Transcriptomic Reversal Screen — SSc Skin scRNA-seq

Generated: 2025-09-18 16:08 | Repo: scleroderma-scvi

Executive Summary

- Atlas-level reversal against LINCS L1000 perturbations across annotated cell types.
- Composite ranking emphasizes total reversal, fibroblast/myofibroblast selectivity, and significance.
- Broad cytotoxics deprioritized; MEK/ERK, EGFR axis, and BET families recur across clusters.
- All results are hypothesis-generating — not clinical guidance.

Shortlist (summary)

base_compound	moa	status	priority_final	total_score	max_rev	neglog10_best_p
PD-0325901	MEK inhibitor	Clinical-stage	3.825211191702425.1	5.157863722237.1	69.089861782002.2	8.089861782008 32
gefitinib	EGFR inhibitor	FDA-approved	2.532581630368546.7	14.533120515214.7	45.742710712531.9	2.742710712531 92
WZ-3105	Unknown/other	Unknown	0.766406616825895.2	15.100374084935.3	35.352156684212.3	5.352156684212389
PD-184352	MEK inhibitor	Clinical-stage	0.553921614707567.3	16.381085503543.2	23.294412240628.4	24.294412240628 44
BI-2536	PLK1 inhibitor	Clinical-stage	0.384484653150285.2	25.227381913202.4	21.435435319456.9	21.435435319456 93
BET bromodomain inhibitor	BET bromodomain inhibitor	Unknown	0.275805214587431.3	31.086666198076.8	18.288710885588.4	18.288710885588 94
JNK-9L	JNK inhibitor	Unknown	0.097095321759894.2	28.126276027872.5	15.105318017733.7	15.105318017733769
BET bromodomain inhibitor	BET bromodomain inhibitor	Clinical-stage	0.161889760962247.3	27.389933487013.3	18.355542651163.9	18.355542651163592
sirolimus	mTOR inhibitor	FDA-approved	0.174531468283768.3	26.108791039883.1	18.463558314551.9	18.463558314551 93
pelitinib	EGFR inhibitor	Unknown	0.437989162439029.5	20.454419486807.1	17.093816405511.8	17.093816405511827
GSK-429286A	Unknown/other	Unknown	0.466606670117856.2	25.728922736705.4	18.288710885588.4	18.288710885588 94
dovitinib	Unknown/other	Unknown	0.661732736803349.4	19.190983007719.9	13.943885324770.4	13.943885324770244
olaparib	Unknown/other	Unknown	1.003007155260799.4	19.701742063221.6	11.630269021921.7	11.630269021921713
KIN001-043	Unknown/other	Unknown	1.335172036296179.3	17.299014731911.8	10.697297659414.8	10.697297659414286
withaferin-a	Unknown/other	Unknown	1.994577252938787.4	17.730771502799.2	10.152577883389.4	10.152577883389414

Dose/Time Consistency (summary)

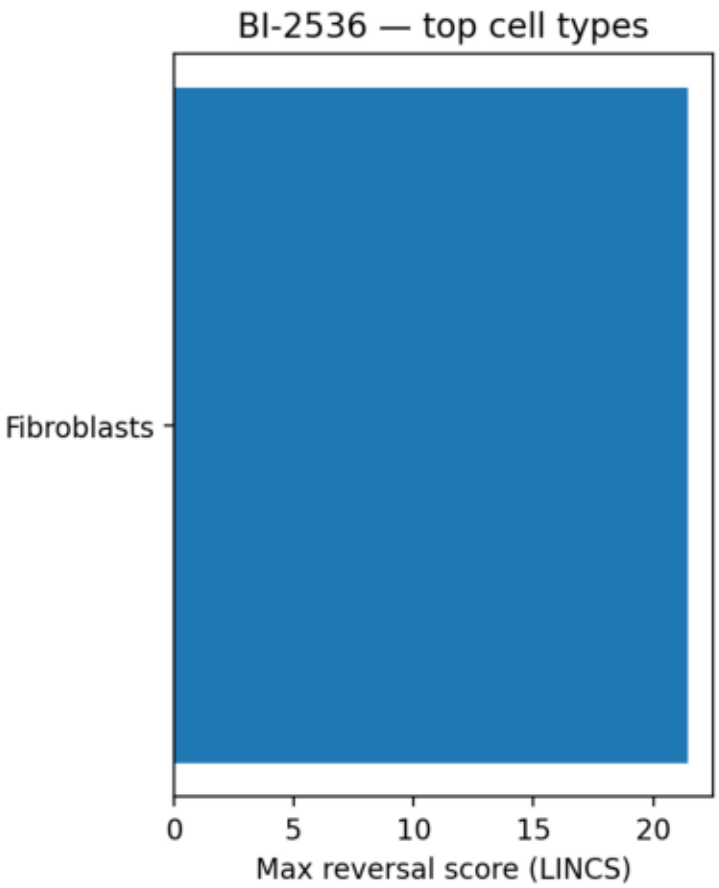
base_compound	n_profiles	times_seen	dose_min	dose_max	score_mean	score_sd	best_p_min
PD-184352	1	24.0	10.0	22.0	1.2941224062844	5.0767731	nan67564584e-23
BI-2536	2	24.0	0.37	19.5	1.0748516261848	3.4697443	6.6197437	58248452e-22
sirolimus	1	24.0	10.0	18.4	1.4635583145519	3.4390753	nan36555272e-19
PD-0325901	6	3.0,24.0	1.11	18.3	1.2491049557055	8.6396024	9.6396024	7706718e-29
GSK-429286A	1	24.0	0.04	18.2	0.2871088558894	5.1438596	nan78551735e-19
I-BET151	4	24.0	1.11	17.9	1.1939568676688	5.2046245	6.2046245	6770615e-19
gefitinib	8	3.0,24.0	0.12	16.3	1.4029746962646	5.8283763	5.8283763	1993481e-24
I-BET	2	24.0	3.33	14.2	1.1704047547741	1.9942145	1.9942145	7057674e-19
WZ-3105	14	24.0	0.04	14.1	1.1769730446385	2.8296031	2.8296031	7445607e-24
pelitinib	3	3.0,24.0	3.33	13.0	1.6648863343539	8.2907139	8.2907139	0412015e-18
dovitinib	2	24.0	3.33	11.3	1.7898361931657	3.1396074	3.1396074	3729023e-14
JNK-9L	6	24.0	0.37	10.9	1.5945696845586	7.3425084	7.3425084	616633e-16
olaparib	3	24.0	0.04	10.3	1.7851022502868	2.7427578	2.7427578	2132749e-12
withaferin-a	3	24.0	1.11	9.7	1.6434845318784	3.4894011	3.4894011	2565754e-13
KIN001-043	7	3.0,24.0	1.11	8.8	1.4067684030862	9.3775143	9.3775143	1118416e-14

