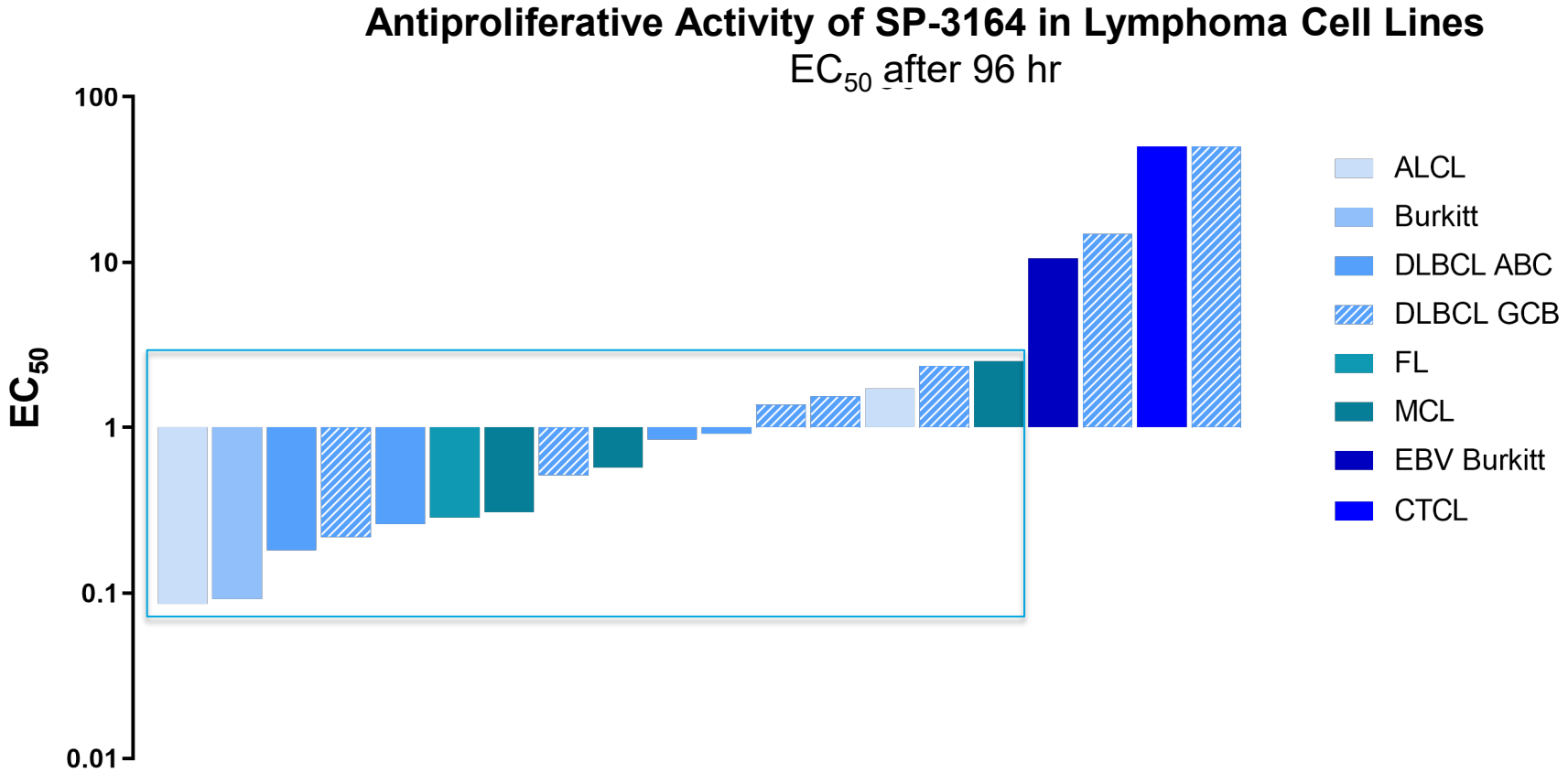
SP-3164 Exhibits Dose-Dependent Aiolos Degradation





- 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)

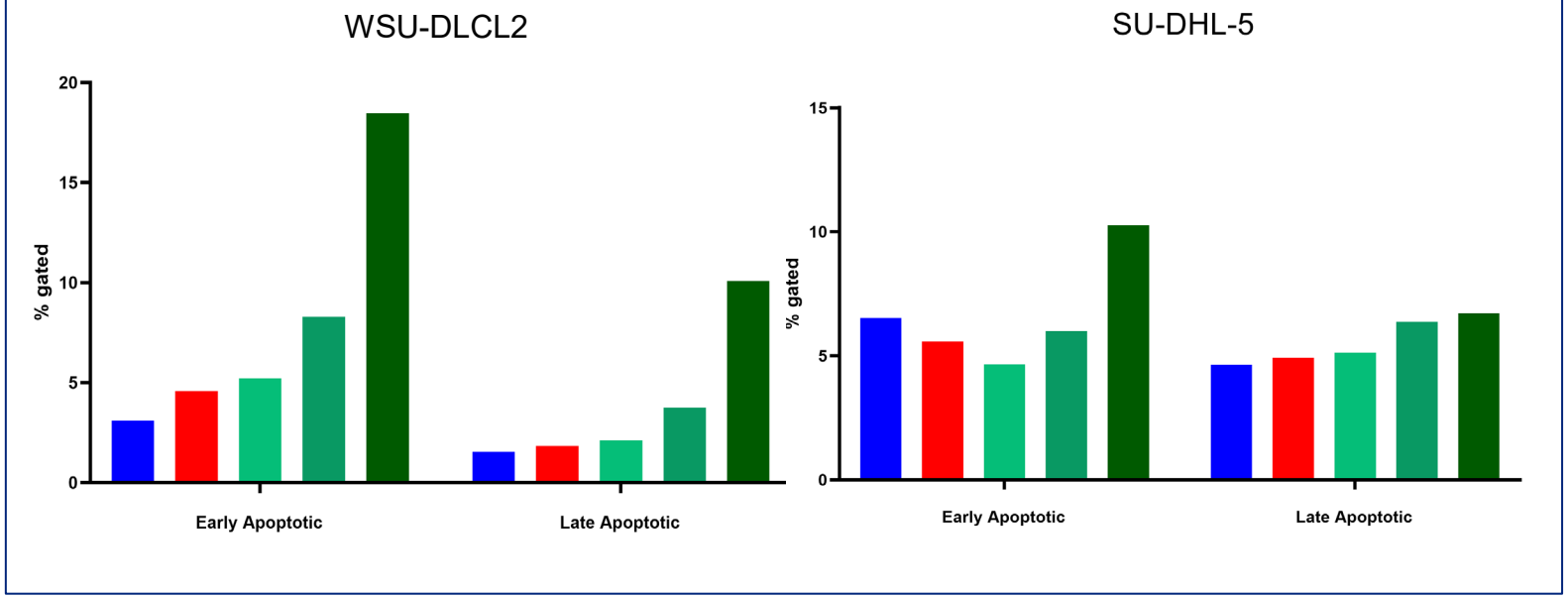
SP-3164 Inhibits Viability in Lymphoma Cell Lines in vitro



