



IMMUNOGEN, INC.

**The 26th International Conference on Monoclonal
Antibodies and Cancer Stem Cells, Corfu, Greece**

Victor S. Goldmacher, Ph.D.

Senior Director, Cell Biology

June 22-24, 2009

Development of IMGN901 for CD56-positive solid tumors and multiple myeloma



Our Broad, Advancing Pipeline and Partners

| Developer | Compound | Phase I | Phase II | Phase III |
|----------------|-----------------------------|---------|----------|-----------|
| ImmunoGen | IMGN242 | | | |
| | IMGN901 | | | |
| | IMGN388* | | | |
| | Others+ | | | |
| Genentech | T-DM1 | | | |
| | 4 other licenses | | | |
| sanofi aventis | SAR3419 | | | |
| | Others+ | | | |
| Biogen idec | BIIB015 | | | |
| Biotest | BT-062** | | | |
| Bayer | Target licensed 4Q08 | | | |
| Other | Multiple | | | |

*Centocor has opt-in rights

**ImmunoGen has opt-in rights

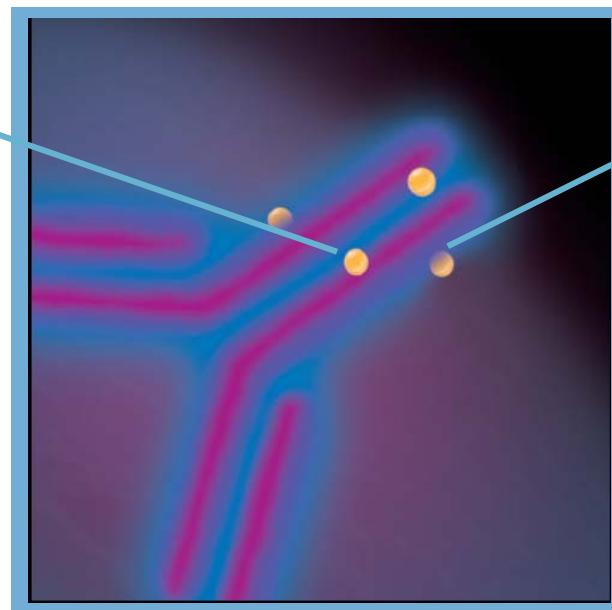
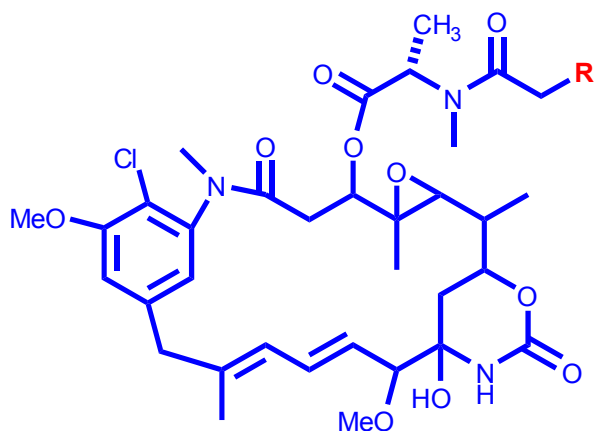
+Is or includes naked antibodies

Proprietary
cell-killing agent
DM1

NCAM-targeting
antibody huN901

Covalent linkage
(*disulfide*)

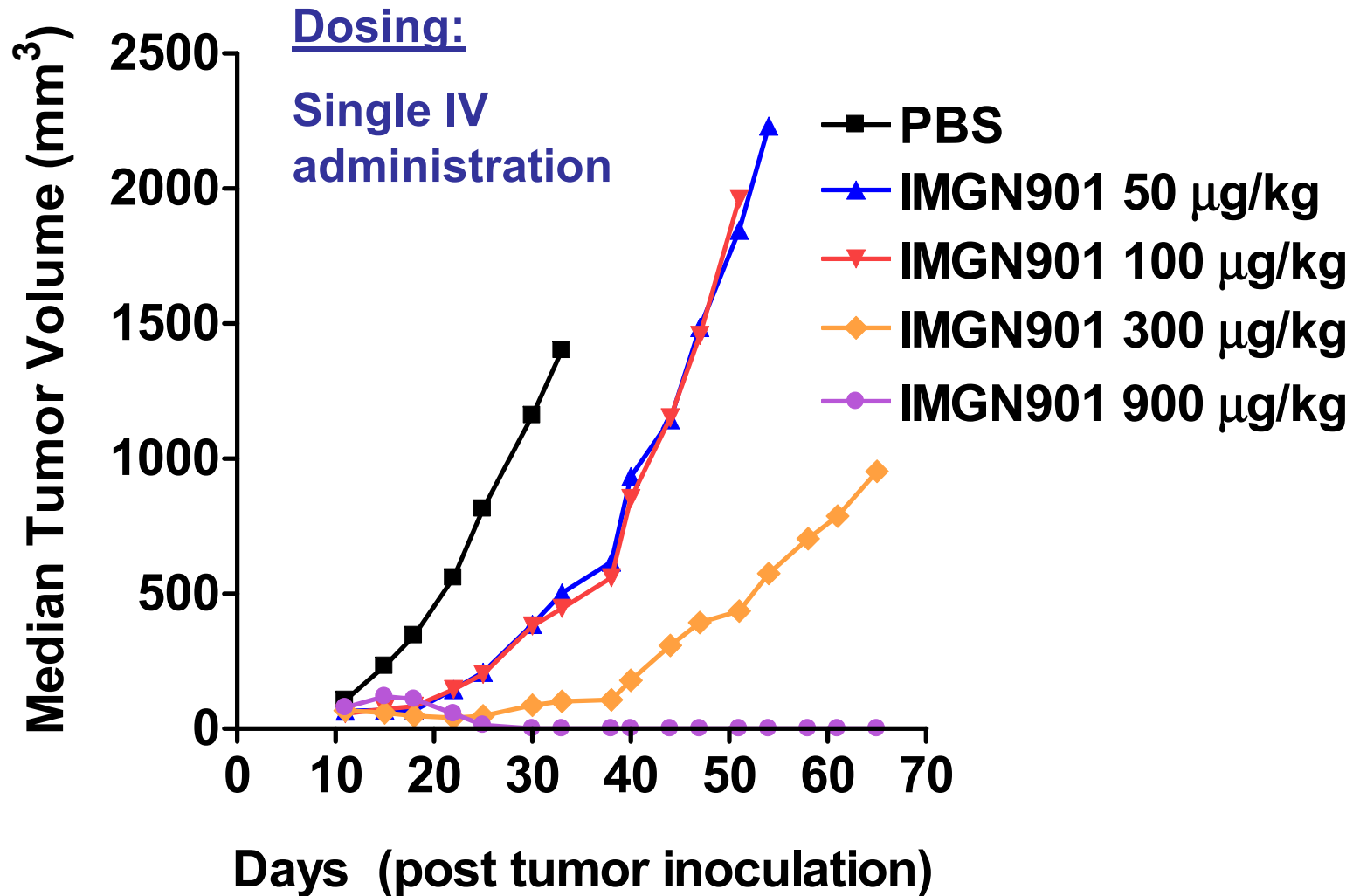
- Stable in blood
- Cytotoxic maytansinoid released inside cell