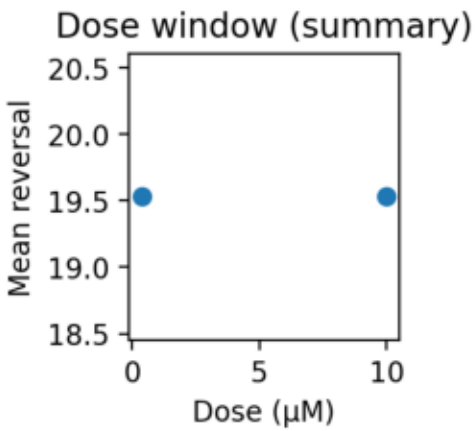
LINCS Coverage (cell types per compound)

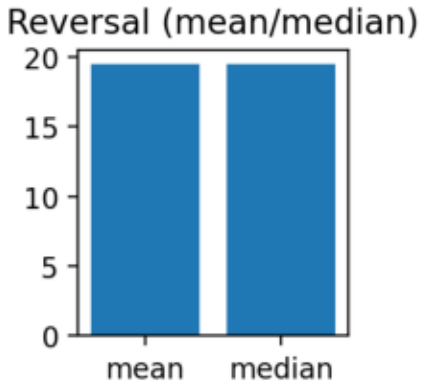
compound	n_celltypes
LJP006 HA1E 24H-CGP-60474-0.37	5
LJP006 HA1E 24H-alvocidib-10	4
LJP006 HA1E 24H-mitoxantrone-3.33	4
LJP006 HME1 24H-gefitinib-0.37	4
LJP006 MCF10A 24H-WZ-4-145-3.33	4
LJP006 HA1E 24H-CGP-60474-3.33	3
LJP006 HA1E 24H-CGP-60474-10	3
LJP006 HA1E 24H-alvocidib-3.33	3
LJP006 HA1E 24H-CGP-60474-1.11	3
LJP006 HCC515 24H-CGP-60474-10	3
LJP006 HME1 24H-AS-605240-3.33	3
LJP006 HME1 24H-PD-0325901-1.11	3
LJP005 A375 24H-PLX-4720-0.04	3
LJP006 HA1E 24H-AZD-5438-10	3
LJP006 A375 24H-alvocidib-10	2
LJP006 HCC515 24H-AT-7519-3.33	2
LJP006 HA1E 24H-alvocidib-0.37	2
LJP005 A375 24H-CGP-60474-1.11	2
LJP005 MDAMB231 24H-WZ-3105-3.33	2
LJP006 A375 24H-JNK-9L-10	2
LJP005 MCF10A 24H-PF-431396-3.33	2
LJP006 A549 24H-mitoxantrone-10	2
LJP006 MDAMB231 24H-CGP-60474-10	2
LJP006 MDAMB231 24H-CGP-60474-0.04	2
LJP006 PC3 24H-CGP-60474-10	2

