GSK ‘916: anti-BCMA ADC

An exciting potential advance in the treatment of Multiple Myeloma

12 December 2017

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A number of adjusted measures are used to report the performance of our business. These measures are defined in our Q3 2017 earnings release and Annual Report on Form 20-F for 2016.

All expectations and targets regarding future performance should be read together with "Assumptions related to 2017 guidance and 2016-2020 outlook" on page 34 of our Q3 earnings release.

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Agenda

Multiple Myeloma market

Luke Miels
President, Global Pharmaceuticals

‘916, a priority asset in GSK oncology pipeline

Axel Hoos, MD, PhD
SVP and Head of Oncology Therapy Area

Results of DREAMM-1 study

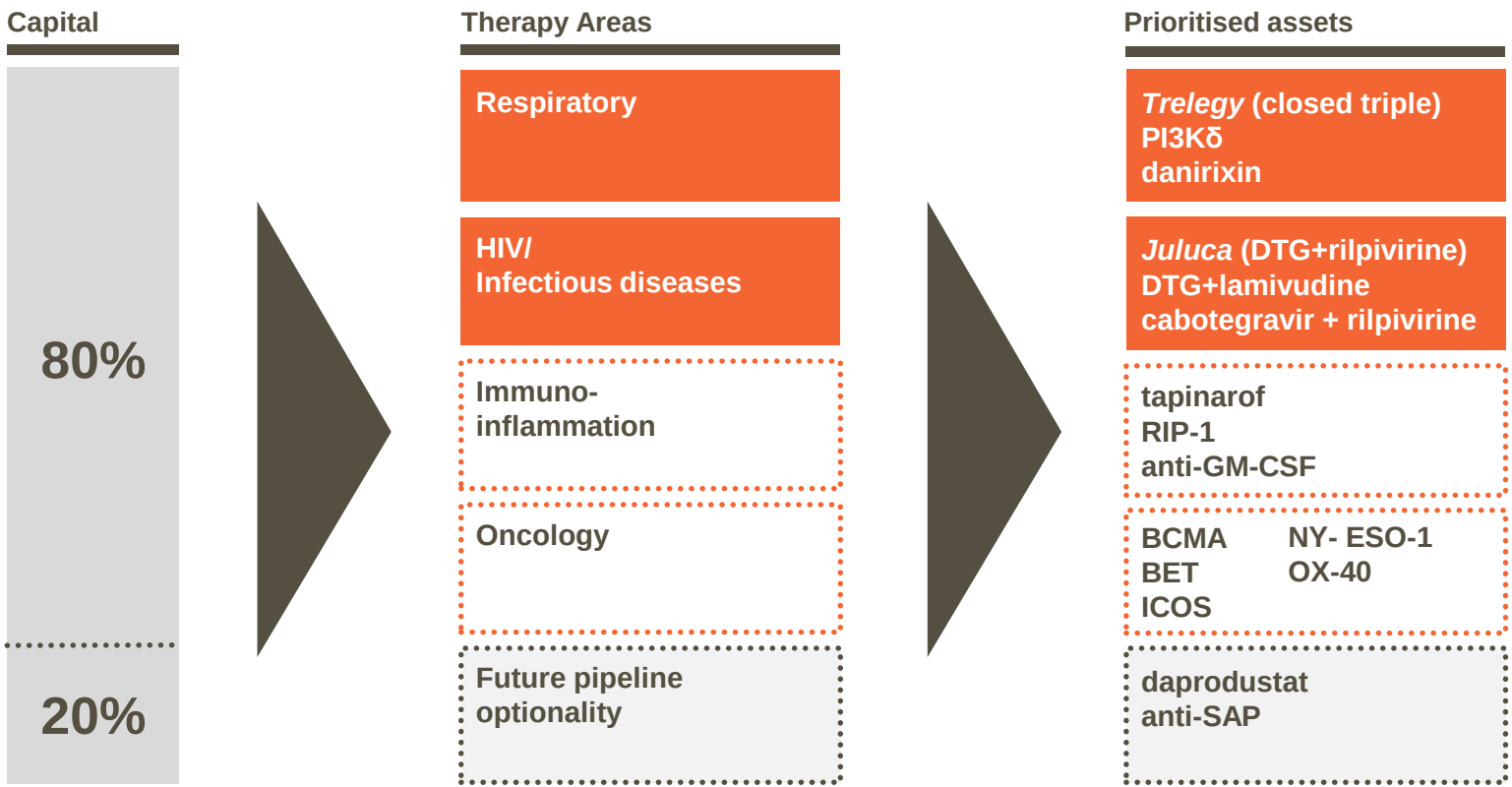
Paul Richardson, MD
Medical Oncology, Dana Farber Cancer Institute