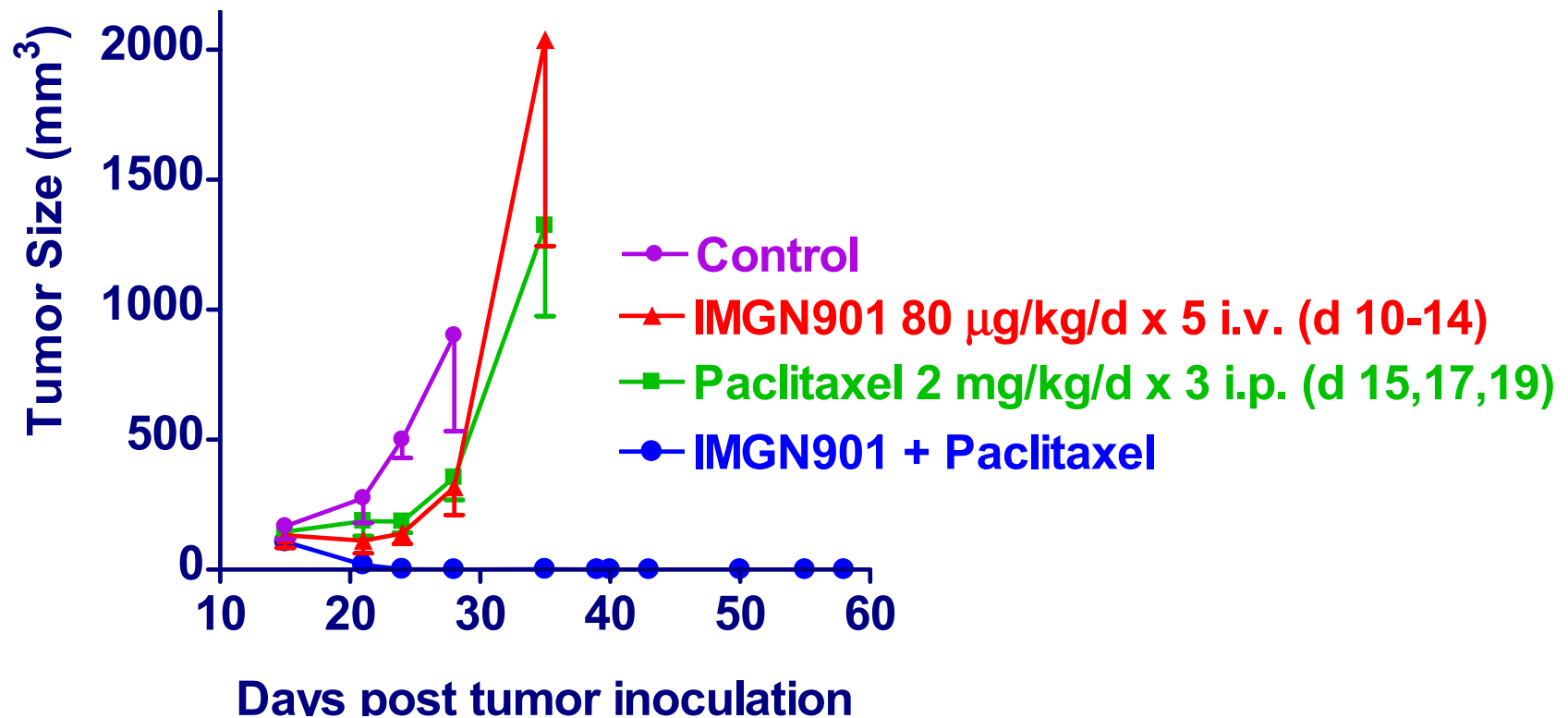
Expression of CD56 by Human Tumors

- **Small Cell Lung Cancer**
 - ✓ 97% (65/67 cases) showed strong uniform cell surface staining
- **Multiple Myeloma**
 - ✓ 78% (43/55cases) showed strong expression
- **Neuroendocrine Tumors**
 - ✓ 78% (88/113 cases) showed strong expression
 - Pancreatic: 56% (9/16); Gastrointestinal: 68% (22/32); Typical and atypical carcinoid of lung: 88% (29/33); Large cell neuroendocrine carcinoma of lung: 80% (4/5)
- **Ovarian Tumors**
 - ✓ 57% (77/135 cases) are CD56-positive
 - Strong expression: Serous papillary carcinoma 58% (23/40); Cystadenocarcinoma 36% (9/25); Adenocarcinoma 31% (8/26)
- **Neuroblastoma**
 - ✓ 100% (15/15 cases)
- **Other Indications**
 - ✓ CD56⁺ leukemia, Wilms' tumor, Merkel cell carcinomas CD56⁺ lymphoma, rhabdomyosarcoma, astrocytoma, schwannoma, osteosarcoma

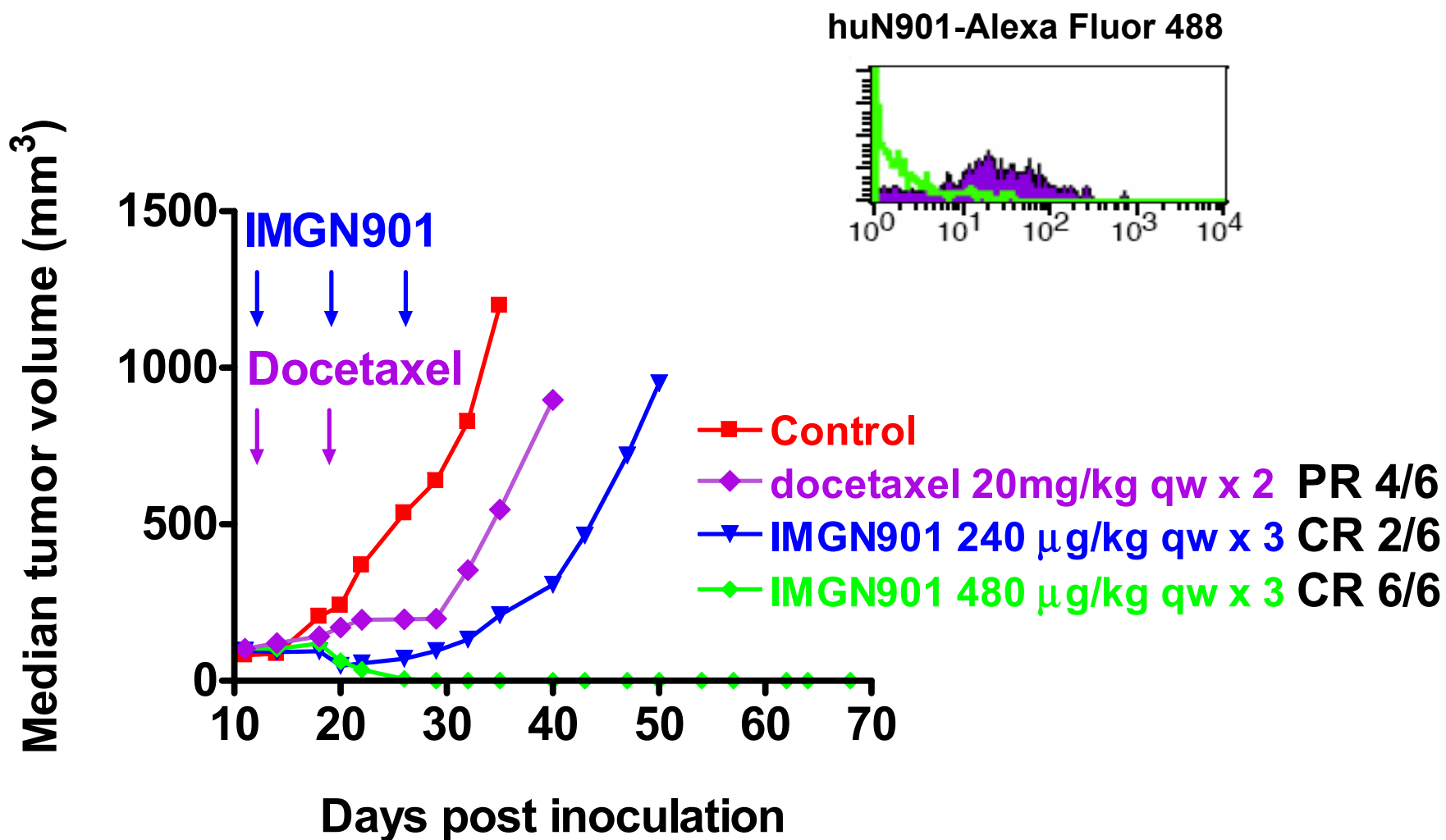
IMGN901 (huN901-DM1) is active in the SW2 small cell lung carcinoma xenograft model in mice

