

# CCS1477: A novel small molecule inhibitor of p300/CBP for the treatment of acute myeloid leukaemia and multiple myeloma

CellCentric

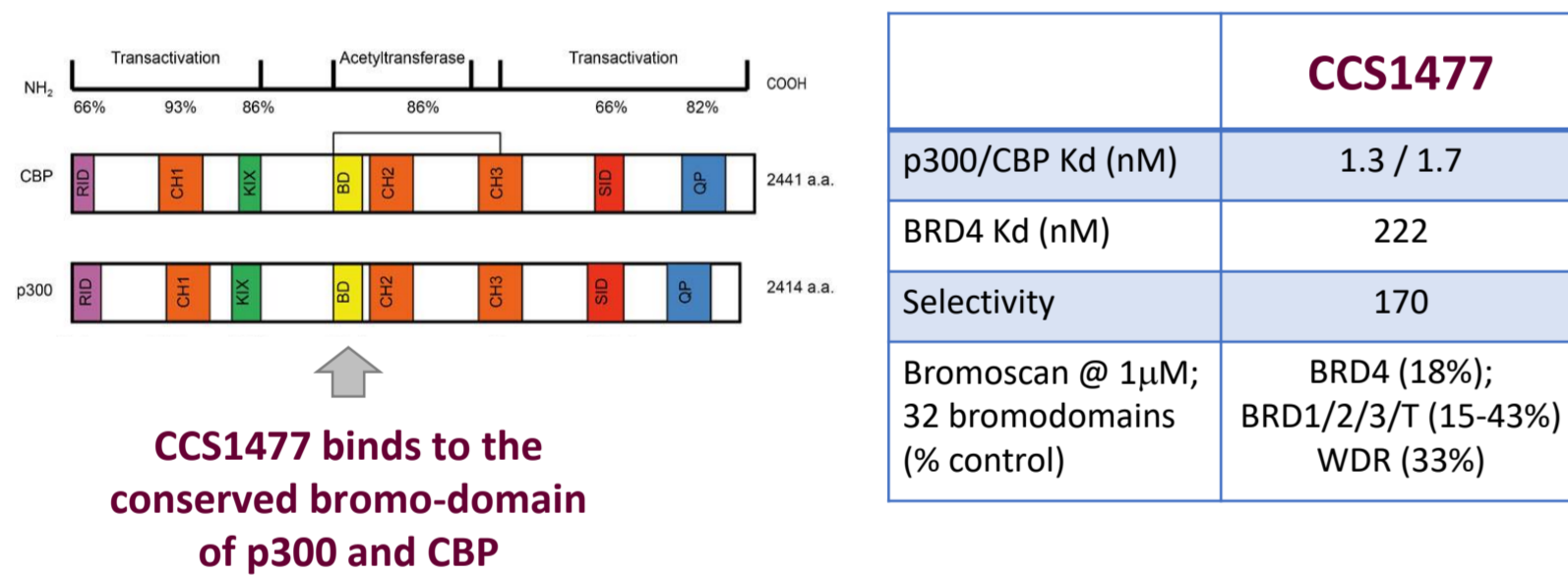
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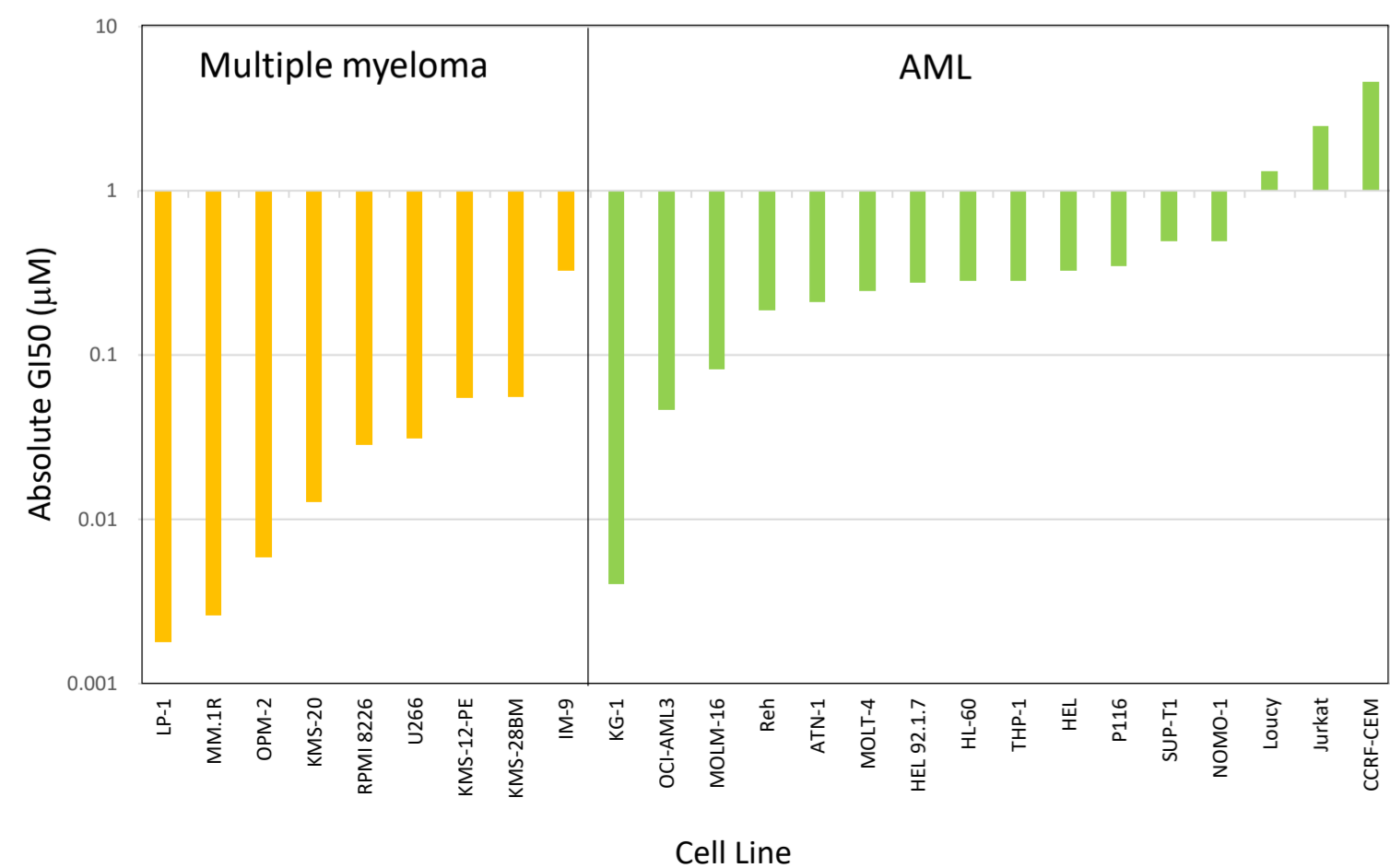
## Introduction