Presentation
20-25 mins

Q&A
20-25 mins

Developing the pipeline in Pharma

Development capital focus on 2 core and 2 potential therapy areas



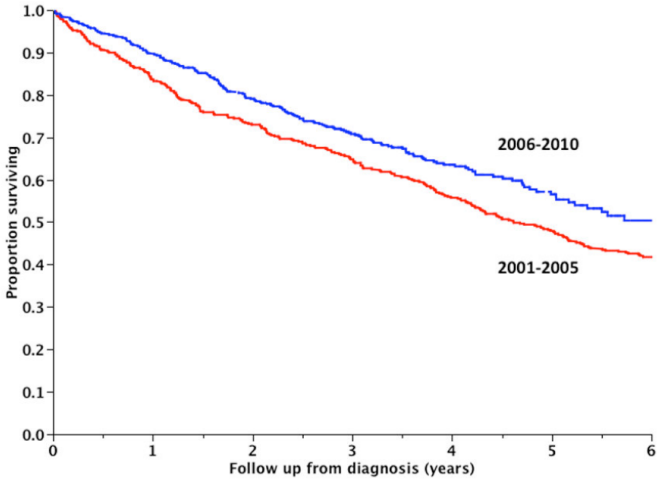
Multiple Myeloma (MM): An incurable hematologic malignancy with high unmet medical need, despite new treatments

Disease background

- Second most common blood cancer
- Myeloma affects major organs of the body which leads to bone disease (~75%), renal compromise, anaemia and infection
- Not curable
- Estimated incidence:
  - Global: 124,000
    - US: 30,000
    - EU5 27,000
    - Japan 8,000

5-year survival data

(most recent survival data available: does not reflect most recent innovations)



Source: Kantar Health; Decision resources; https://seer.cancer.gov/statfacts/html/mulmy.html
Kumar, S. et al., Leukemia (2014)

Market growth creates opportunity for innovation

Key Drivers of Growth

- Aging population – increasing incidence
- Longer duration of therapy, multiple lines
- Innovation
  - Efficacy remains key driver of acceptance of new agents
  - *Darzalex*‡ (daratumumb anti-CD38 mAb) among a new class, gaining acceptance due to efficacy profile vs previous standard of care (SoC)
  - High interest in new interventions, targets and modalities, including ‘916, CAR-Ts
- Shift towards combination therapies