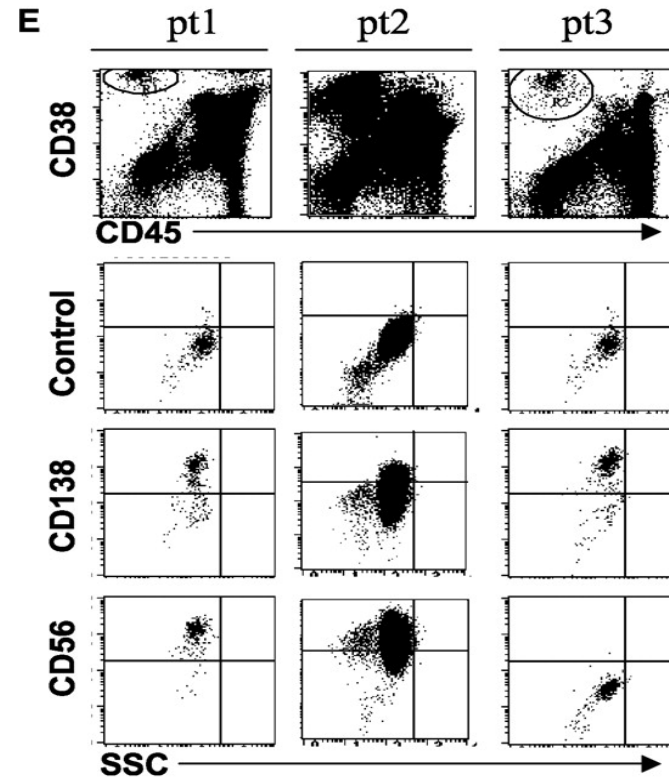
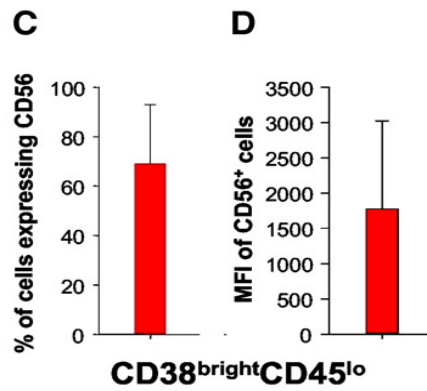
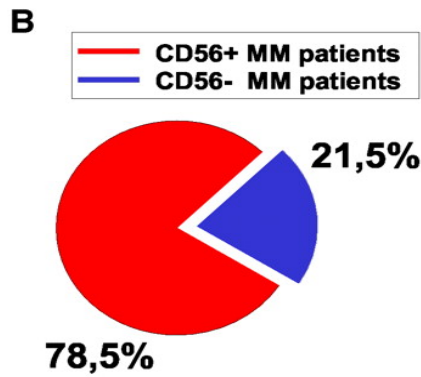
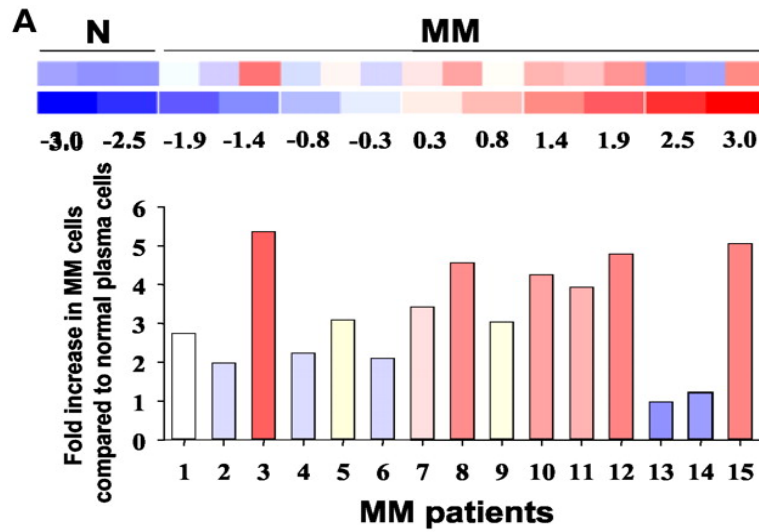


IMGN901 + Paclitaxel combination therapy in SCLC NCI N417 xenograft model in mice



Activity of IMGN901 in the COLO720E ovarian xenograft model

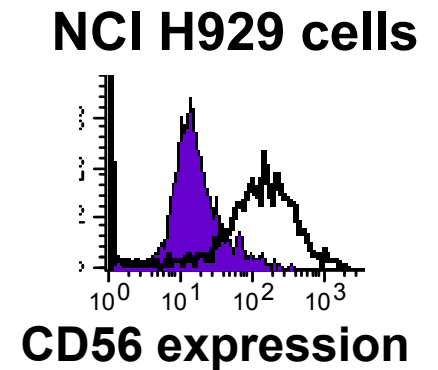
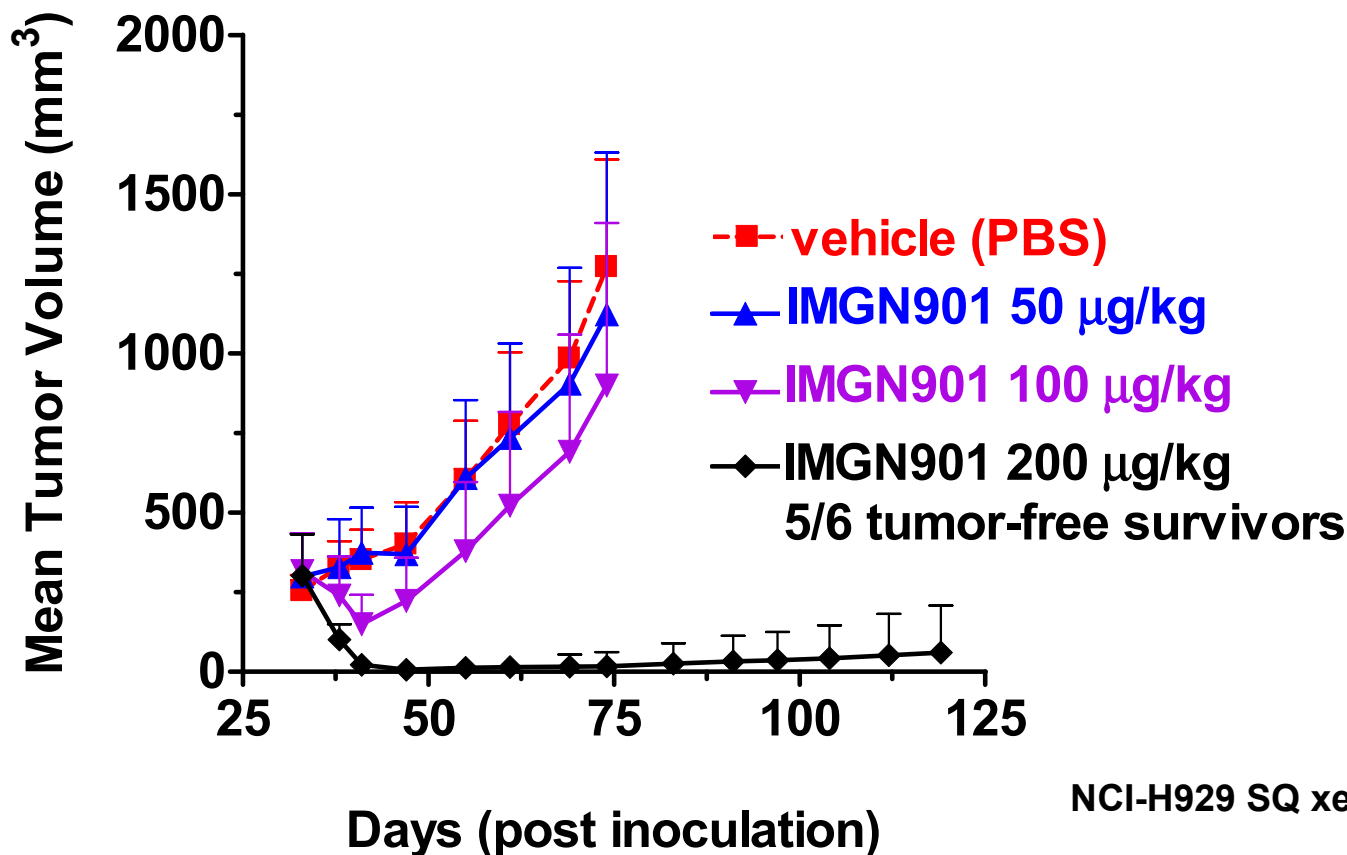