One-pager — BI-2536

BI-2536

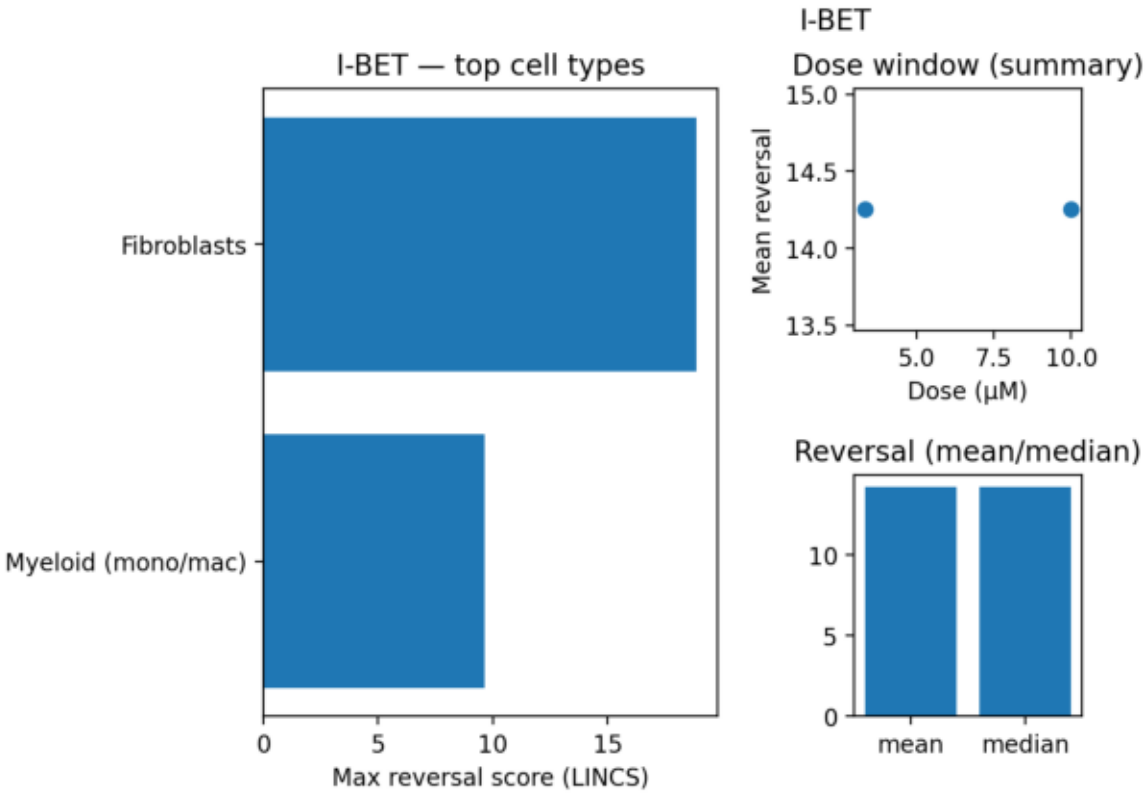






MOA: PLK1 inhibitor
Status: Clinical-stage
Priority: 0.38
Max rev: 21.44
−log10(p): 21.44
Targets present: 1
Missing: nan

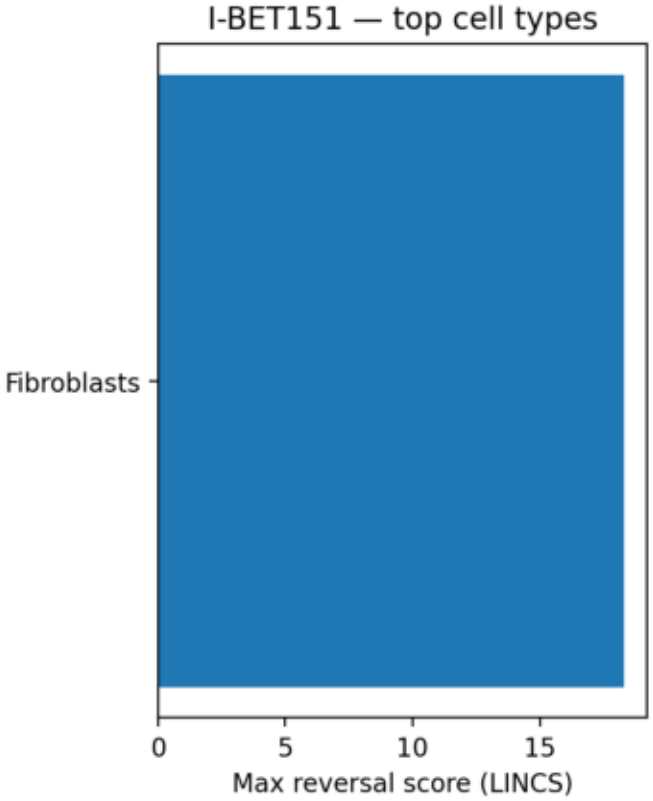
One-pager — I-BET

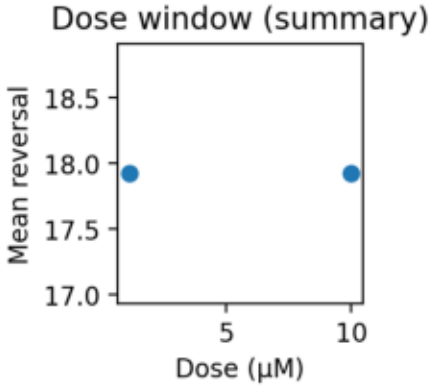


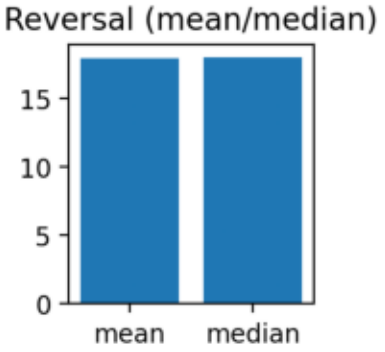
MOA: BET bromodomain inhibitor
Status: Clinical-stage
Priority: -0.16
Max rev: 18.86
−log10(p): 18.86
Targets present: 0
Missing: BRD2,BRD3,BRD4