- E1A binding protein (p300) and CREB binding protein (CBP) are two closely related histone acetyl transferase proteins with oncogenic roles in acute myeloid leukemia (AML) and multiple myeloma (MM)
- CCS1477 is a potent, selective and orally bioavailable p300/CBP bromodomain inhibitor, currently in Phase I/II clinical trials
- Here we report the pre-clinical characterization of CCS1477 and its therapeutic application in AML and MM

## 1. CCS1477 is a potent and selective inhibitor of p300/CBP bromodomains

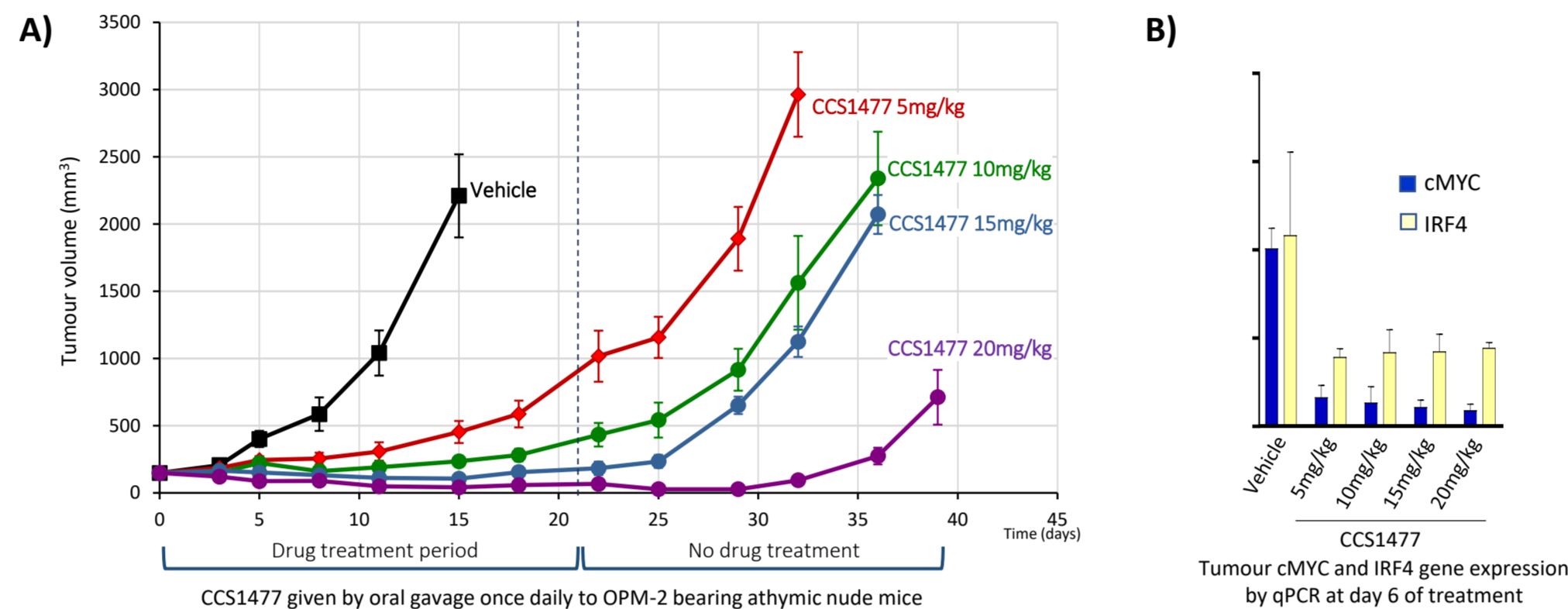


## 2. CCS1477 is a potent inhibitor of proliferation in a panel of multiple myeloma and AML cell lines *in vitro*



Proliferation was measured by CellTiter Glo after treatment with CCS1477 for 72h

## 3. CCS1477 causes tumour regression in a xenograft model of multiple myeloma (OPM-2); continued inhibition following drug withdrawal



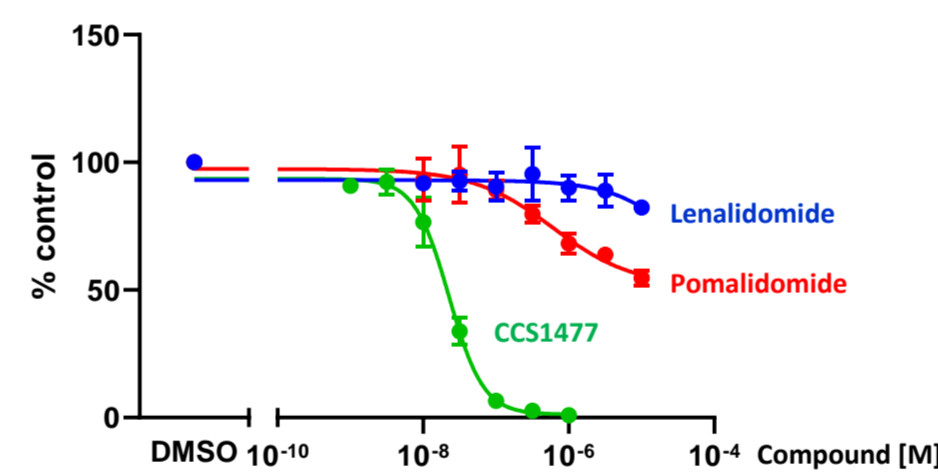
## 4. CCS1477 inhibits proliferation in lenalidomide resistant cell lines