Tassone, P. et al. Cancer Res 2004;64:4629-4636

Activity of IMGN901 in the NCI-H929 model

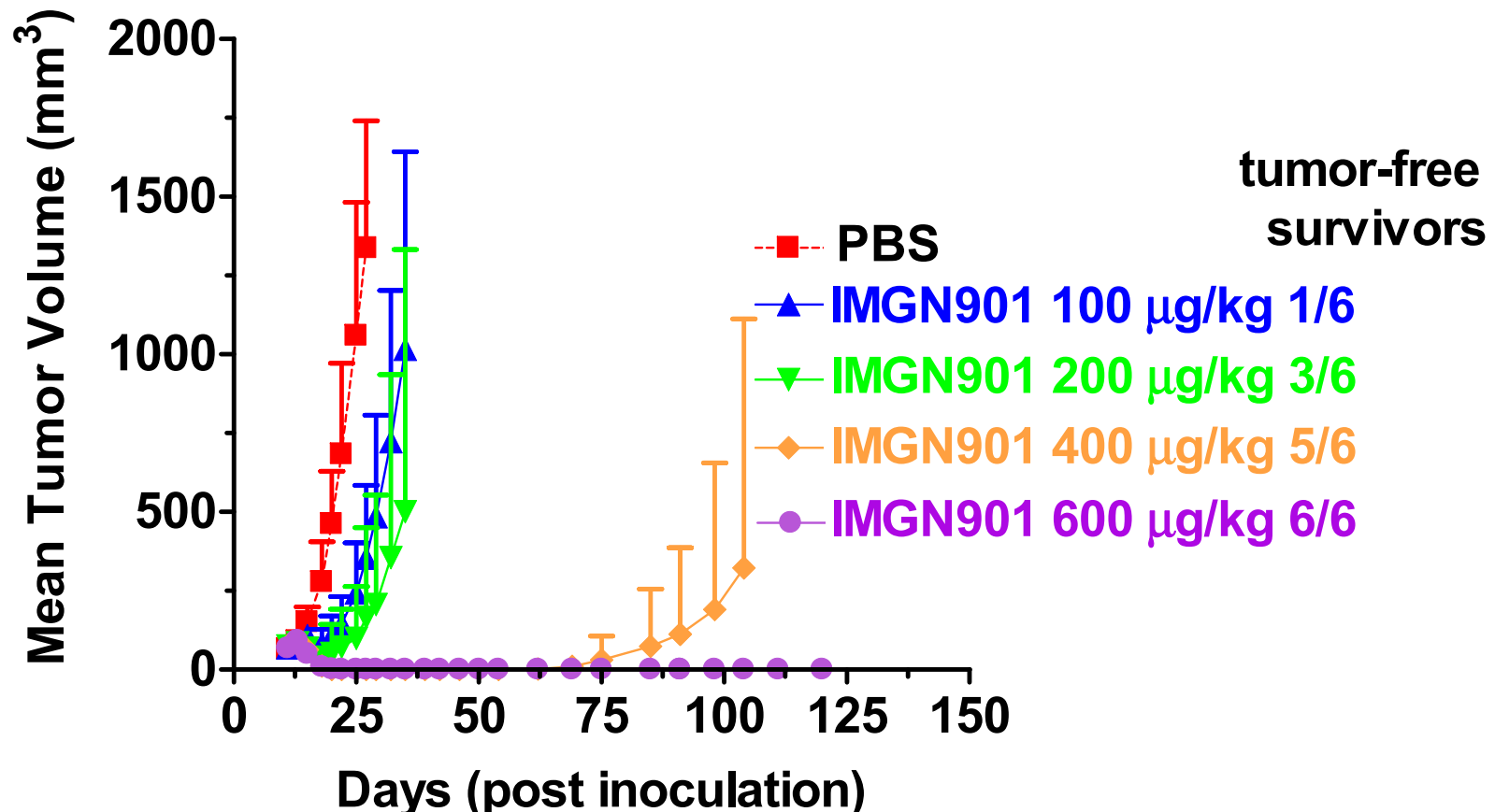
Highly sensitive



NCI-H929 SQ xenografts in CB17 SCID mice

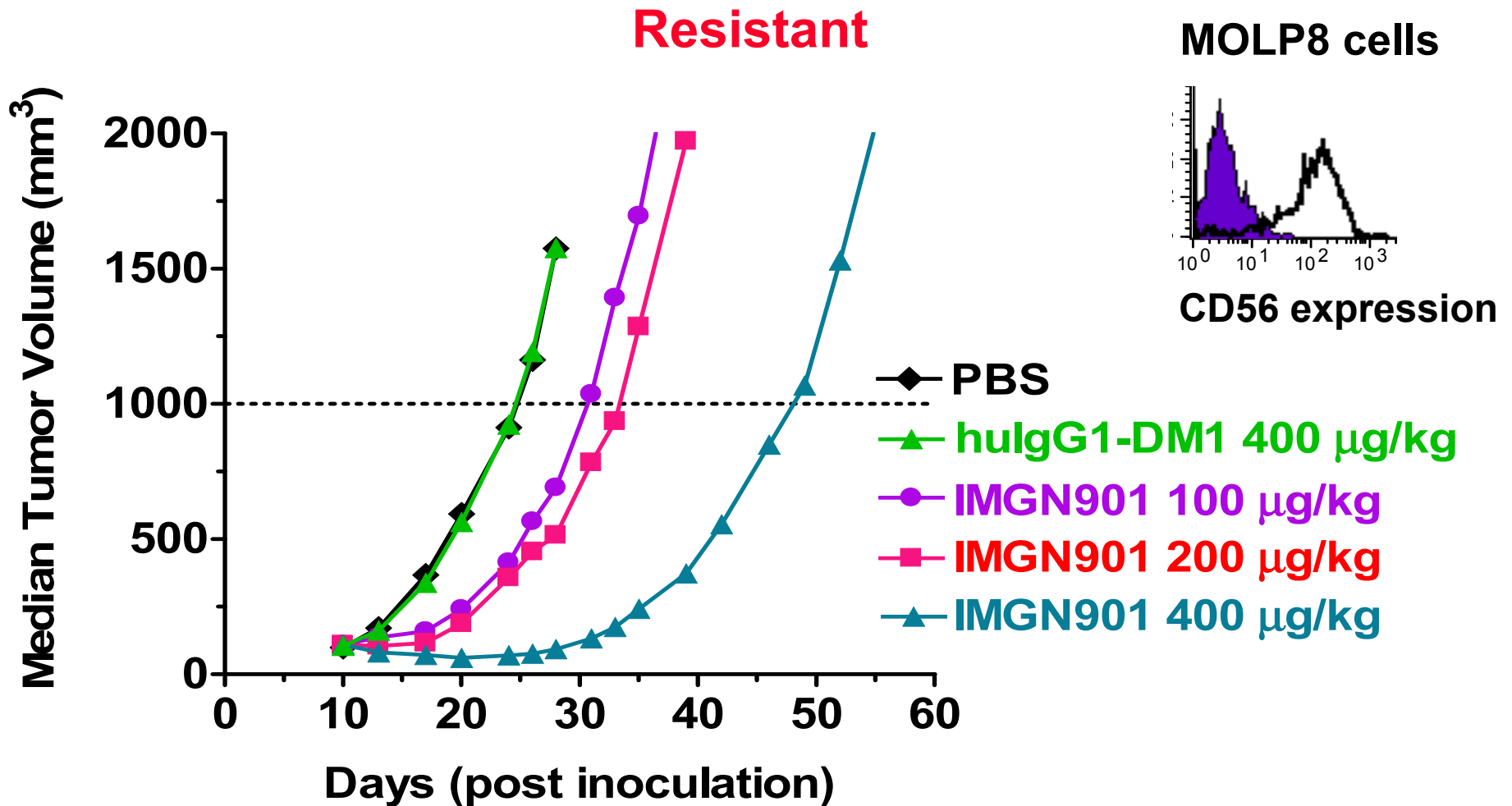
Activity of IMGN901 in the OPM2 model

Moderately sensitive



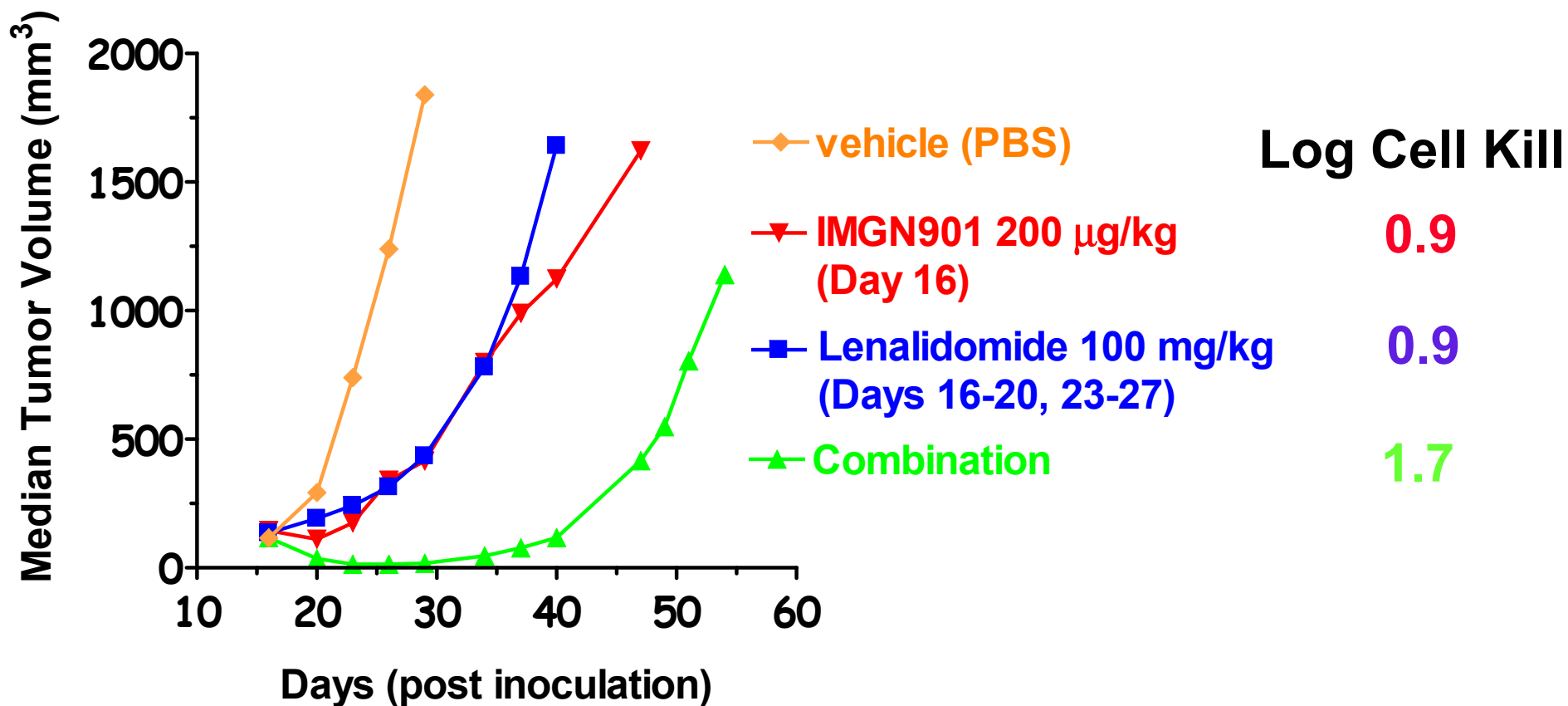
OPM2 SQ xenografts in CB17 SCID mice

Activity of IMGN901 in the MOLP8 model

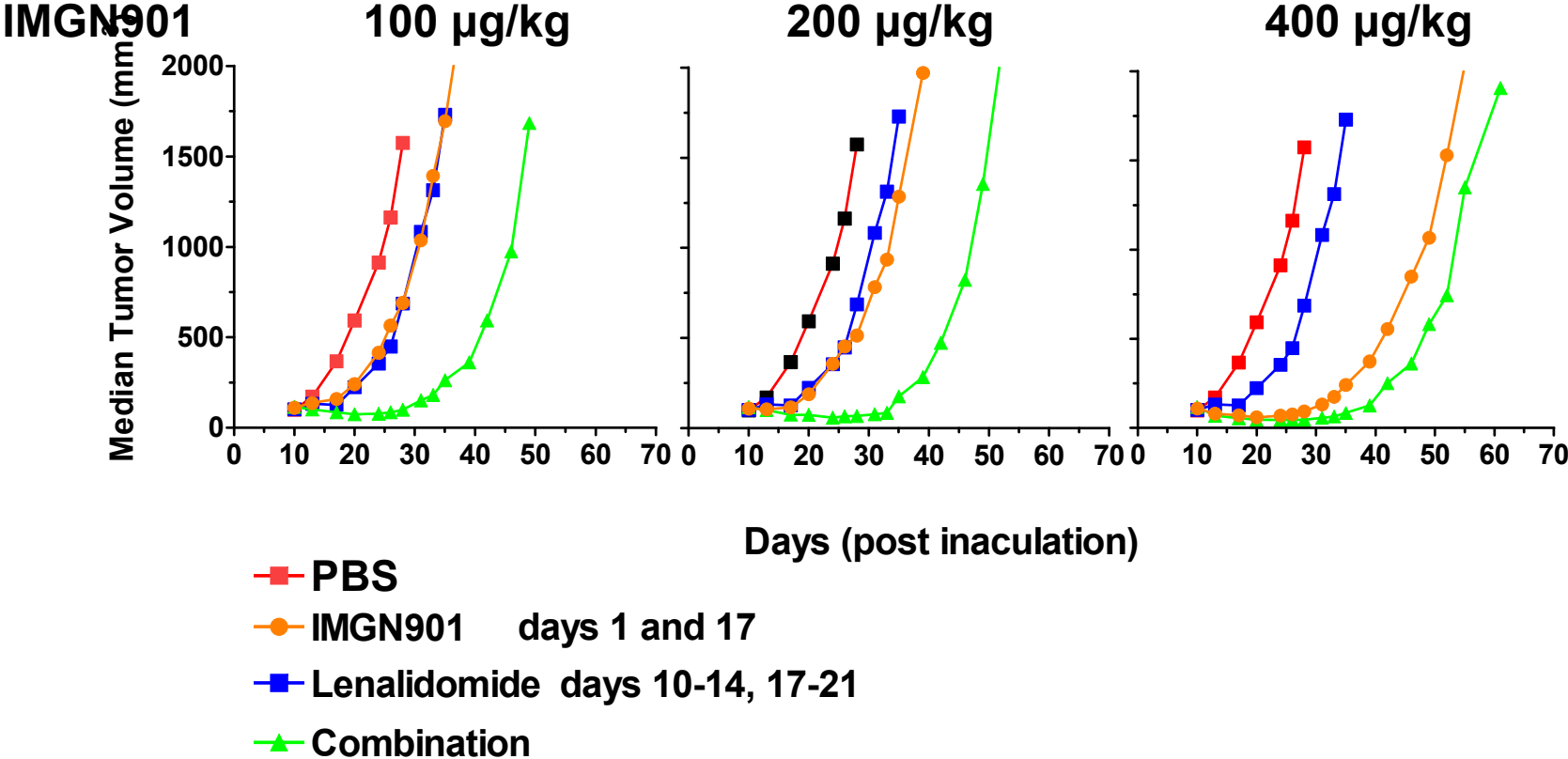


MOLP8 SQ xenografts in CB17 SCID mice

Combination of IMGN901 + Lenalidomide OPM2 model additive-to-synergistic