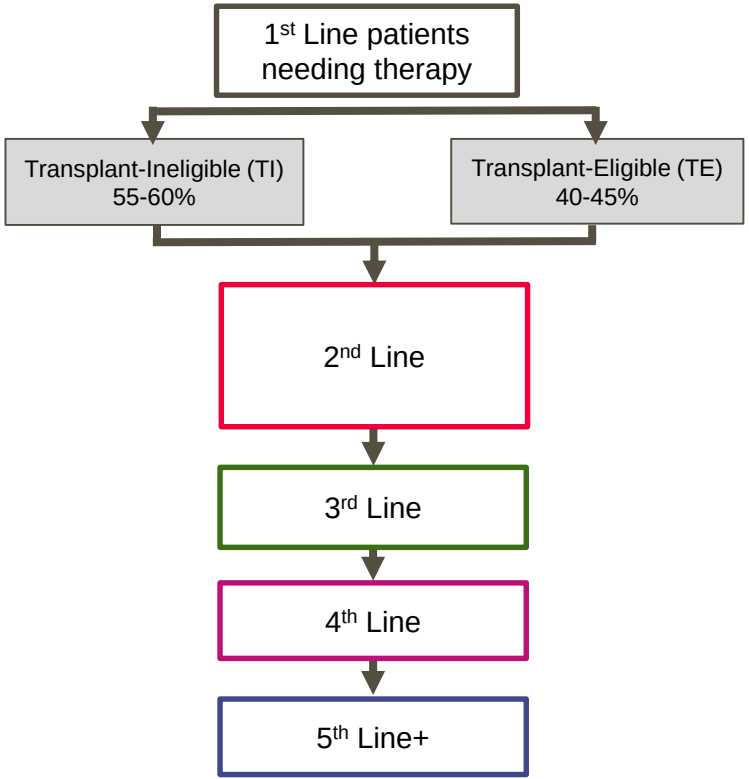
Market value ~$12bn in 2016, +40% vs 2015

Growth expected to continue: +16% CAGR 2016-22 to $29bn[1]

1. EvaluatePharma MM report (accessed 31 July 2017)

Fragmented treatment paradigm*

Opportunity for new entrants



1st Line therapy (followed by maintenance)

- *Velcade*‡ / *Revlimid*‡ (*Thalomid*‡) / Dex based regimens (SoC);
- *VelRevDex*‡ preferred (US);
- *VelMelPrednisone*‡ (TI; Ex US)

- Switch/Re-treat 1st Line regimen
- 2nd gen Proteasome Inhibitor (*Kyprolis*‡, *Ninlaro*‡) ±*RevDex*‡
- *DarzalexRevDex*‡; *DarazalexVelDex*‡; *EmplicitiRevDex*‡

- *PomDex*‡; *DarzalexPomDex*‡;
- *EmplicitiRevDex*‡; *Kyprolis*‡±Dex

- *Darzalex*‡; *PomDex*‡;
- Treatments that have not been used before

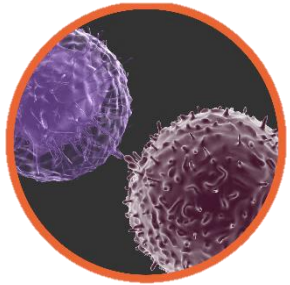
- Best Supportive Care,
- Clinical trial

*Source: GSK Market Research based on various publications and treatment guidelines. Regimen preference vary by regions and patient performance status; Maintenance therapy is mostly in the US