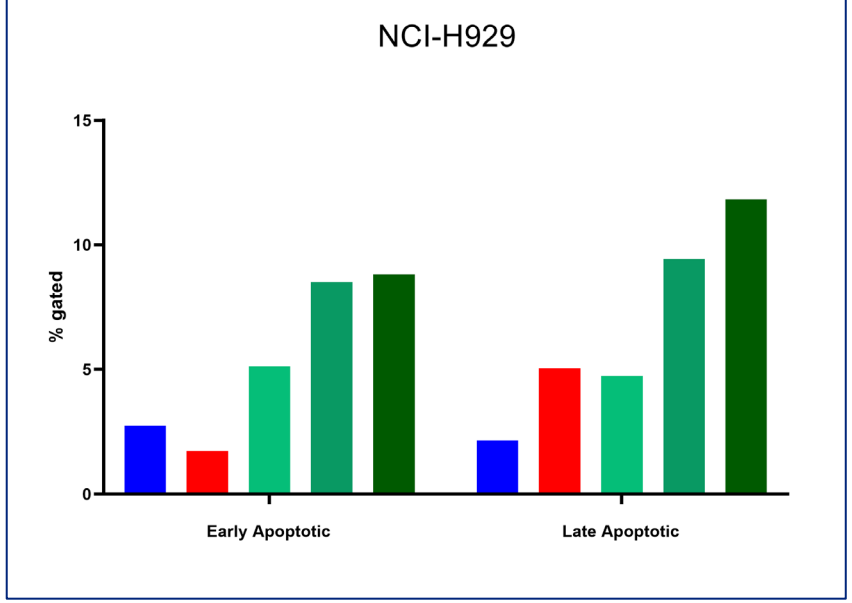
In a panel of 20 lymphoma cancer cell lines representing various subtypes, SP-3164 demonstrated potent antiproliferative activity within 96 hrs of dosing in 16 cell lines (average EC_{50} <1 µM, range 0.092-2.523 µM).

SP-3164 Induces Apoptosis in Lymphoma and Myeloma Cells

Lymphomas



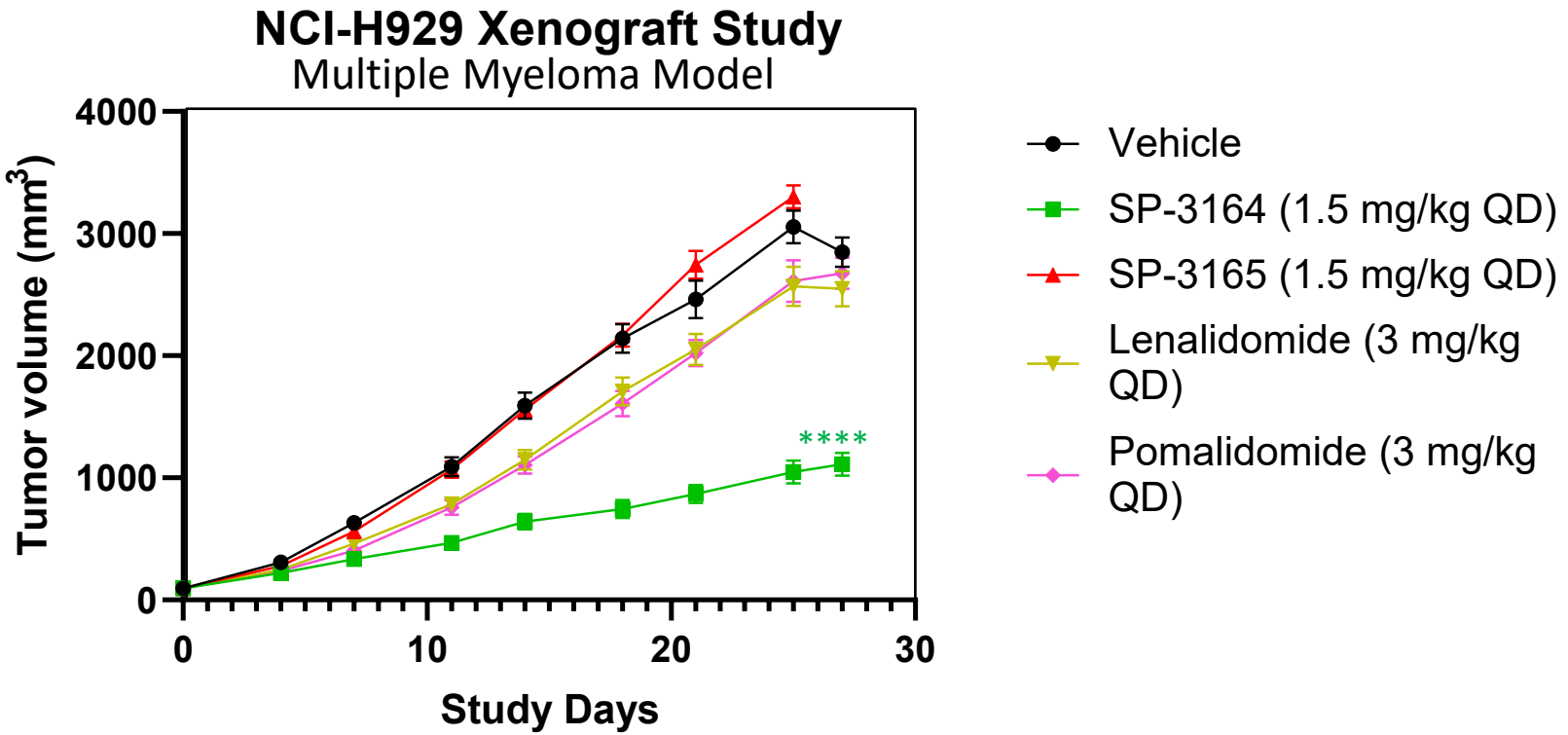
Multiple Myeloma



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

SP-3164 Shows Significant TGI Compared to Other IMiDs®

In MM H929 Xenograft Model



- SP-3164: exhibits significant TGI compared to approved IMiDs for MM1
- SP-3165: No significant TGI, rather a trend towards supporting tumor growth