### A) Intrinsic resistance

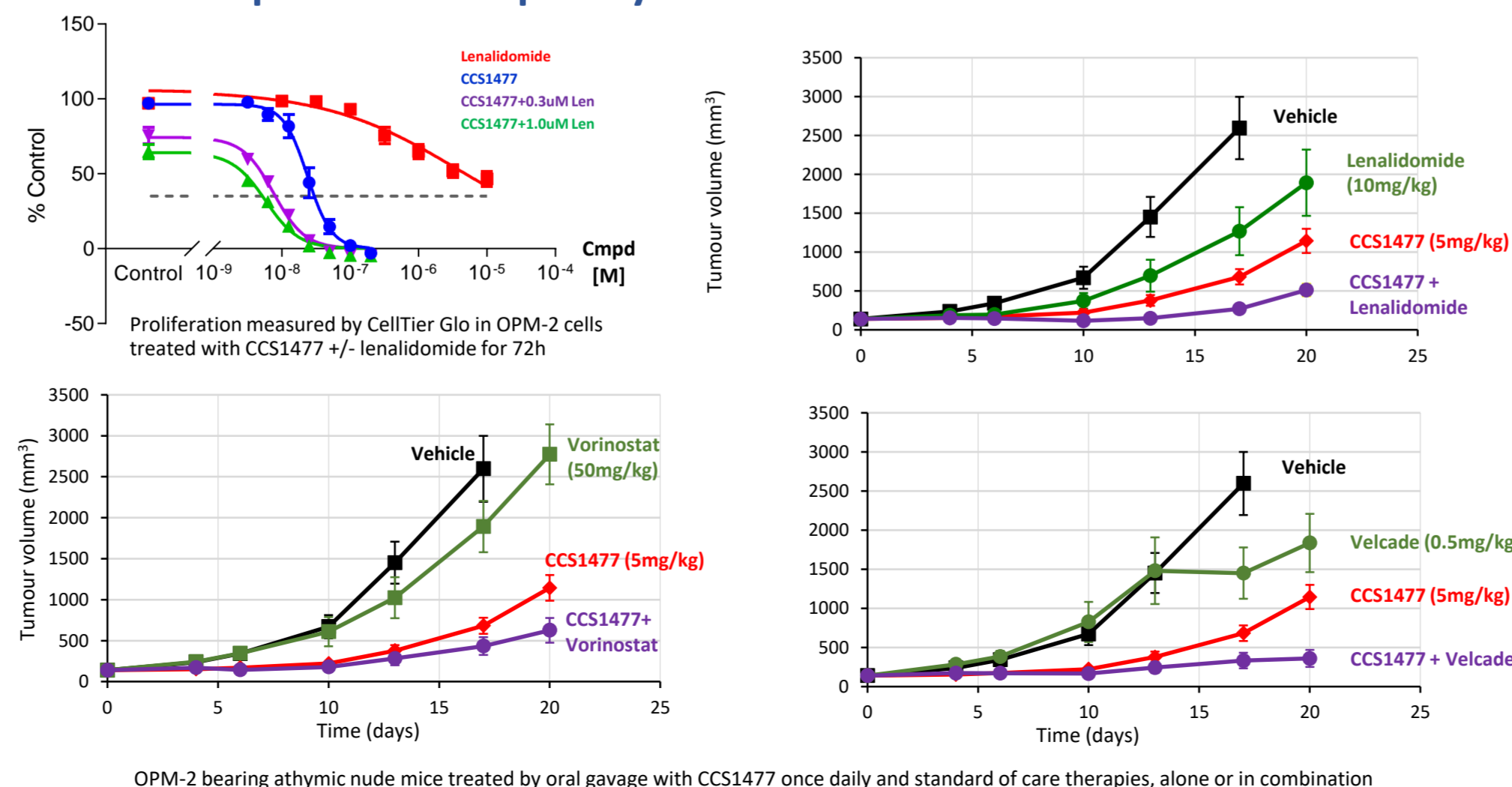
	Cell Line	Lenalidomide GI50 (µM)	CCS1477 GI50 (µM)
Lenalidomide resistant	RPMI-826	>10	0.006
	LP1	>10	0.006
	KMS-11	>10	0.041
Lenalidomide sensitive	OPM-2	0.102	0.005