One-pager — I-BET151

I-BET151

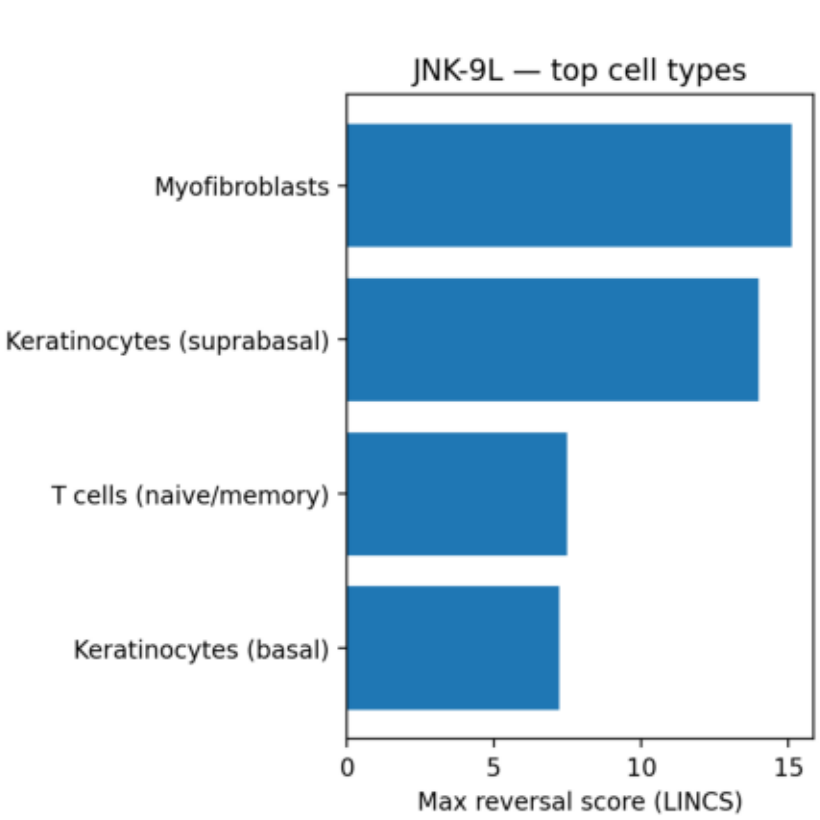


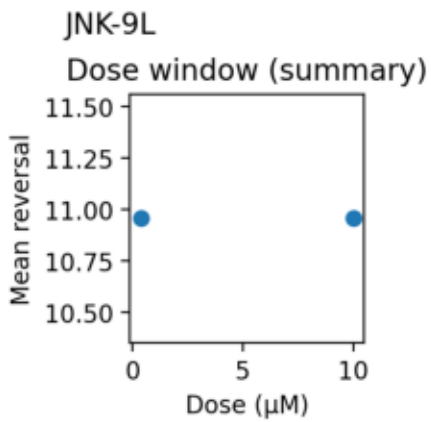


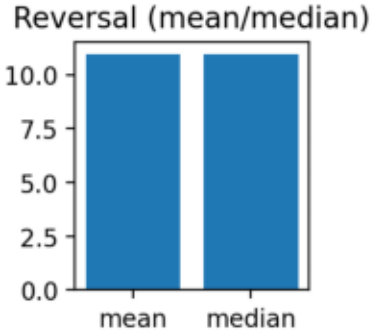


MOA: BET bromodomain inhibitor
Status: Unknown
Priority: 0.28
Max rev: 18.29
−log10(p): 18.29
Targets present: 0
Missing: BRD2,BRD3,BRD4