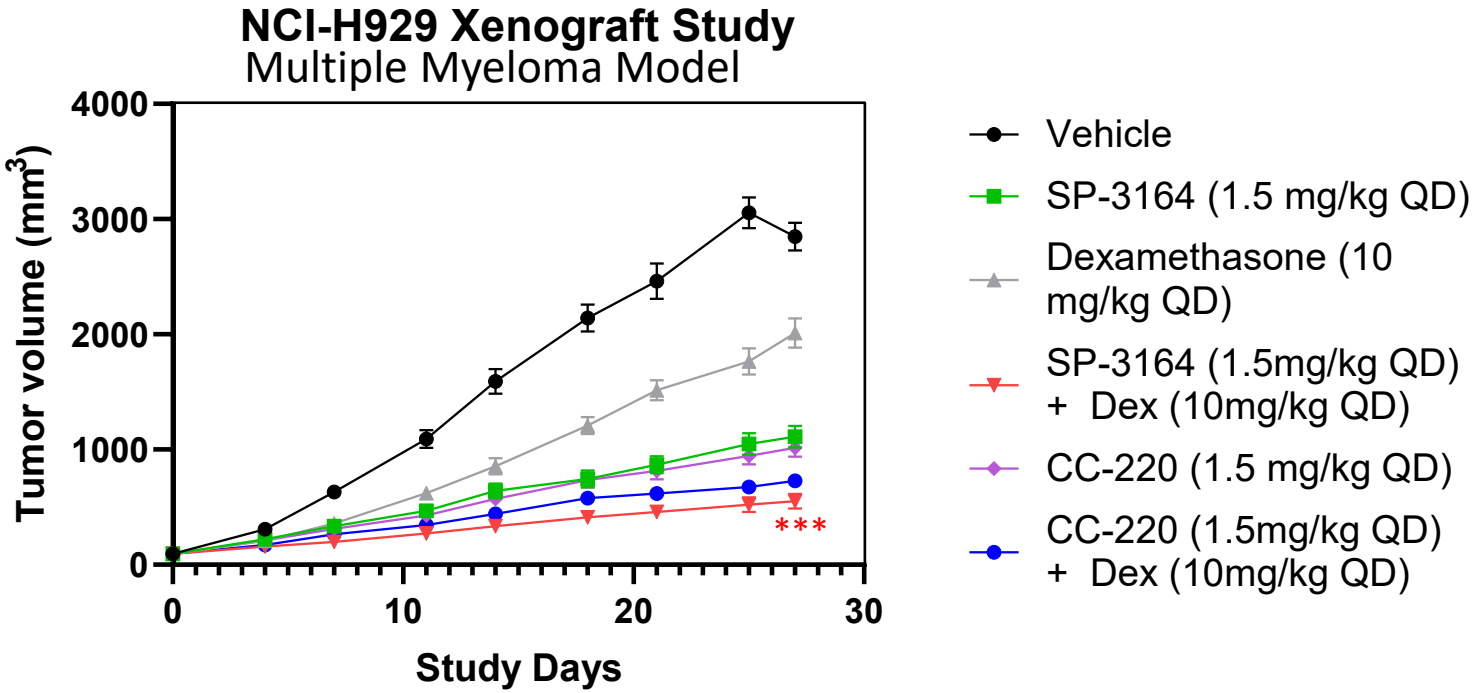
1. Revlimid® (lenalidomide) and Pomalyst® (pomalidomide)

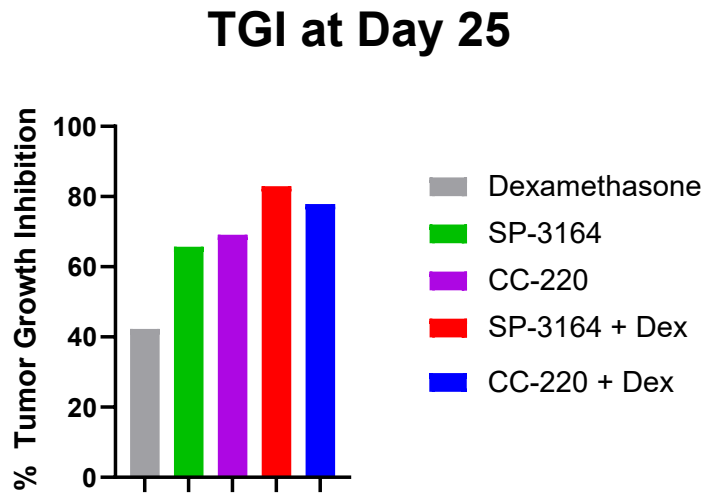
Abbreviations: Tumor Growth Inhibition (TGI), Multiple Myeloma (MM)

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

SP-3164 Shows Enhanced TGI In Combo With Dexamethasone

Comparable activity to CC-220





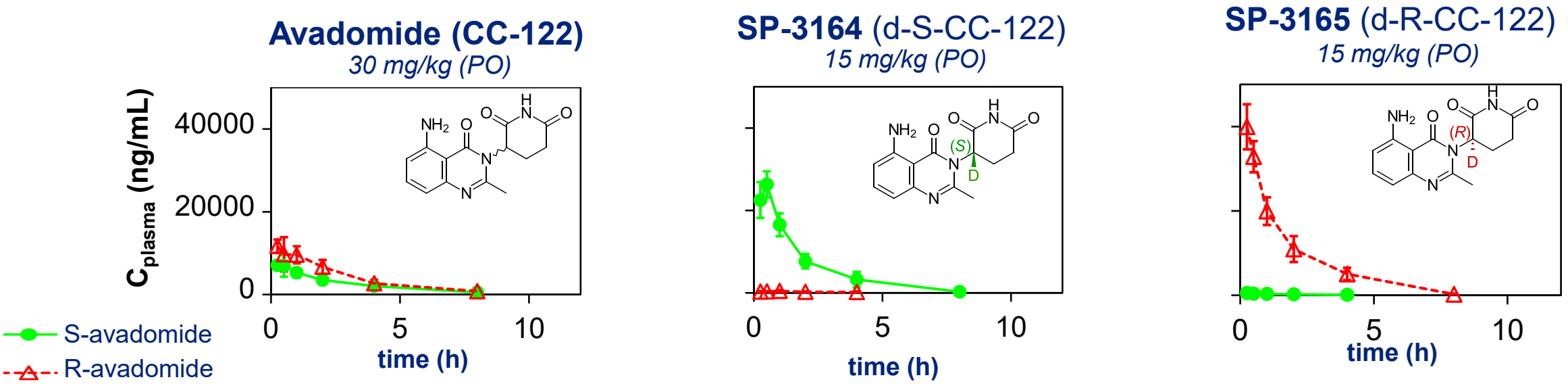
- **Combo SP-3164 + dexamethasone (Dex) showed increased TGI vs either agent alone.**
  - Compared favorably to CC-220 (iberdomide) + Dex
  - **Future studies with combos of SP-3164 and MM standard-of-care (SOC) agents**