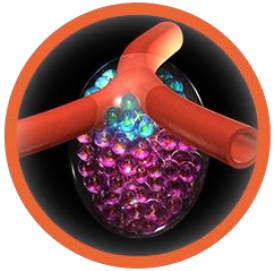
Oncology R&D

Maximising survival through transformational medicines and combinations

Immuno-Oncology



Cell & Gene Therapy



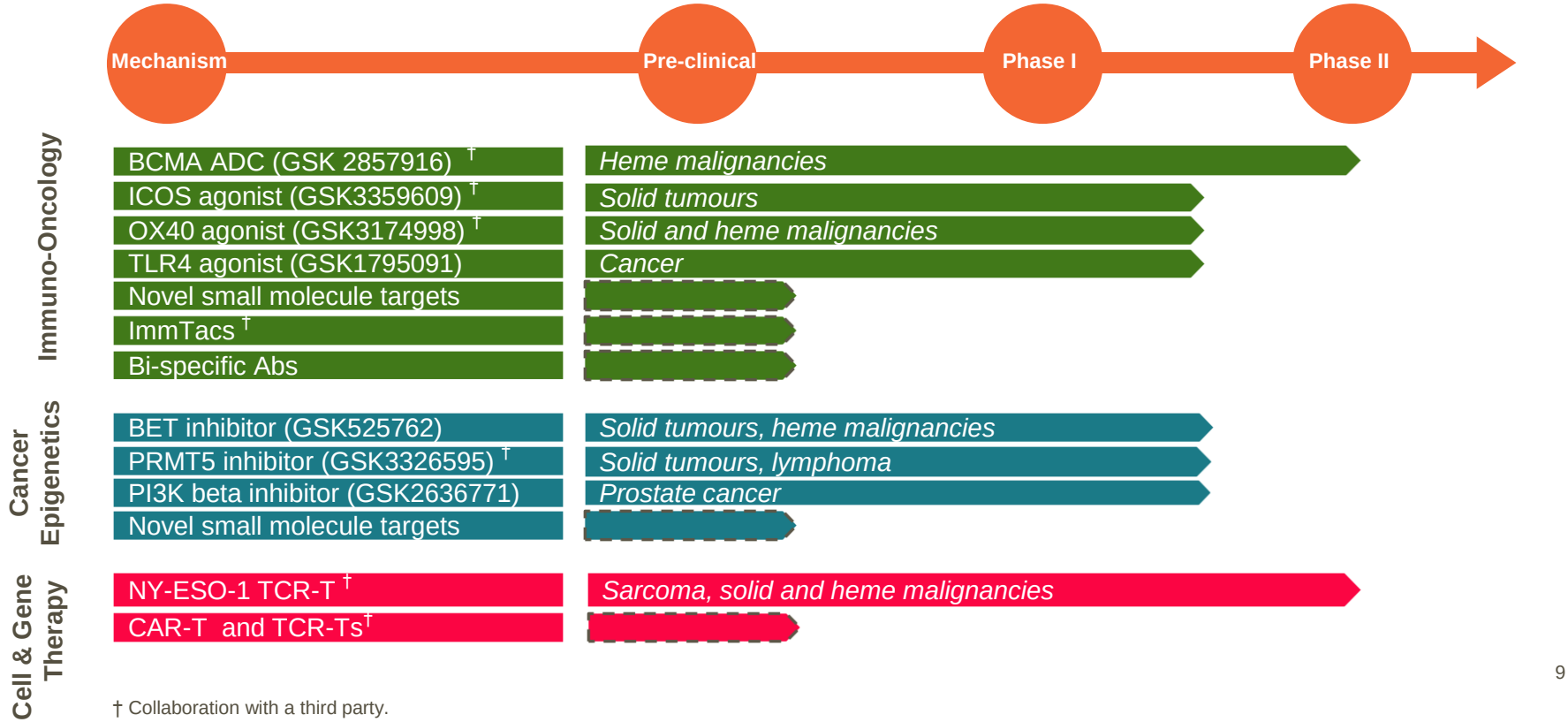
Cancer Epigenetics

GSK pipeline

Long-term survival & cures	First-in-class medicines	Reprogram cancer cells Stimulate anti-tumour immunity Cells as medicines	Combination therapy

Innovative & emerging oncology pipeline

BCMA is the lead asset



† Collaboration with a third party.

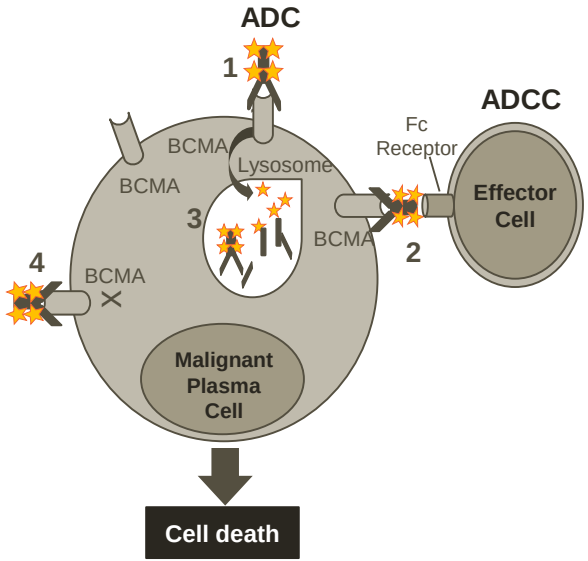
First-in-class anti-BCMA agent with multiple modes of action