One-pager — JNK-9L

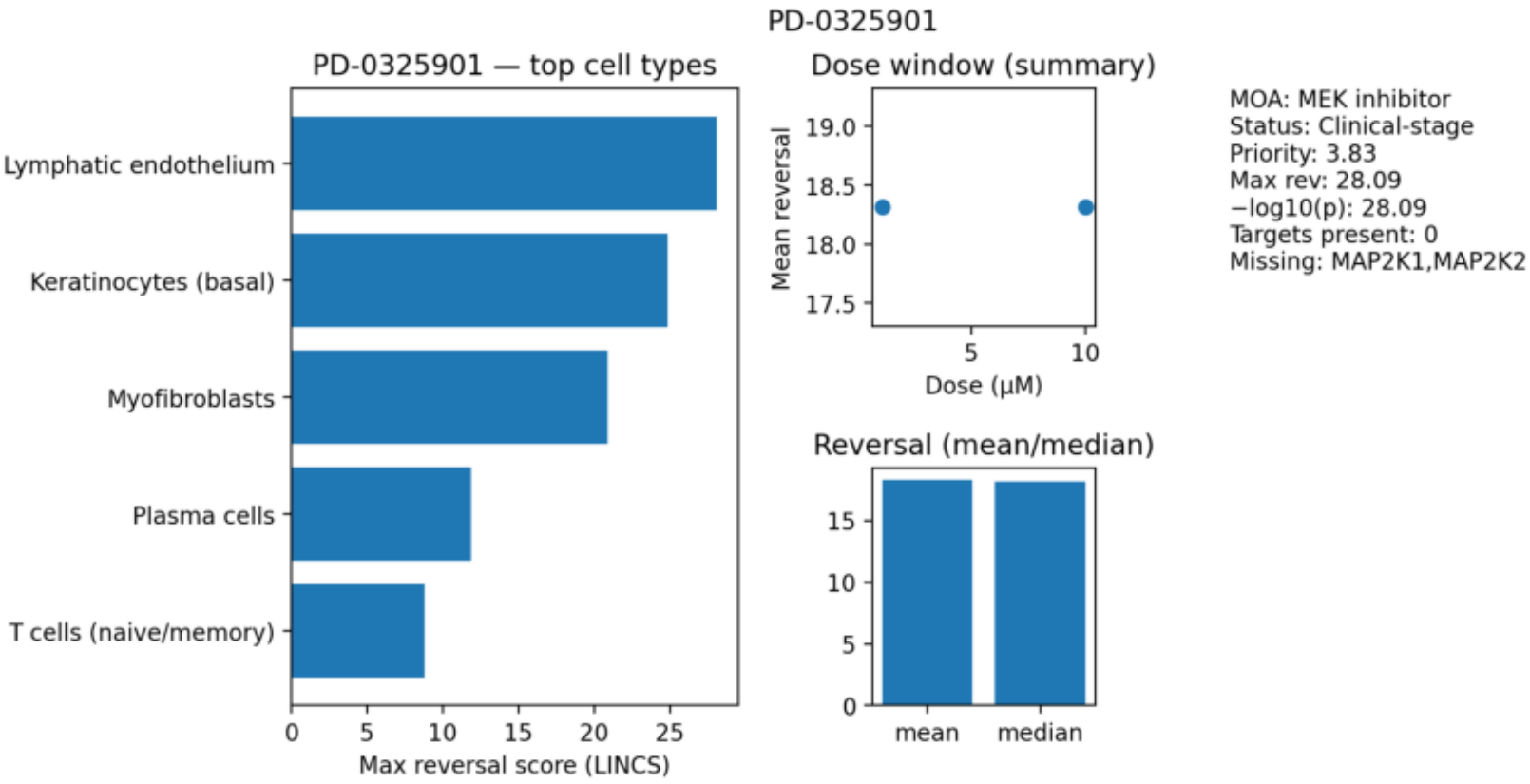






MOA: JNK inhibitor
Status: Unknown
Priority: 0.10
Max rev: 15.11
−log10(p): 15.11
Targets present: 0
Missing: MAPK8,MAPK9

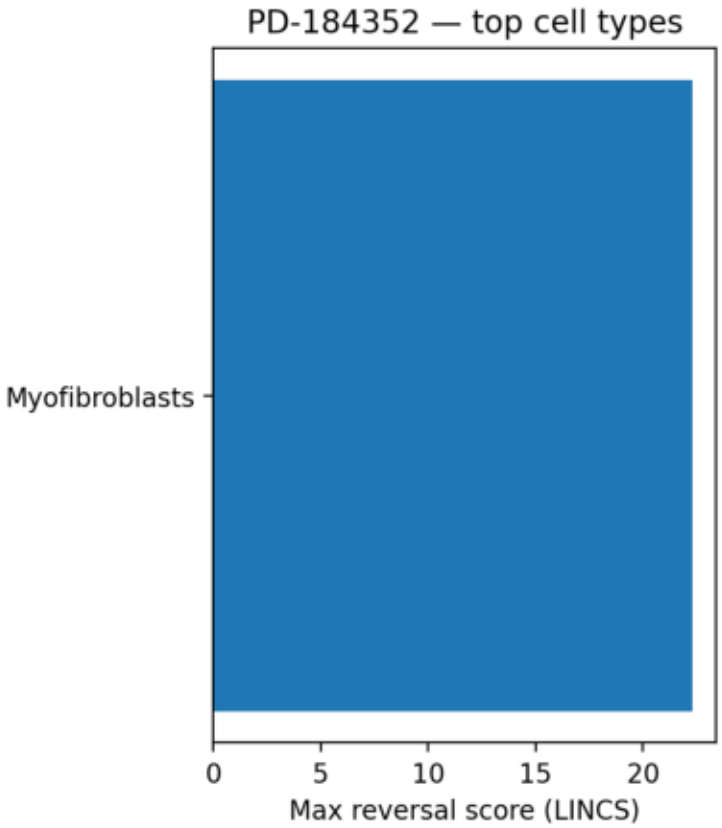
One-pager — PD-0325901

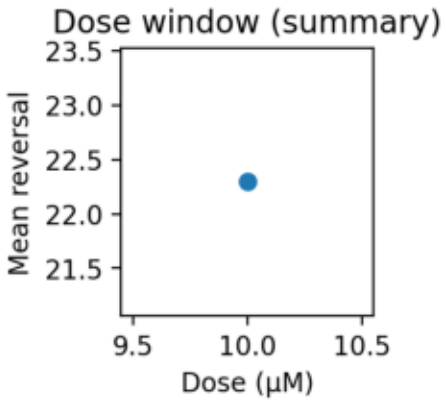


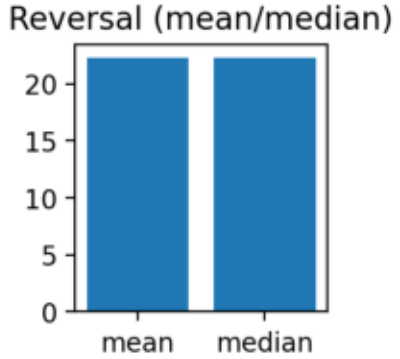
MOA: MEK inhibitor
Status: Clinical-stage
Priority: 3.83
Max rev: 28.09
−log10(p): 28.09
Targets present: 0
Missing: MAP2K1,MAP2K2