Abbreviations: Tumor Growth Inhibition (TGI)

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

SP-3164 *In Vivo* Pharmacokinetics - Stabilization Demonstrated

Exclusive Exposure to Single Enantiomers in Mice



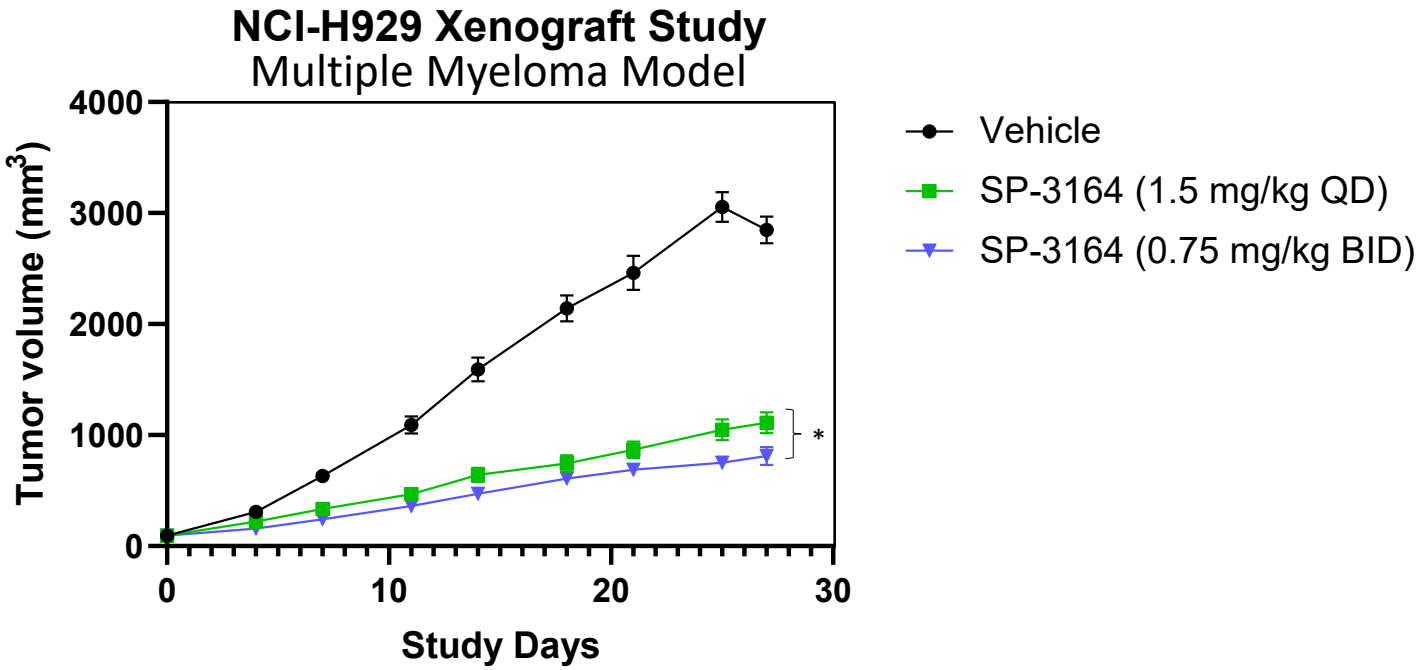
Avadomide (CC-122): Stereoselective for undesired R-enantiomer after dosing (R>S)

- Little to no interconversion with deuterium-stabilized enantiomers
- Increased Cmax with single enantiomer vs racemate* → opportunity to lower doses in clinic
- SP-3164 has a shorter Tmax and t1/2 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: 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

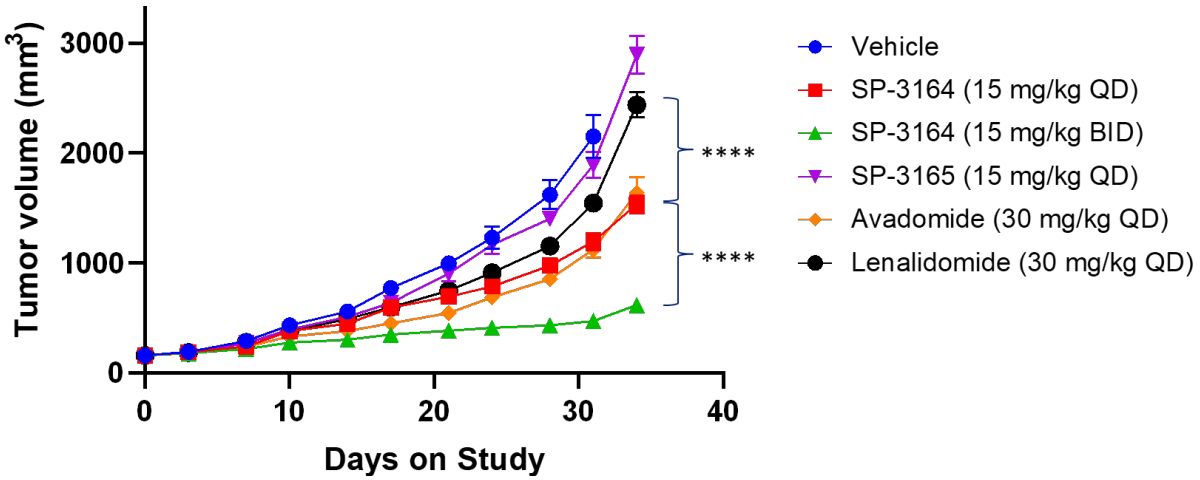
Abbreviations: Tumor Growth Inhibition (TGI)