The agent	– GSK'916 is a humanised IgG1 antibody targeting BCMA (B-cell maturation antigen)
	  – Linked to the anti-mitotic agent MMAF
	  – Afucosylated to enhance ADCC

The target	– BCMA plays a key role in plasma cell survival – It is found on the surfaces of plasma cells and is overexpressed on malignant plasma cells – Not expressed in healthy tissues
Key attributes	– New modality in multiple myeloma: first ADC – Easy and convenient to administer: 1h infusion q3w – No pre-medication for infusion reactions – Pre-medication with steroid eye drops – New MoA enabling diverse combinations

Four mechanisms of action:

1. ADC mechanism
2. ADCC mechanism
3. BCMA receptor signaling inhibition
4. Immunogenic cell death

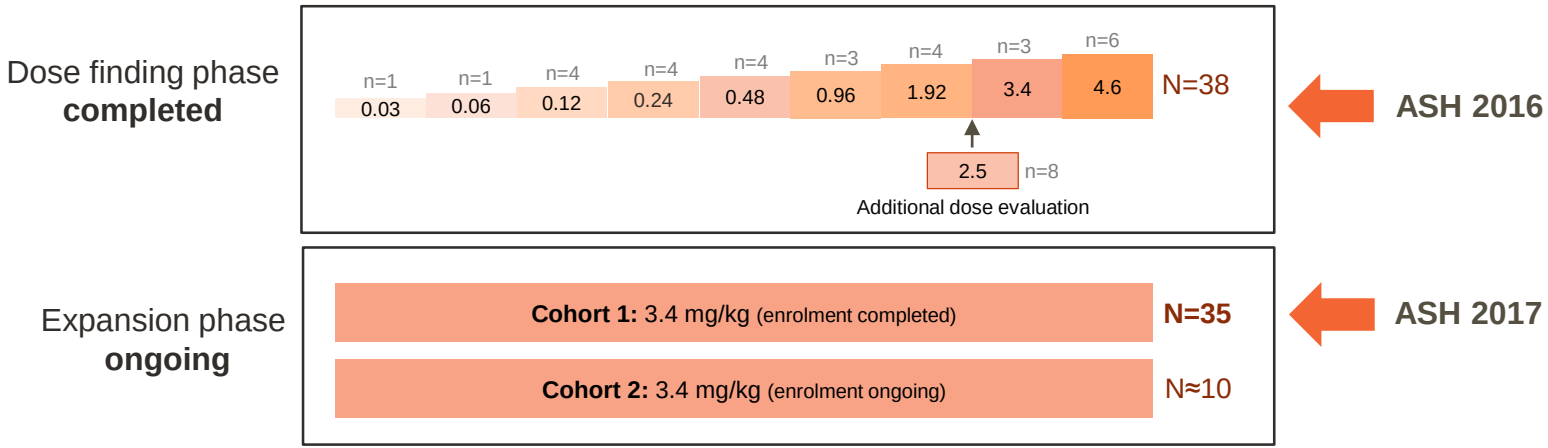


ADC, antibody-drug conjugate; ADCC, antibody-dependent cell-mediated cytotoxicity; BCMA, B-cell maturation antigen; MMAF, monomethyl auristatin-F

DREAMM-1: study design

DRiving **E**xcellence in **A**pproaches to **M**ultiple **M**yeloma

- Patients enrolled **regardless of BCMA expression levels**
- **No dose limiting toxicities** observed in dose finding phase - 38 patients with relapsed/refractory multiple myeloma
- Expansion phase:
  - Cohort 1: relapsed/refractory MM (enrolment complete); data presented at 59th ASH Annual Meeting (Dec 2017)
    - 57% had **5+ prior lines of treatment**
  - Cohort 2: BCMA-positive relapsed DLBCL or follicular lymphoma (enrolment ongoing)