One-pager — PD-184352

PD-184352

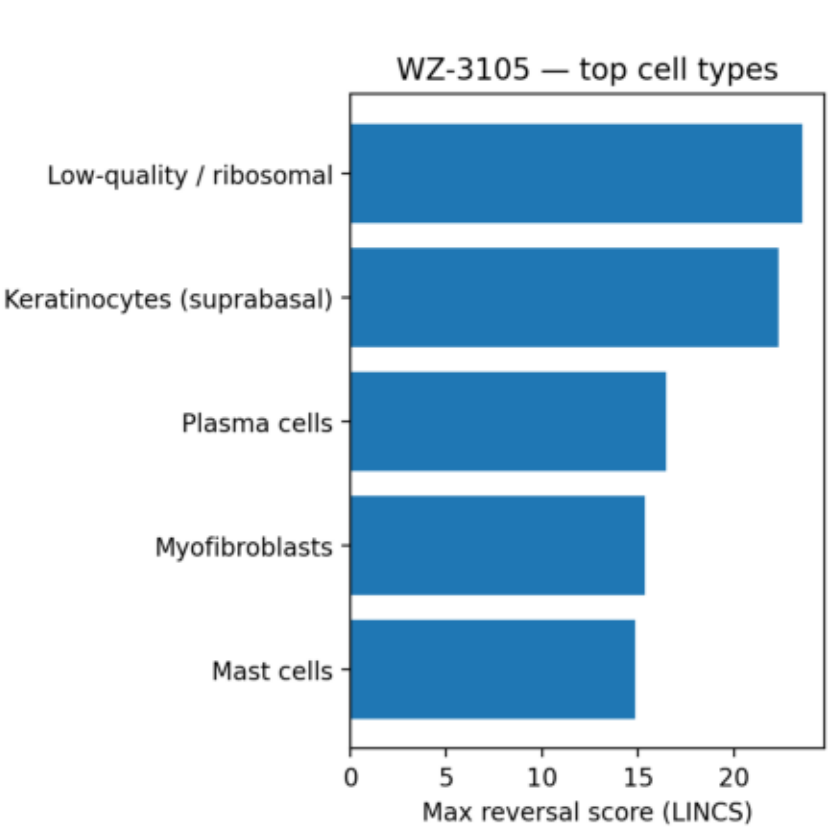


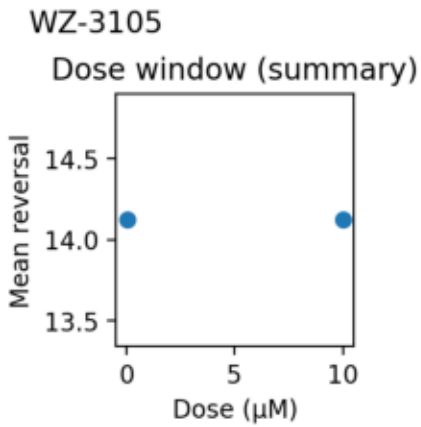


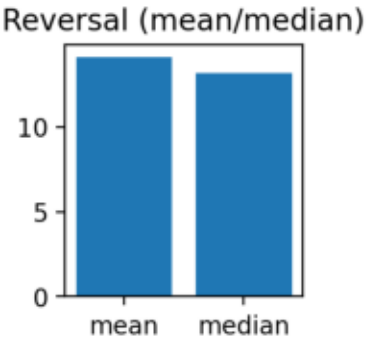


MOA: MEK inhibitor
Status: Clinical-stage
Priority: 0.55
Max rev: 22.29
−log10(p): 22.29
Targets present: 0
Missing: MAP2K1,MAP2K2