* $p \leq 0.05$

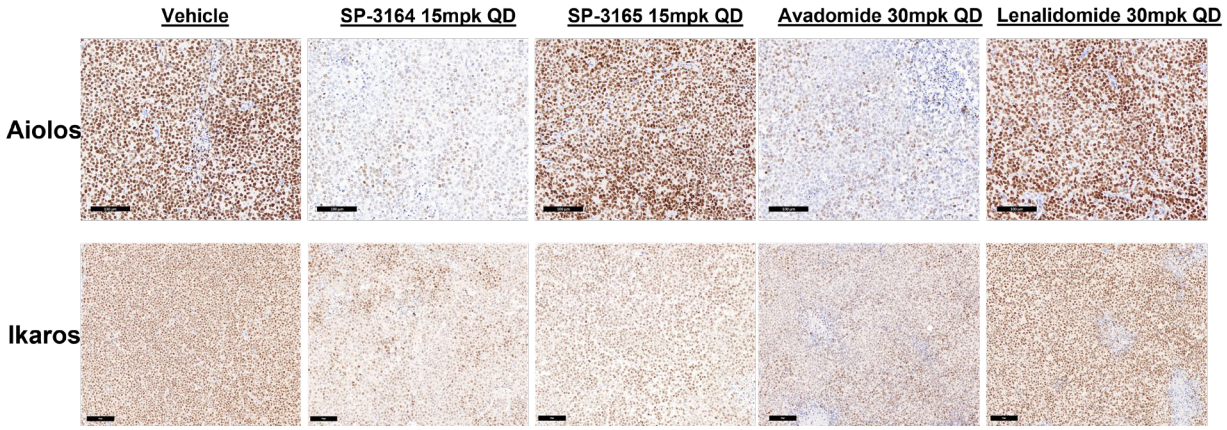
SP-3164 Demonstrates Single-Agent Activity in DLBCL