DLBCL: diffuse large B-cell lymphoma

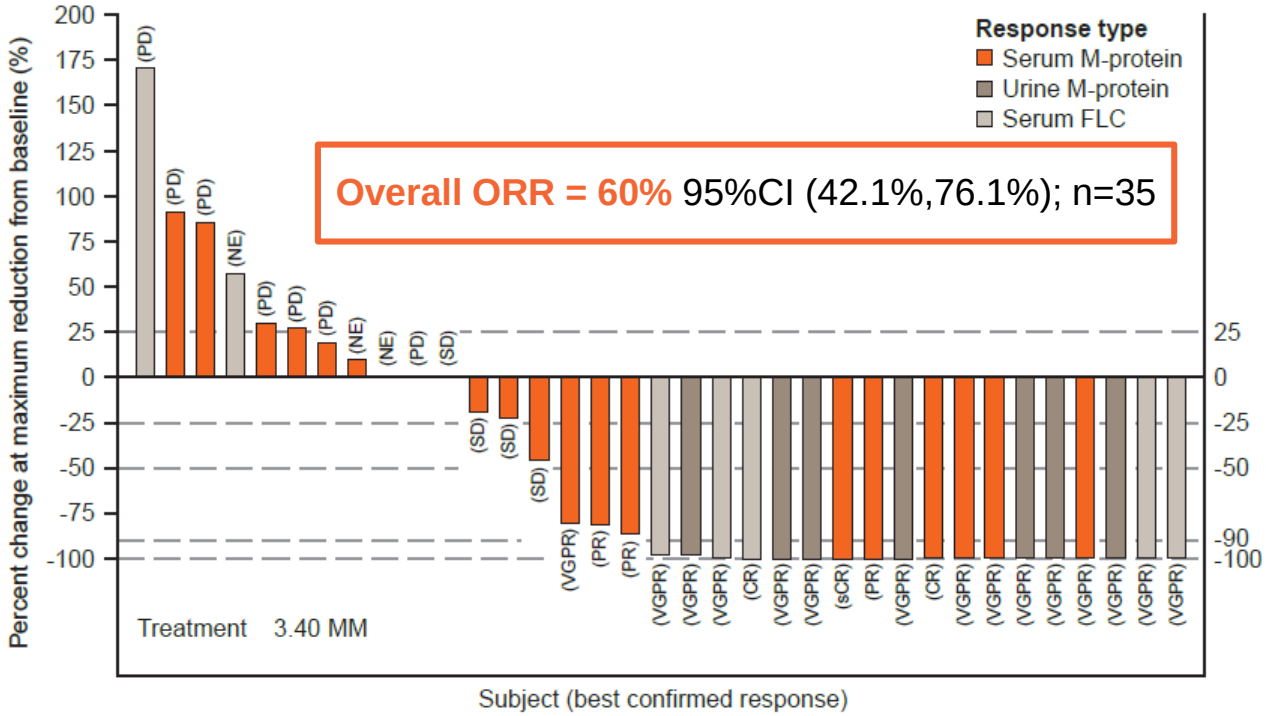
DREAMM-1 Part 2: Demographics and baseline characteristics

Characteristic	Part 2 (N=35)
Age (years), median (min, max)	60 (46–75)
Females/males, %	51/49
≥5 prior lines, n (%)	20 (57)
ASCT	31 (89)
IMiDs, n (%) Lenalidomide Pomalidomide Thalidomide **Refractory to IMiD**	**35 (100)** 33 (94) 21 (60) 12 (34) **32 (91)**
PI, n (%) Bortezomib Carfilzomib **Refractory to PI, n (%)**	**35 (100)** 34 (97) 28 (80) **34 (97)**
Daratumumab, n (%) **Refractory to daratumumab, n (%)**	**14 (40)** **13 (37)**
Refractory to IMiD/PI, n (%)	**31 (89)**
Refractory to IMiD/PI and prior daratumumab, n (%)	**12 (34)**
Cytogenetics risk, n (%)* High risk Other (non-high risk, not done, or missing)	 10 (29) 25 (71)