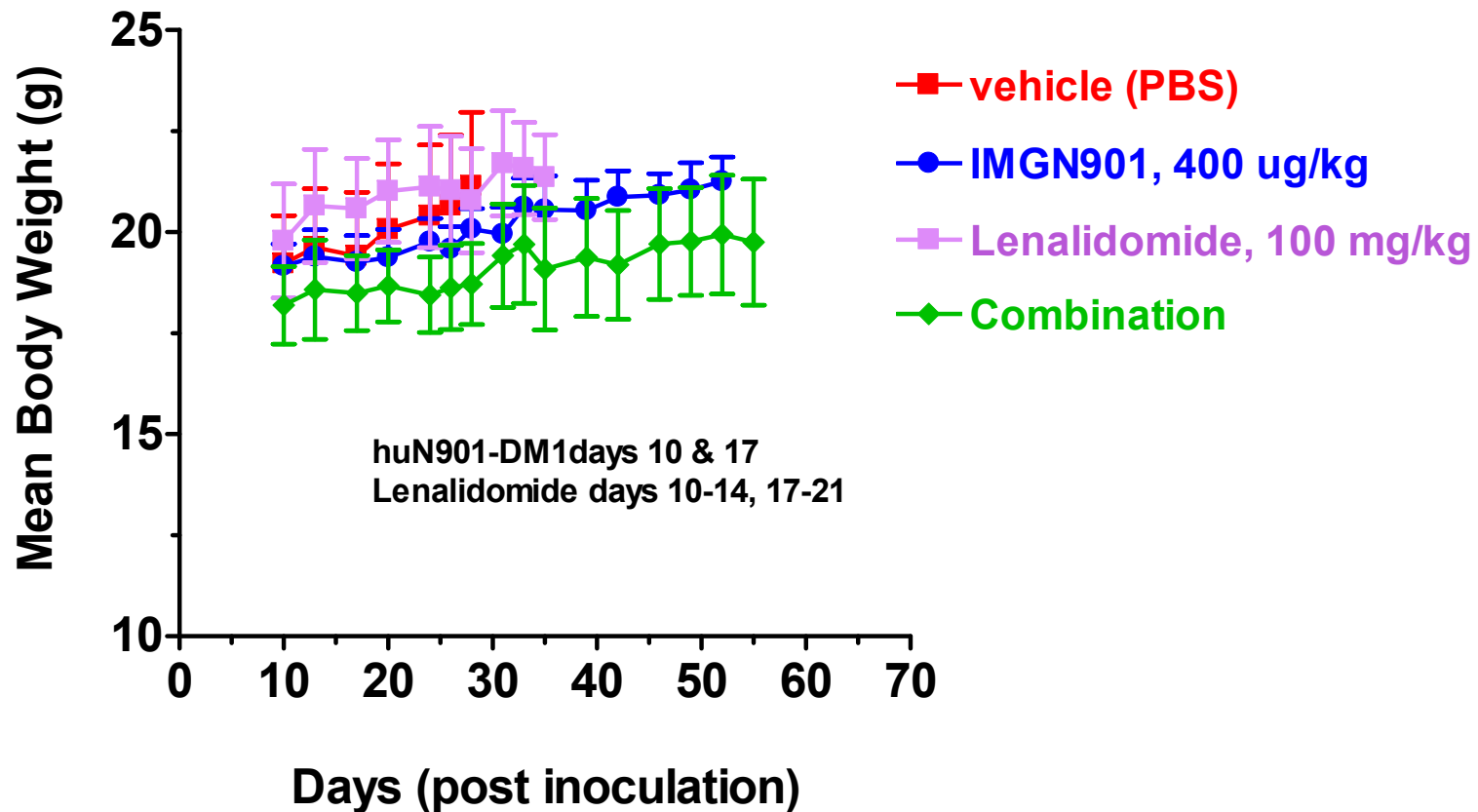
Combination of IMGN901 + Lenalidomide in MOLP8 model **additive-to-synergistic**



| Agent | Log Cell Kill | Partial regressions |
|--------------------------|---------------|---------------------|
| IMGN901 (100 µg/kg) | 0.4 | 0/6 |
| Lenalidomide (100 mg/kg) | 0.3 | 0/6 |
| Combination | 1.2 | 0/6 |
| IMGN901 (200 µg/kg) | 0.5 | 0/6 |
| Lenalidomide (100 mg/kg) | 0.3 | 0/6 |
| Combination | 1.3 | 3/6 |
| IMGN901 (400 µg/kg) | 1.3 | 2/6 |
| Lenalidomide (100 mg/kg) | 0.3 | 0/6 |
| Combination | 2 | 6/6 |