Mouse DLBCL (WSU-DLCL2) Xenograft Model

Tumor Volume ±SEM

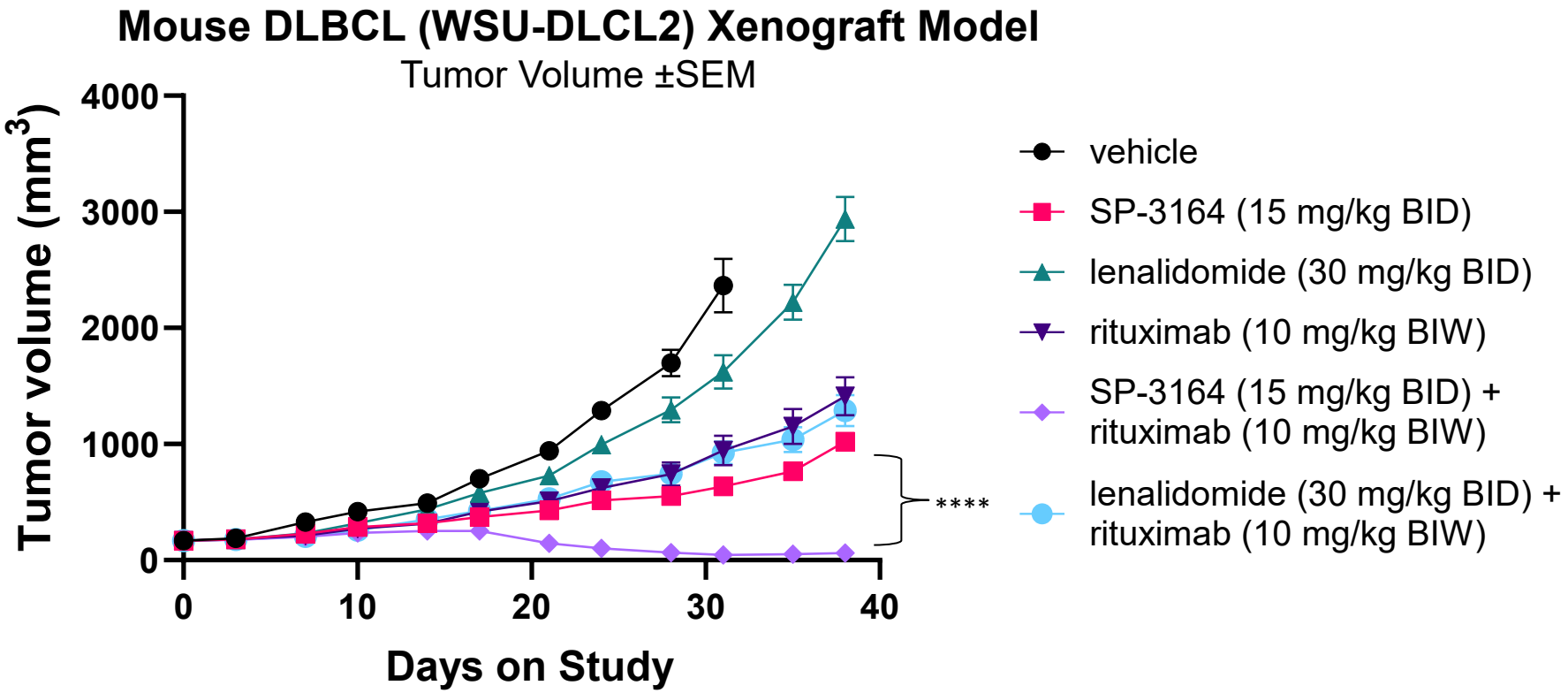


Degradation of Aiolos and Ikaros in tumors



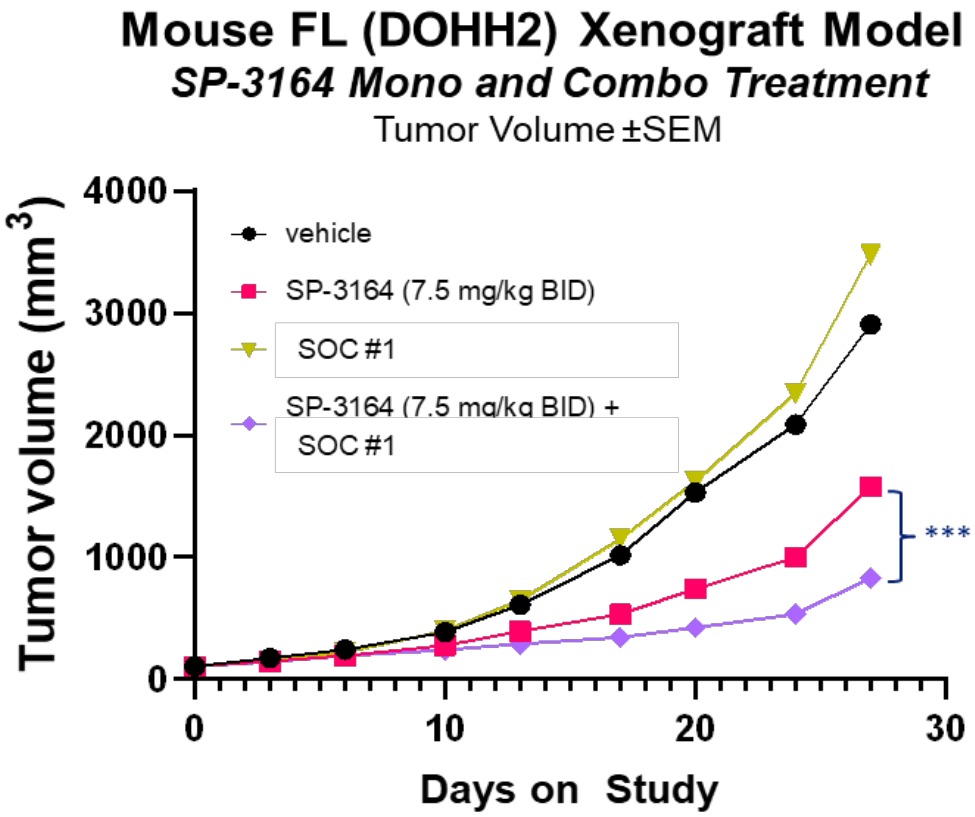
- SP-3164 demonstrated pronounced antitumor activity as single agent outperforming lenalidomide and comparable to avadomide while SP-3165 lacked significant antitumor activity (**** $p \leq 0.0001$).
- Due to SP-3164's shorter $t_{1/2}$ vs. avadomide, SP-3164 was studied BID resulting in the largest inhibitory effect.
- Treatment with SP-3164 caused degradation of Aiolos and Ikaros in tumors (representative IHC images at t=6hr).

SP-3164 Shows Synergistic Activity with Rituximab in DLBCL



- SP-3164 combination with rituximab was compared to approved regimen, lenalidomide and rituximab in WSU-DLCL2 DLBCL model.
- Combination of SP-3164 and rituximab resulted in sustained regressions with 50% of mice being tumor-free, significantly better than the lenalidomide and rituximab regimen (****p ≤0.001).

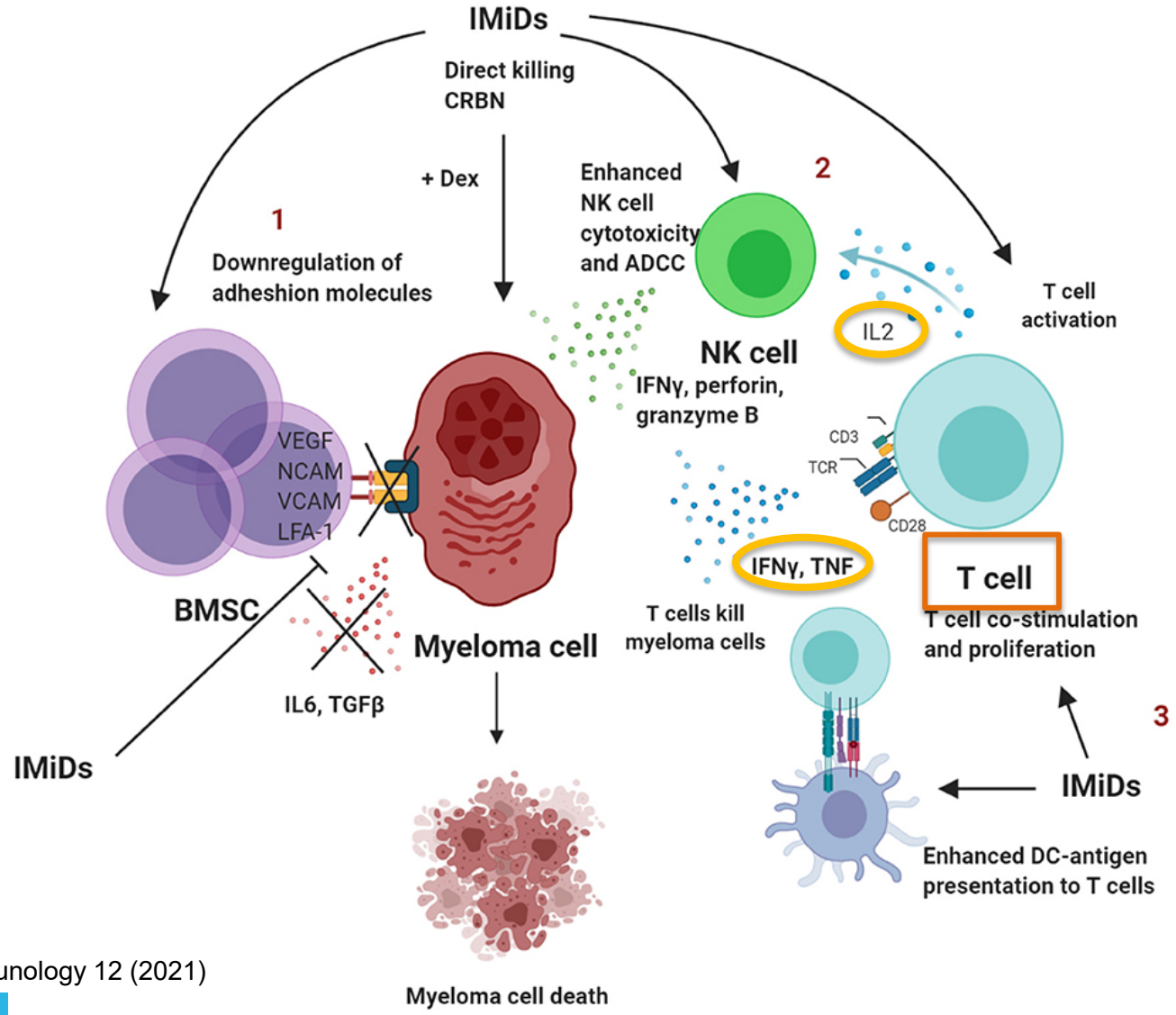
SP-3164 Shows Improved Activity Over And Significant Synergy With SOC Agents in Follicular Lymphoma



- SP-3164 shows single agent tumor growth inhibition (TGI) in a Follicular Lymphoma model and is significantly better than the standard of care (SOC) agent
- In combination with a SOC agent, SP-3164 causes tumor regressions.