One-pager — WZ-3105

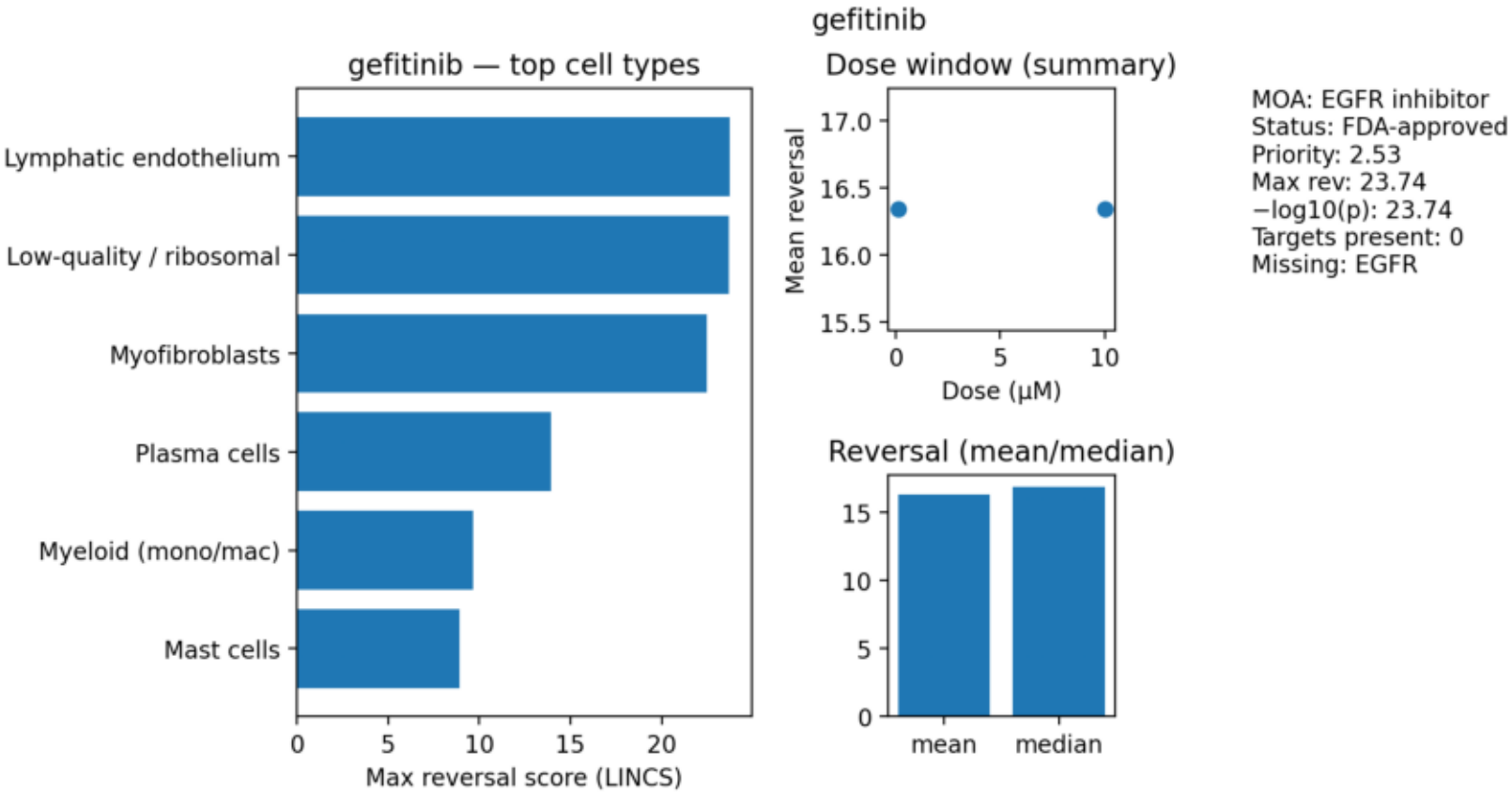






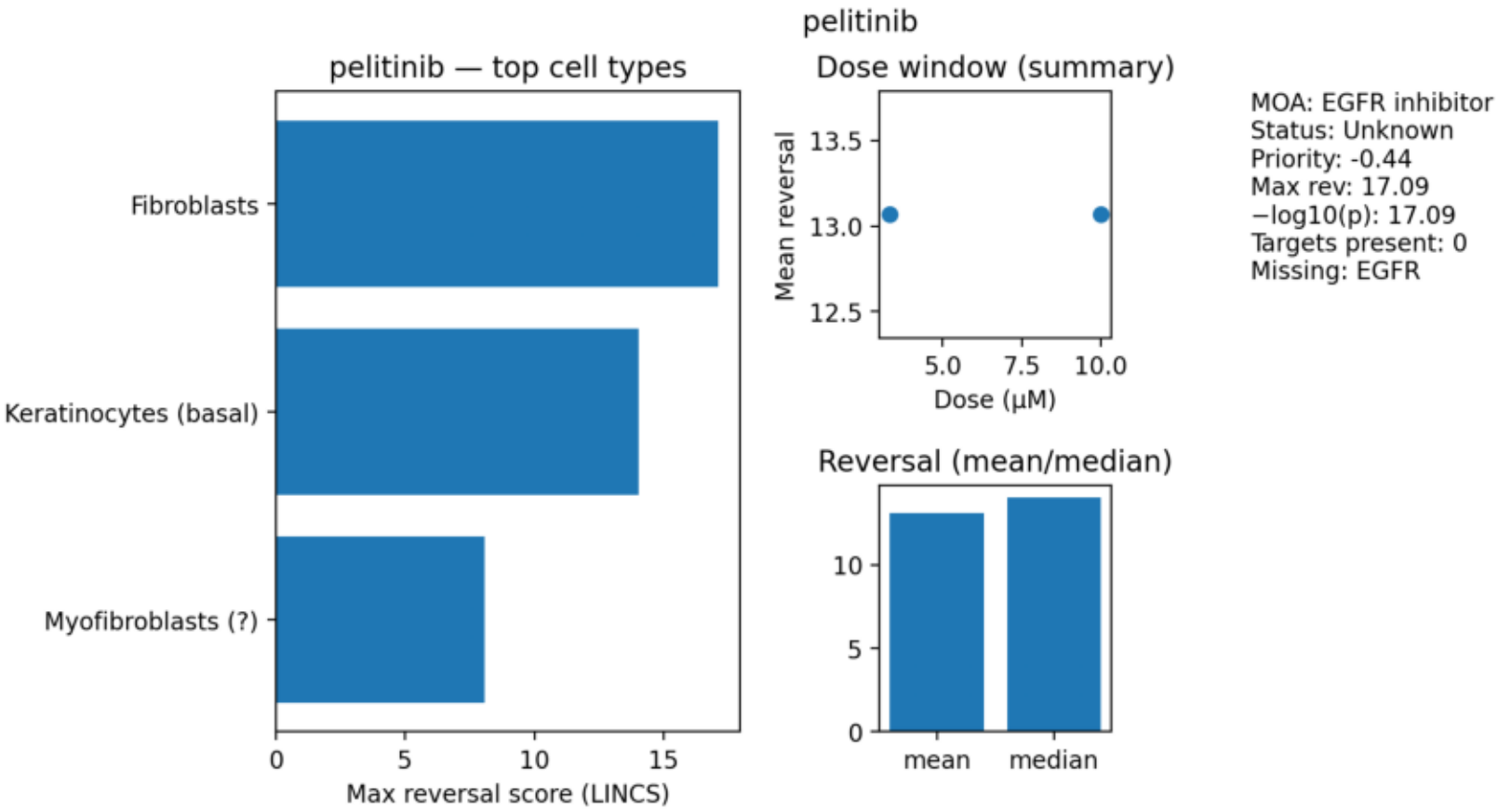
MOA: Unknown/other
Status: Unknown
Priority: 0.77
Max rev: 15.35
−log10(p): 15.35
Targets present: 0
Missing: nan