No toxicity in combination of high dose IMGN901 (400 $\mu\text{g}/\text{kg}$) plus high dose Lenalidomide

MOLP-8 Xenografts in CB.17 SCID Mice
Mean Body Weight

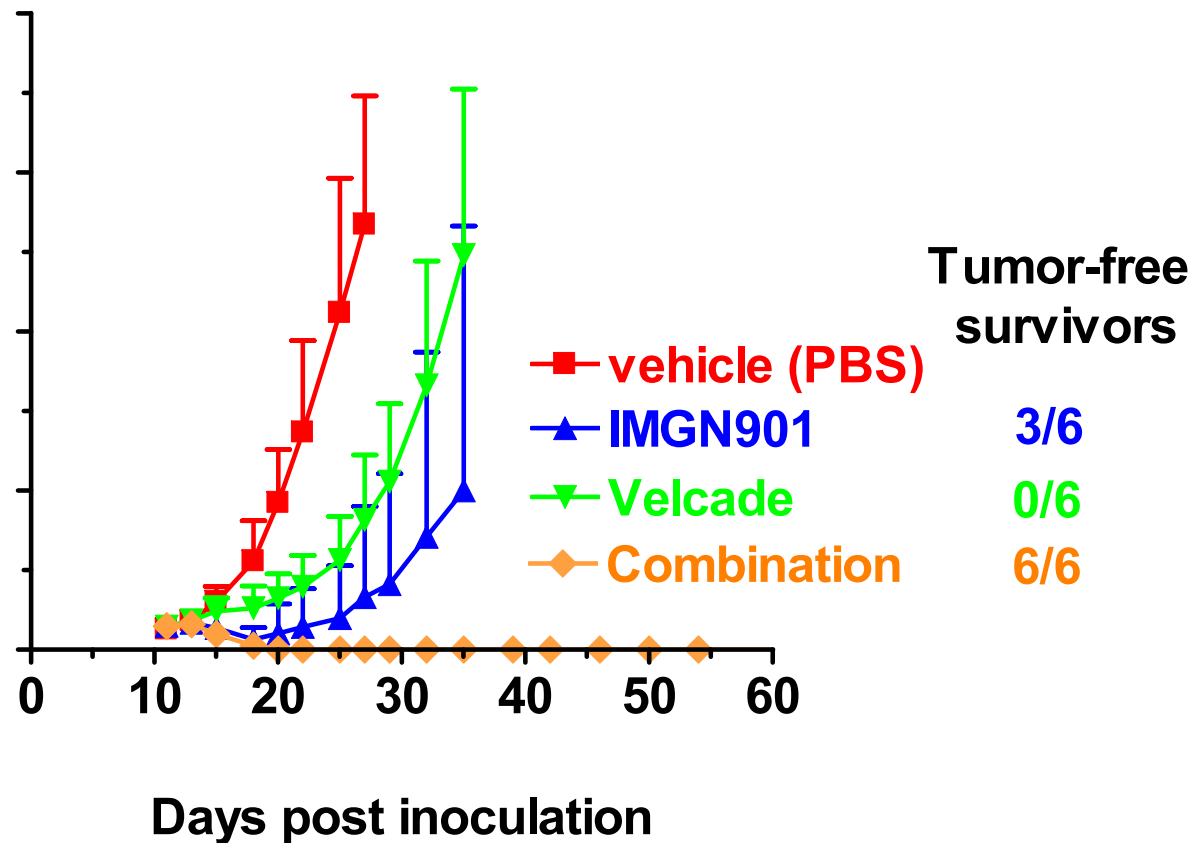


Combination of IMGN901 + Velcade/OPM2 tumors:

synergistic

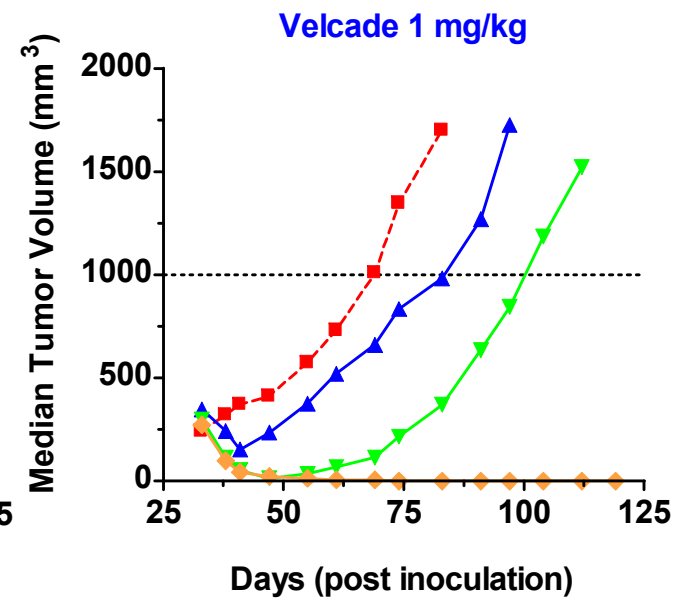
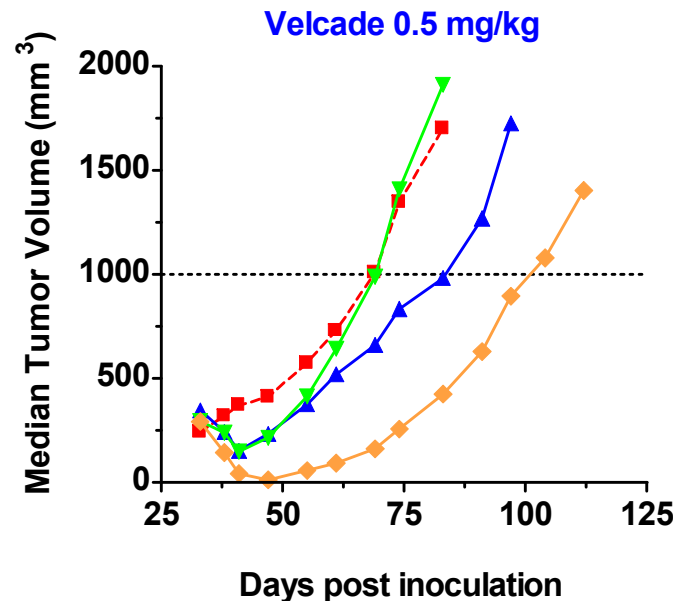
CB.17 SCID Mice