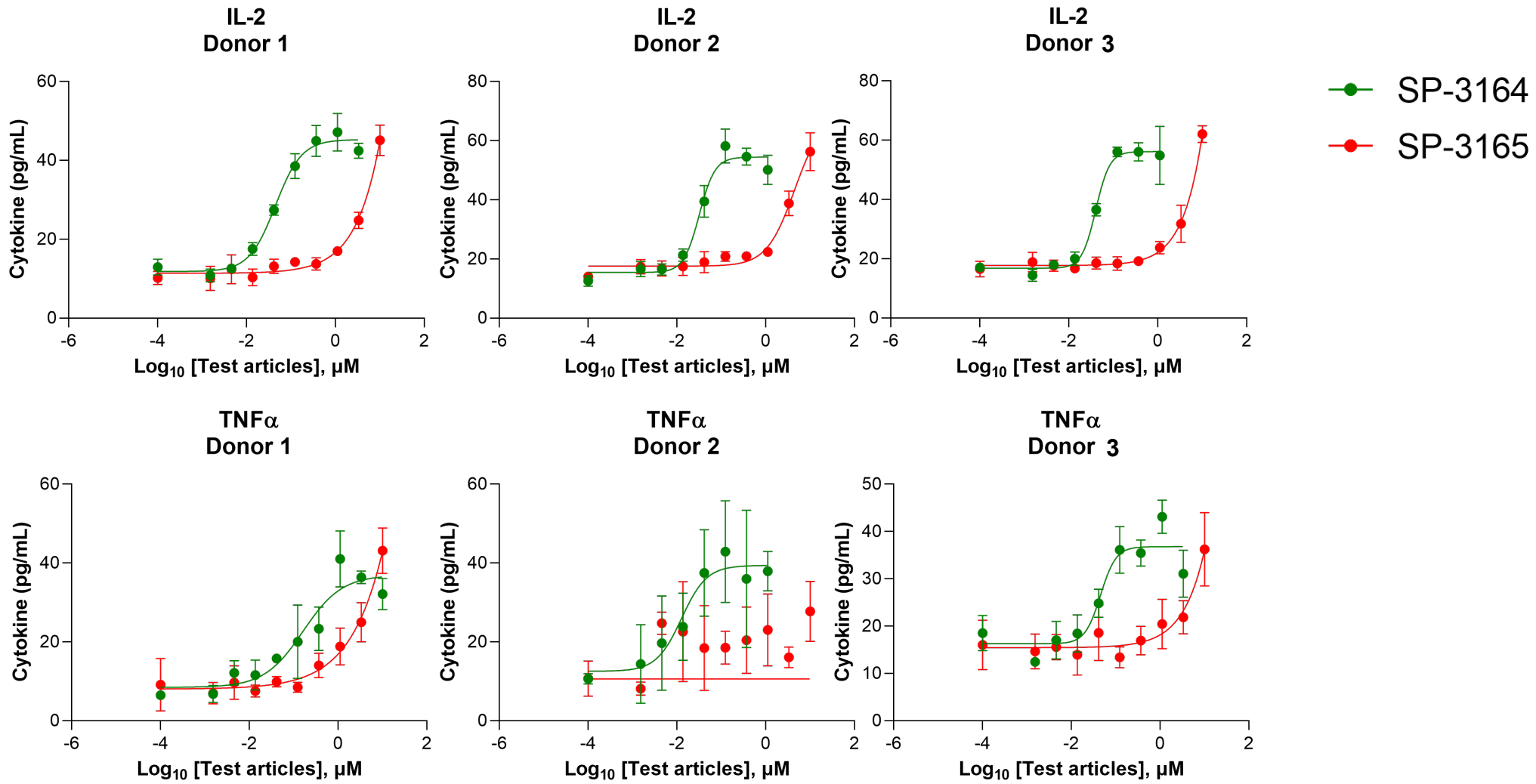
1. Standard of care details available under CDA