One-pager — gefitinib



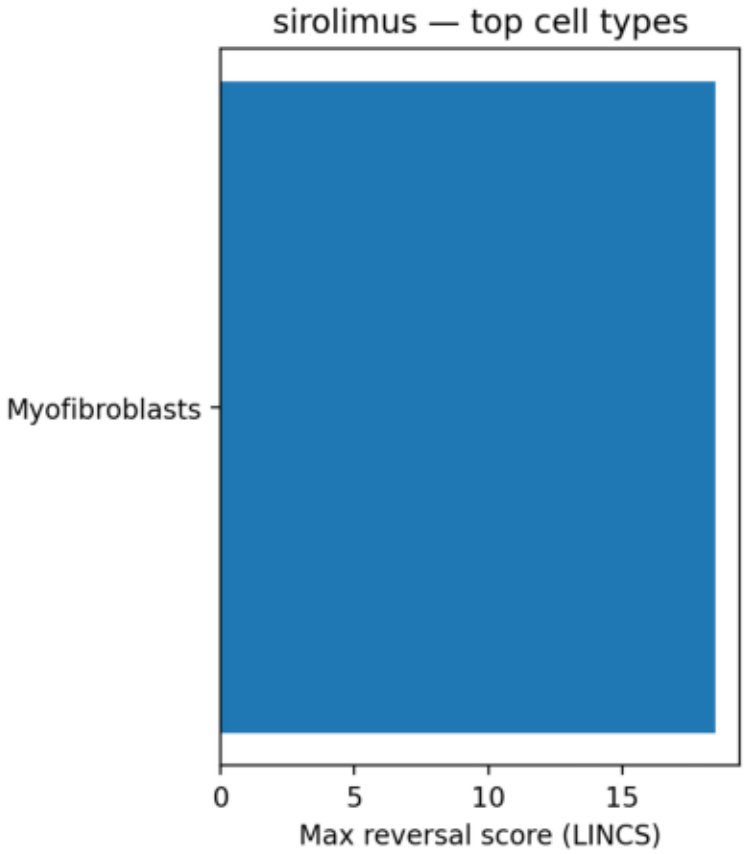
MOA: EGFR inhibitor
Status: FDA-approved
Priority: 2.53
Max rev: 23.74
−log10(p): 23.74
Targets present: 0
Missing: EGFR

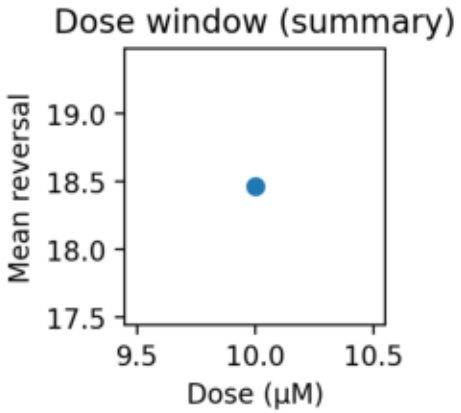
One-pager — pelitinib

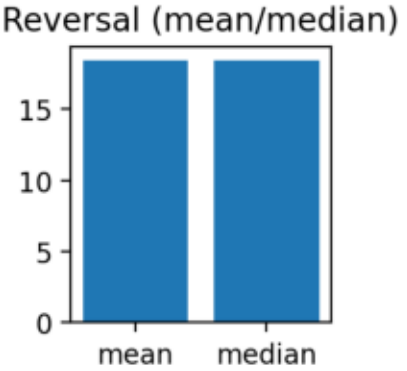


One-pager — sirolimus

sirolimus







MOA: mTOR inhibitor
Status: FDA-approved
Priority: -0.17
Max rev: 18.46
−log10(p): 18.46
Targets present: 0
Missing: MTOR