IMGN901 200 μ g/kg + Velcade 1 mg/kg



In vivo combination of IMGN901 + Velcade/H929 large tumors

IMGN901 100 µg/kg



- **Vehicle (PBS)**
- ▲ **IMGN901**
- ▼ **Velcade**
- ◆ **Combination**

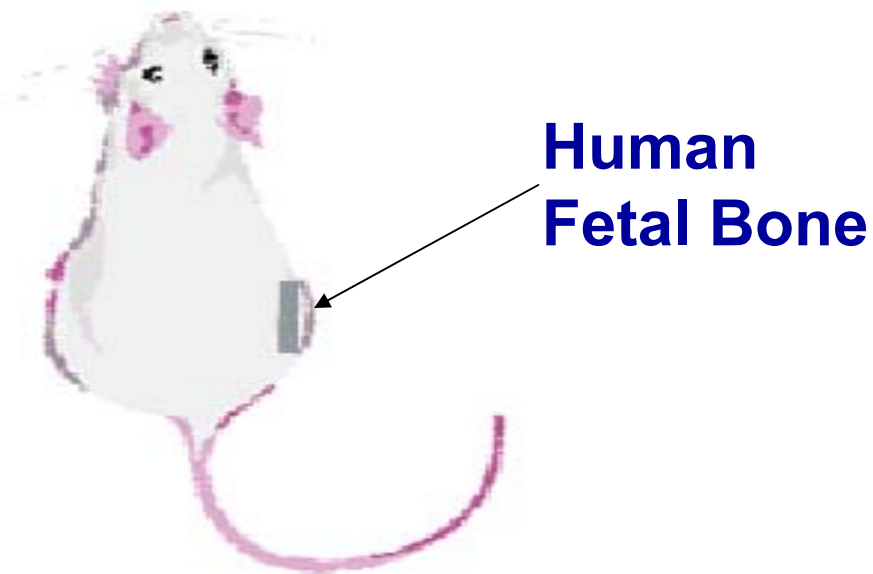
| | |
|---------------------|-----|
| Log kill TFS | |
| 0 | 0/6 |
| 0 | 0/6 |
| 0.5 | 1/6 |

| | |
|---------------------|-----|
| Log kill TFS | |
| 0 | 0/6 |
| 0.5 | 1/6 |
| 0.5 | 5/6 |

IMGN901 *in vivo* combination studies in multiple myeloma summary

| | Bortezomib (Velcade) | Lenalidomide | Melphalan | Thalidomide |
|----------|--|---|--|--|
| Efficacy | Additive to synergistic | Additive to synergistic | Additive to synergistic | Additive to synergistic |
| Toxicity | Schedule dependent additive toxicity at high IMGN901 dose + Velcade at MTD | No toxicity at a high IMGN901 dose + high dose Lenalidomide | Additive at high IMGN901 dose + melphalan at MTD | No toxicity at a high IMGN901 dose + high dose Thalidomide |

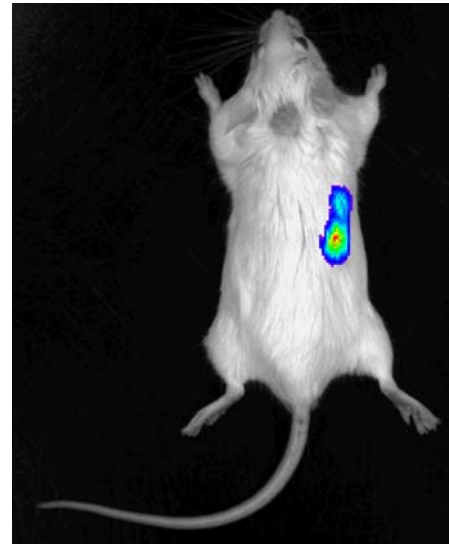
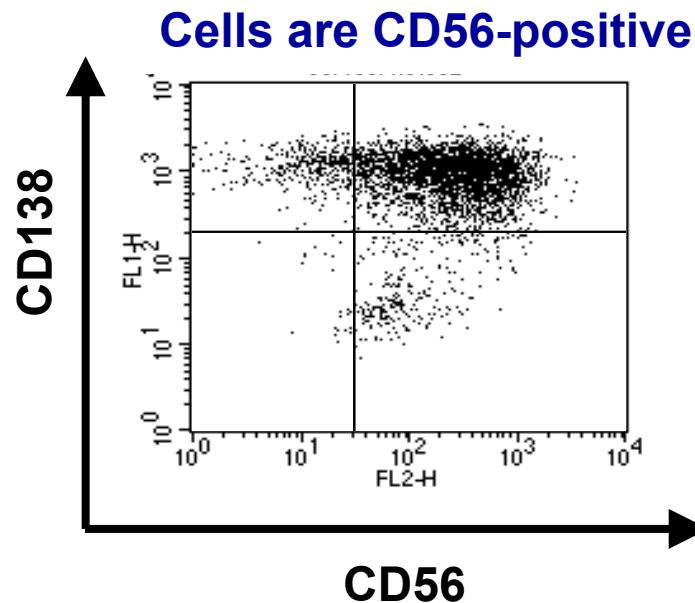
SCID-hu Mouse Model for Primary Myeloma



Yaccoby et al., *Blood* 1998;1999

The early-stage bone-marrow stroma-dependent MM model BN

stroma-dependent growth in vitro and bone-chip-dependent growth as murine xenografts (the latter at the initial stage of small tumors)

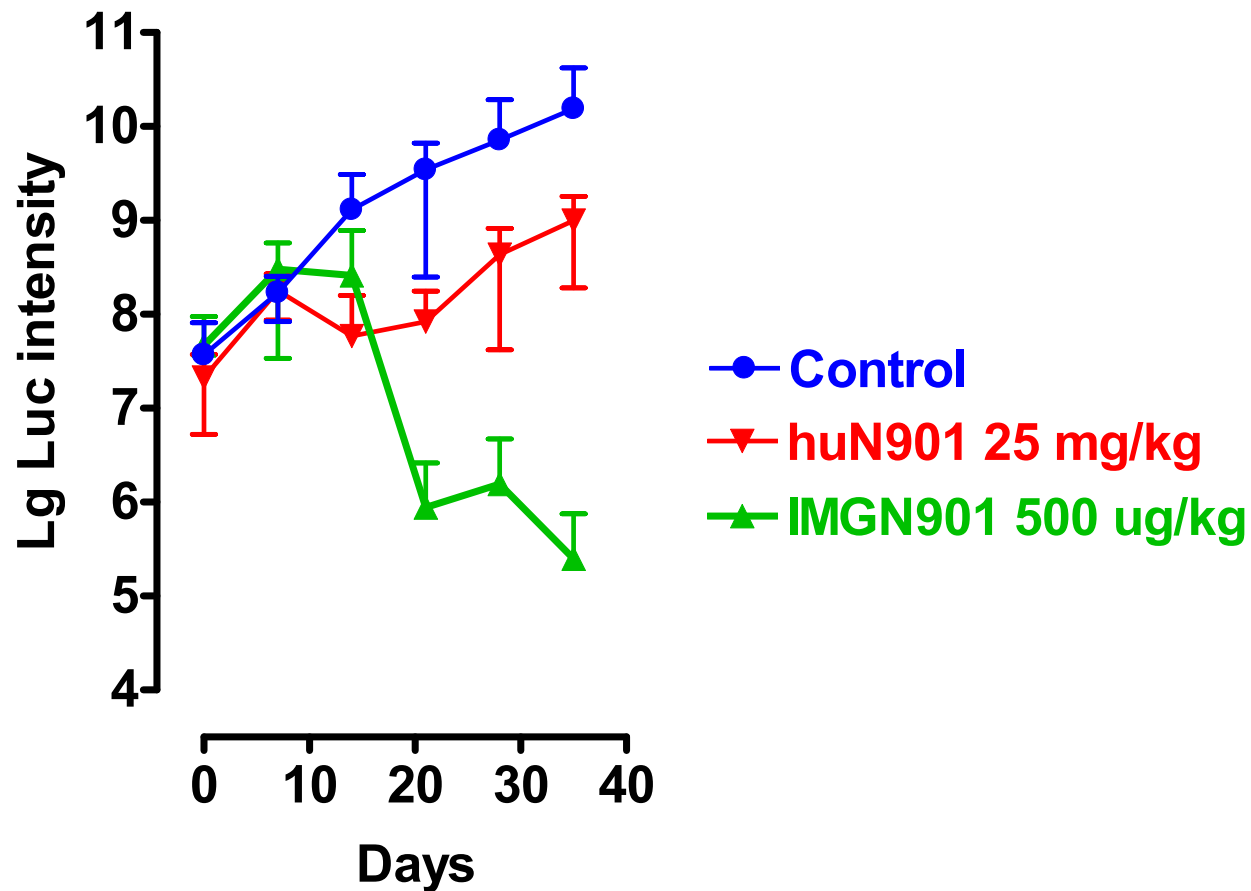


cells transduced with luciferase to enable live imaging

Six weeks after construction of the model, BN cells injected directly into the implanted human bones (1×10^5 cells/mouse)