ASCT, autologous stem cell transplant; IMiD, immunomodulator; PI, proteasome inhibitor

*Patients with any of the following genetic abnormalities were considered high risk: t(4:14), del17, t(14:16), t(14:20), nonhiperdiploidy, or gain 1q

Transformational efficacy in multiple myeloma: ORR

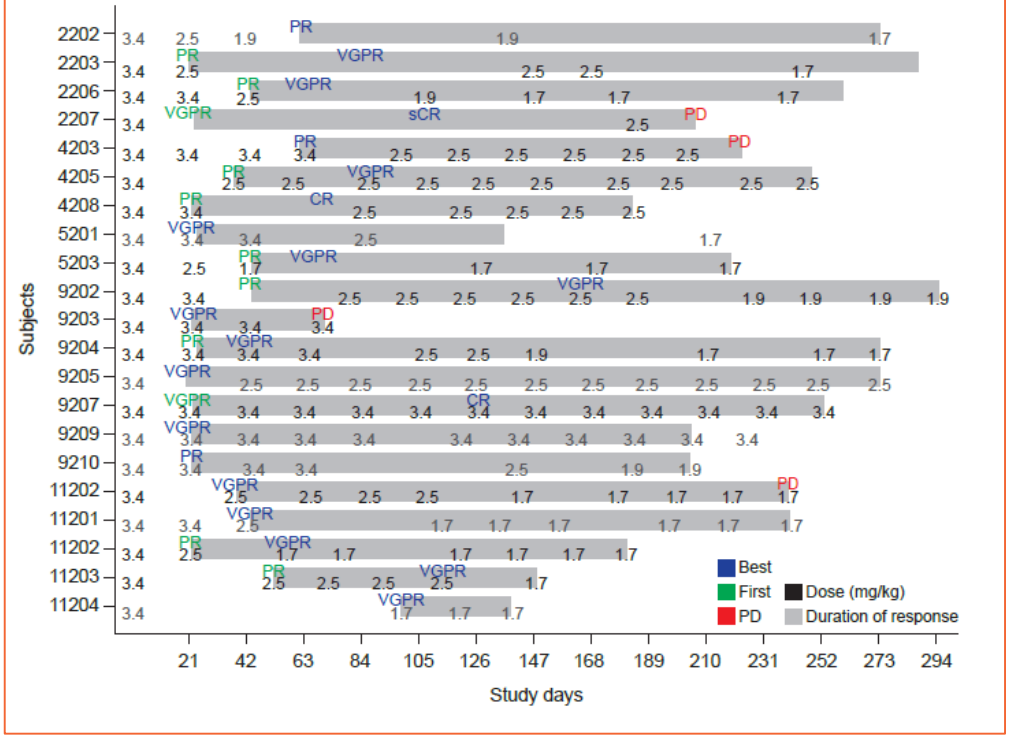


Transformational efficacy in refractory populations

Patients refractory to IMID and PI (n=31) ORR=58% [95%CI (39.1%,75.5%)]

Patients previously treated with daratumumab (n=14) ORR=43% [95%CI (17.7%,71.1%)]