SP-3164 Exhibits Immune Modulation Effects

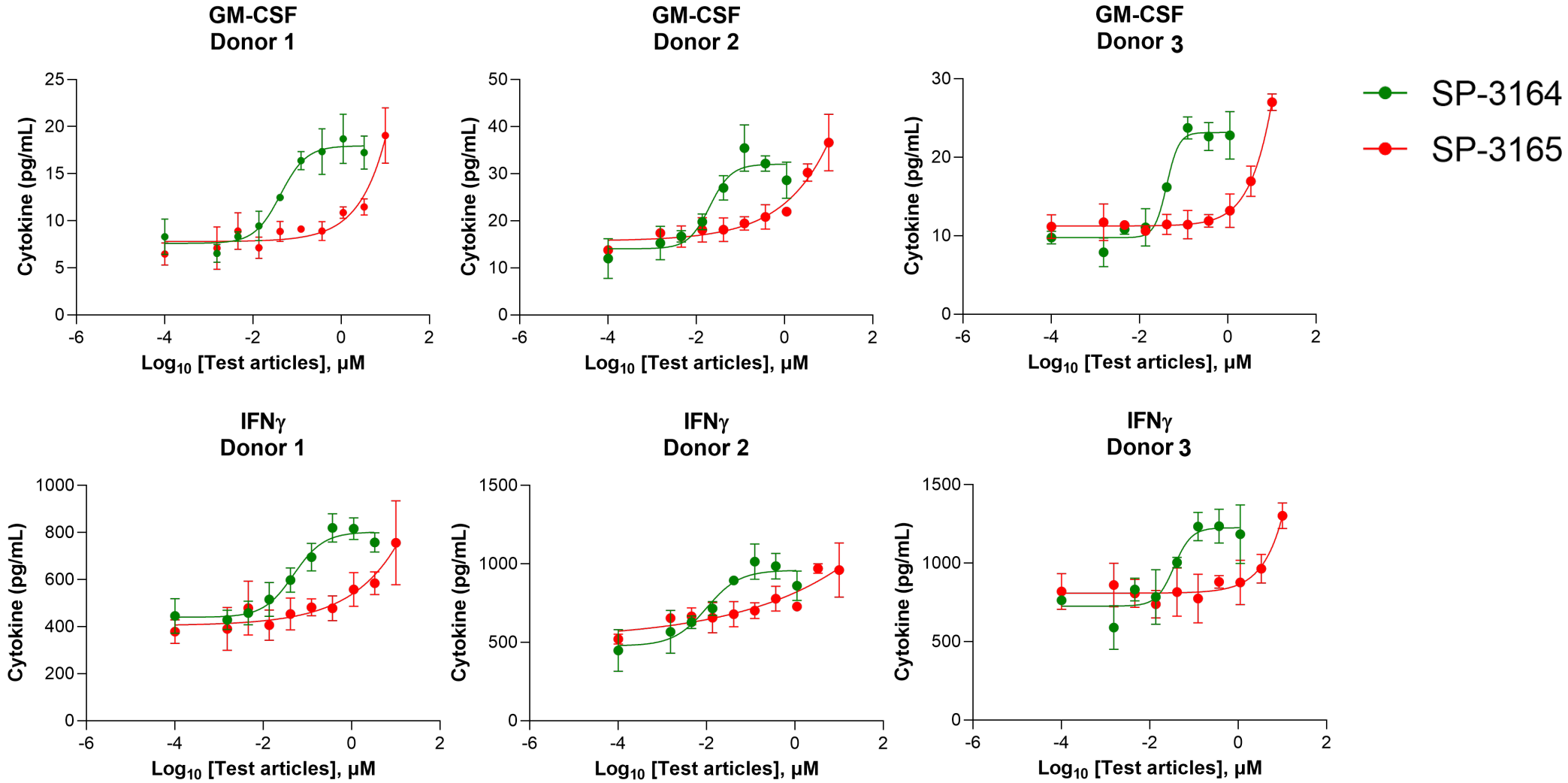


D'Souza, C. et al. Frontiers in Immunology 12 (2021)

SP-3164 Exhibits Immune Modulation Effects



SP-3164 Exhibits Immune Modulation Effects



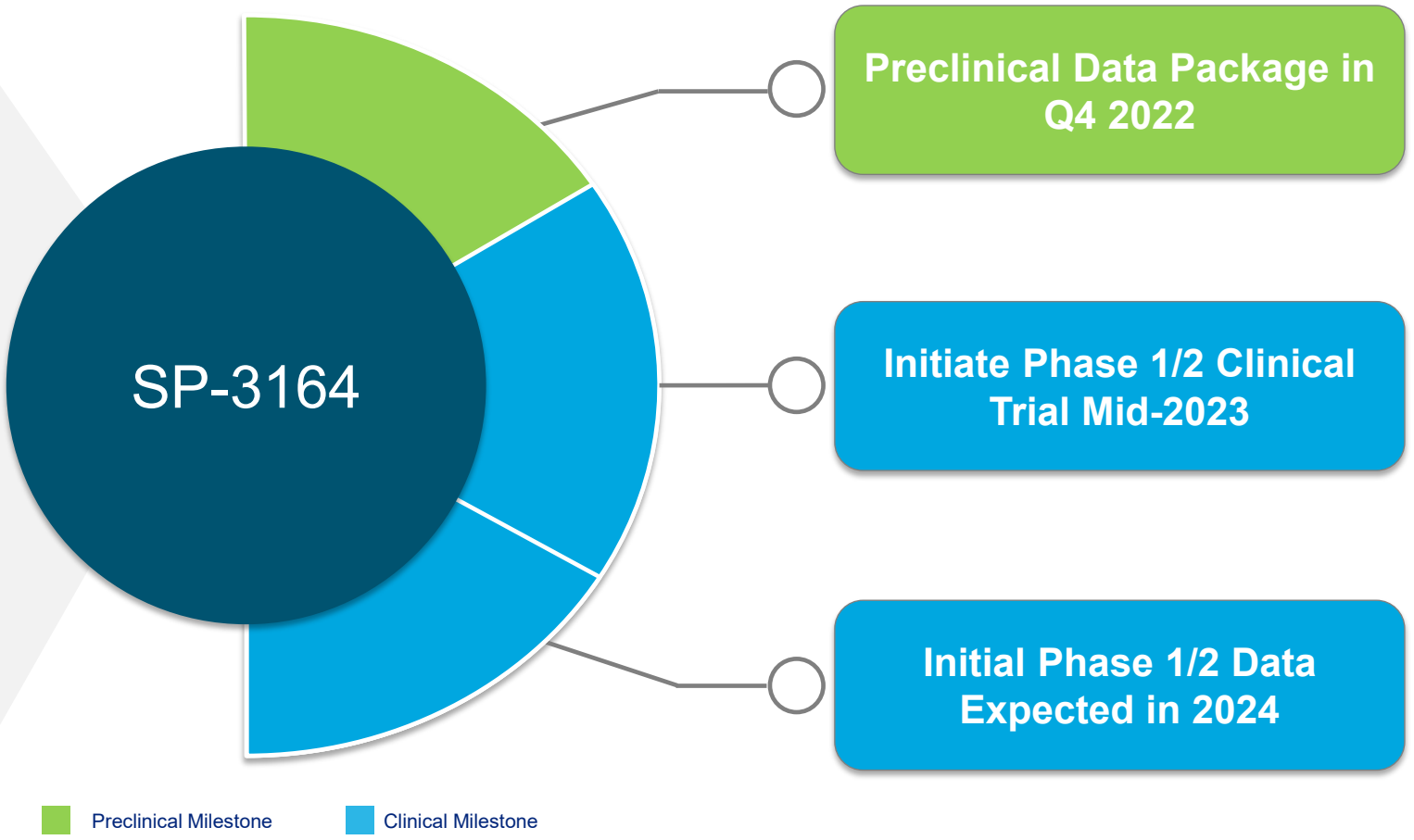
SP-3164 Current Status and Upcoming Milestones

Completed

- FDA Pre-IND meeting process
- API CMC optimization
- GMP API batch
- Drug product CMO contracting
- GLP toxicology CRO contracting & scheduling
- Initial in vitro and in vivo studies
- Dose ranging toxicology
- Multiple Myeloma and Lymphoma advisory boards

Ongoing and Upcoming

- Drug product formulation development
- GLP toxicology
- In vitro IND enabling studies
- Extensive in vivo single agent, combination therapy and comparator studies



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
- 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.
- In in vivo DLBCL studies, SP-3164 showed synergistic activity with rituximab (anti-CD20), resulting in tumor regressions and performing significantly better than the approved regimen, lenalidomide and rituximab.

Future Directions

- Explore SP-3164 in other heme malignancies and solid tumors
- Continue assessing PK/PD effects to better understand clinical dosing
- Continue exploring immuno-oncology effects and potential combinations for SP-3164
- The presented data support clinical investigation of SP-3164 and a trial is planned for 2023

Acknowledgements

Daniela Santiesteban, PhD
Justine Delgado, PhD
Sheila DeWitt, PhD*
Vincent Jacques, PhD*
Ray Starrett, MSc
Nadeem Mirza, MD, MPH
Steve Horrigan, PhD
Jim Goebel, PhD

* Employees of DeuteRx, a collaboration partner with Salarius

Thank you!

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