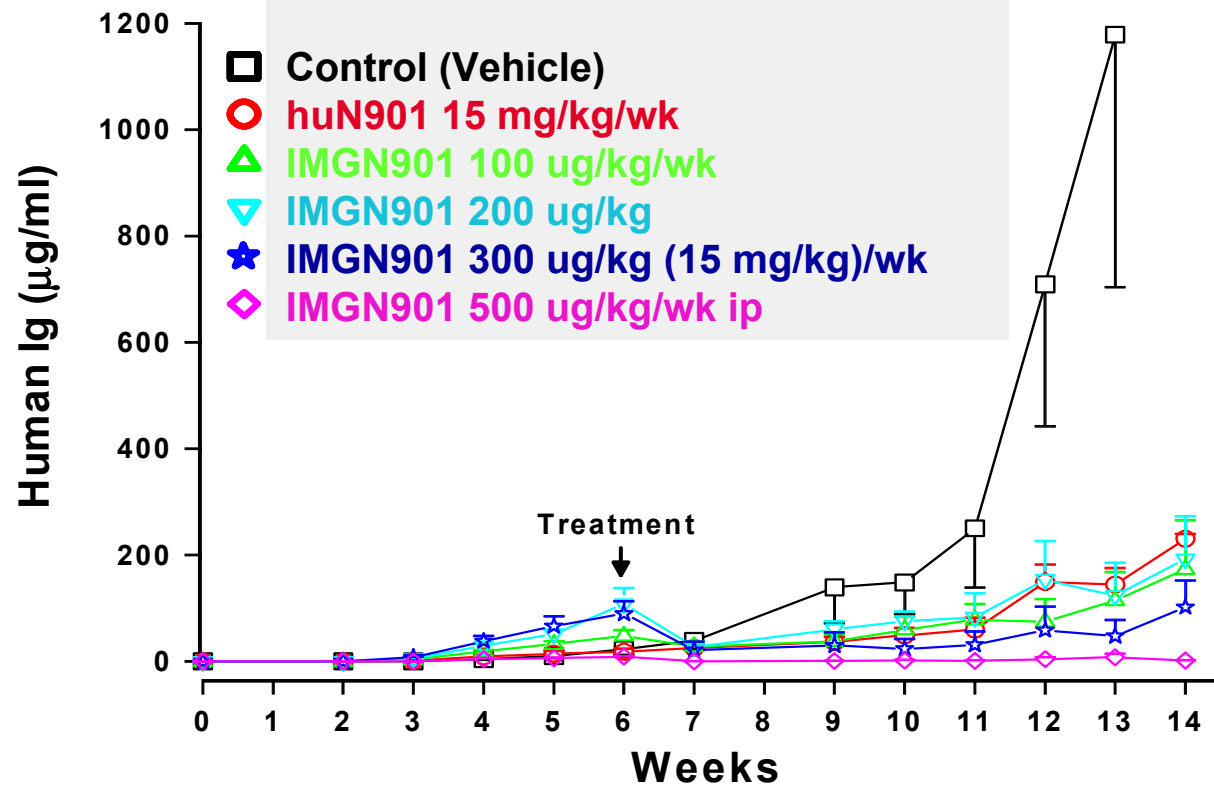
MM growth monitored by the level of human immunoglobulin (hlg) in the sera and /or by luciferase-dependent live imaging

Effects of IMGN901 and huN901 at the initial stage of growth of BN xenografts in SCID mice. Treatment initiated on week 3



IMGN901 and huN901 antibody suppresses the growth of the early-stage MM BN model

Upon establishment of MM, mice were randomly assigned to the following groups (all n=5 except the last n=2); injections i.p.:



IMGN901 Clinical Trials

- **Ph I/II (all CD56+ diseases) given IV weekly x4 every 6 wks, completed**
 - **Ph I dose-escalation trial in CD56+ solid tumors**
Ph II portion in relapsed SCLC
- **Ph I given IV daily for 3 days every 3 wks in CD56+ solid tumors – ongoing**
- **Ph I given IV weekly x 2 every 3 wks in CD56+ multiple myeloma (MM) – ongoing**
- **Initiate Ph I combination trial in MM**

Early Evidence of Clinical Efficacy

Small Cell Lung Carcinoma

- 2 PRs as 3rd-line treatment – 1 for 24 weeks; 1 for 8 weeks
- 19 patients had clinically meaningful stable disease as \geq 2nd-line treatment

Supportive data in non-pulmonary small-cell carcinoma

- 1 CR in a patient with progressive Merkel Cell Carcinoma (“primary small cell carcinoma of the skin”) – has been progression free for >3 years
- 1 PR (unconfirmed) as 3rd-line treatment – patient with small cell carcinoma of the cervix
- Stable disease noted in patients with neuroendocrine tumors

IMGN901 in Multiple Myeloma

Evaluation of Available Clinical Data

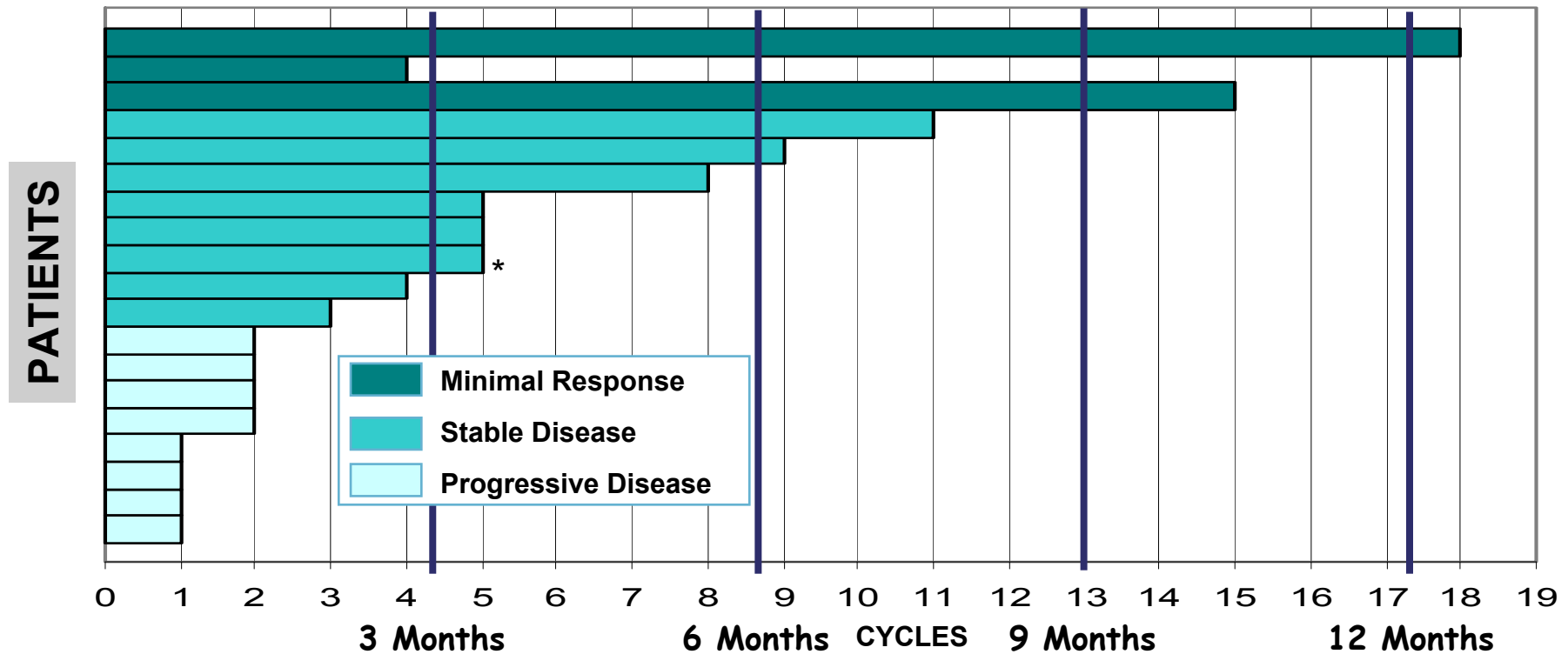
- **Trial design**

- Patients with relapsed/refractory CD56+ MM after treatment with approved agents
- Ph I – dose escalation (*current stage*) to be followed by a Ph I expansion cohort in up to 40 CD56+ MM pts to be treated at MTD
- Dose weekly for 2 weeks every 3 weeks

- **Status at time of ASH (12/08)**

- N=19
- Dose range – 40 to 140 mg/m²
- Average of 6 prior treatments – typically included bortezomide, lenalidomide, thalidomide

IMGN901 – Extended Benefit Seen in Patients Who Failed Approved MM Therapies



Many patients remained on IMGN901 longer than on agents received earlier in the course of their disease

Reported at ASH, December 2008

* Treatment ongoing (140 mg/m²/week) at time of ASH

Acknowledgements

ImmunoGen

Department of Cell Biology:

Olga Ab

Yelena Kovtun

Klaudia Foley

Laura Bartle

Preclinical Studies/Department
of Pharmacology:

Robert Lutz

Kathy Whiteman

John Lambert, Executive VP
and Chief Scientific Officer

James O'Leary, VP and Chief
Medical Officer

Albert Qin, Medical Director

University of Arkansas Myeloma Institute for Research and Therapy

Shmuel Yaccoby, Associate Professor of Medicine and
Physiology in the Myeloma Institute for Research and
Therapy

Rinku Saha

Xin Li

Angela Pennisi