Lenalidomide resistant and sensitive cells lines were treated with CCS1477 for 5days. Proliferation was measured by CellTiter Glo

### B) Acquired resistance

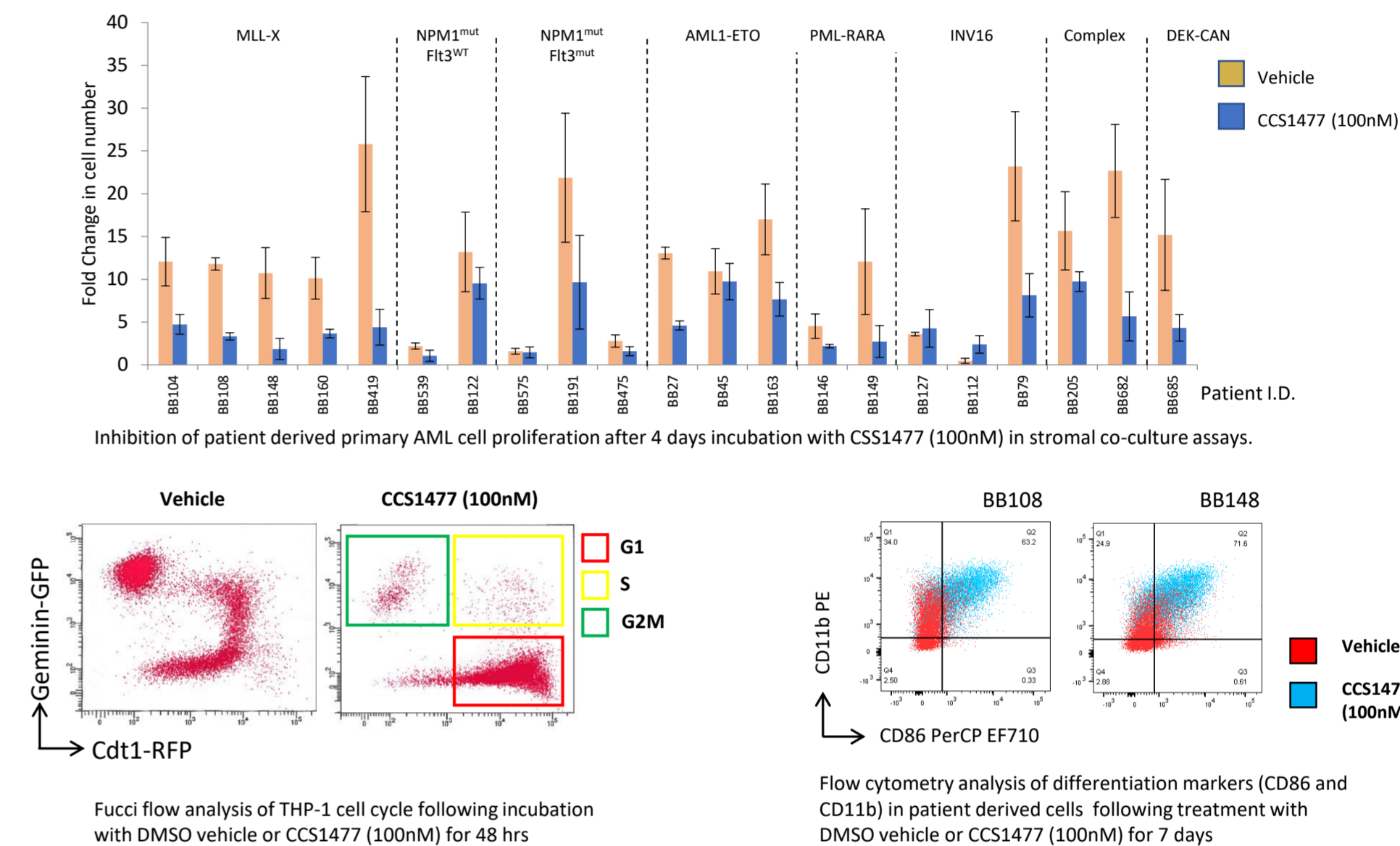


## 5. Superior efficacy and combination benefit of CCS1477 with standard of care therapies for multiple myeloma

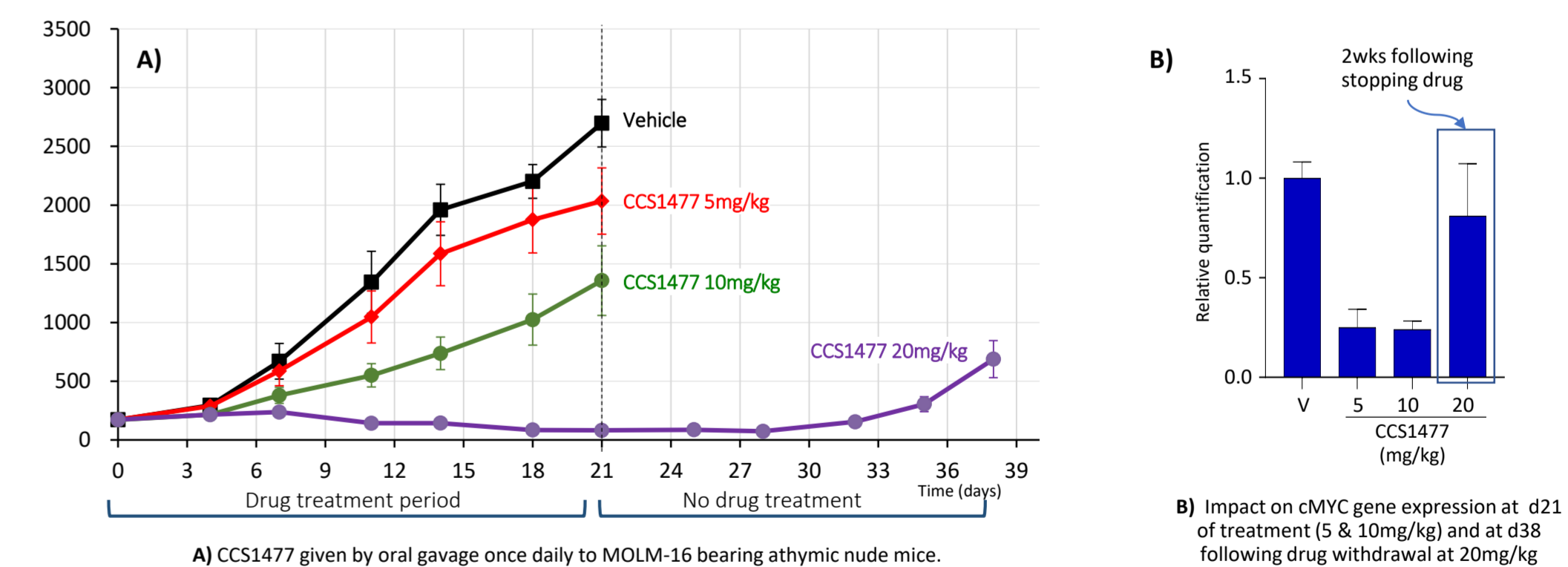


OPM-2 bearing athymic nude mice treated by oral gavage with CCS1477 once daily and standard of care therapies, alone or in combination

## 6. CCS1477 inhibits proliferation, causes G1 cell cycle arrest and induces differentiation in human AML primary cells



## 7. Tumour regression after CCS1477 treatment in a xenograft model of AML (MOLM-16): continued inhibition following drug withdrawal



## Summary

- CCS1477 is a potent and selective small molecule inhibitor of the bromodomain of p300/CBP
- Pre-clinical data presented here, support the clinical development of CCS1477 in MM and AML, either as monotherapy or in combination with standard of care therapies, incl. lenalidomide
- CCS1477 is the first p300/CBP inhibitor to be tested clinically in a Phase I/II trial of haematological malignancies, including MM, AML and NHL (NCT04068597)

**Conflict of interests:** Nigel Brooks and Neil Pegg are employees and stockholders in CellCentric Ltd. There are no relationships to disclose for Meera Raja, Barbara Young, Gary Spencer or Tim Somerville.

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