DREAMM-1 Part 2: Response characteristics

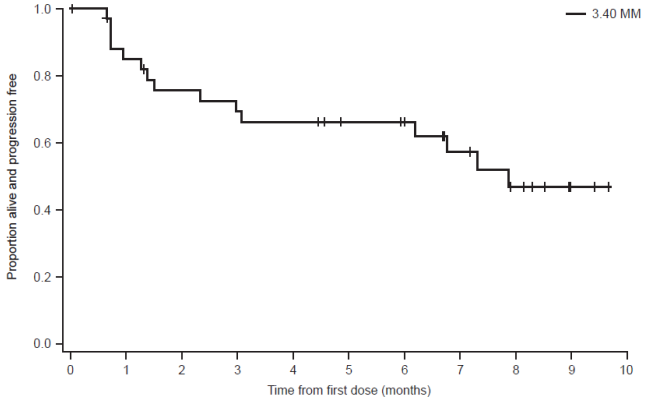


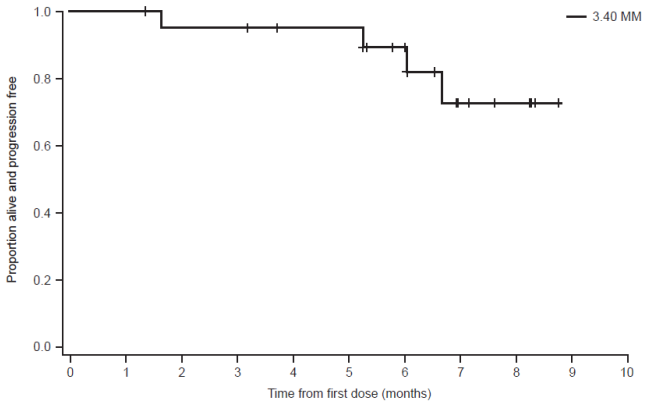
Response characteristics:

- Early response seen after 1-2 doses
- Mostly durable
- Dose reductions did not lead to loss of response

CR, complete response; PD, progressive disease; PR, partial response; sCR, stringent complete response; VGPR, very good partial response

DREAMM-1 Part 2: Efficacy – progression-free survival and duration of response





Progression free survival

Number of subjects	**35**
Progressed or died	15 (43%)
Censored, f/u ended	3 (9%)
Censored, f/u ongoing	17 (49%)

Progression-free survival (months)	
Q1 (95% CI)	2.3 (0.7, 6.8)
Median (95% CI)	**7.9 (3.1, -)**
Q3 (95% CI)	N/A

Duration of response

Number of subjects	**21**
Progressed or died	4 (19%)
Censored, f/u ended	0
Censored, f/u ongoing	17 (81%)

Duration of response (months)	
Q1 (95% CI)	6.7 (1.6, -)
Median (95% CI)	**N/A (6.7, -)**
Q3 (95% CI)	N/A

CI, confidence interval; f/u, follow-up; N/A, not available; Q, quartile

Manageable safety profile - summary

Most frequent adverse events
- Corneal events 63%
- Thrombocytopenia 49%

Corneal events - mostly low grade (9% G3)
- Manageable with steroid eye drops
- Dose reductions

Hematologic AEs (including thrombocytopenia)
- Frequent in MM population due to disease

Infusion Related Reactions (IRR) 23%
- Occur at first dose without premedication
- Manageable
- Do not recur with subsequent doses

GSK'916 single agent has transformational efficacy

Drug, Sponsor	Line of Therapy; Trial	ORR	mPFS	mOS
[1]*Kyprolis*‡ (IV), monotherapy Amgen	3L+, Single arm, N=266	23.7%	3.7m	15.6m
[2]*Darzalex*‡ (IV), monotherapy Janssen	4L+, Single arm, N=106	29.2%	3.7m	17.5m
GSK'916 (IV), monotherapy	***5 median lines (40% Darzalex‡ treated), Single arm, N=35***	***60% (43% in Darzalex‡ exposed)***	***7.9m (6.8m in Darzalex‡ exposed)***	***NA***

1: Siegel et al. Blood (2012); 2: Lonial et al., Lancet (2016). GSK'916 data presented at ASH 2017

GSK ’916: expected next steps

Breakthrough therapy designation from FDA

EMA granted PRIME designation

Orphan drug designation from the EMA and FDA for multiple myeloma

	2018	2019	2020 +
Monotherapy in Multiple Myeloma	Pivotal phase 2 start: 4th line	Pivotal data readout 4th line	Filing & launch
Combination therapy with SOC in Multiple Myeloma	Phase 1/2 start: 2nd line		Data readout and pivotal trial start 2nd line
Novel combination therapy in Multiple Myeloma	Phase 1/2 start		Data readout and pivotal trial start
Lymphoma		Phase 1/2 lymphoma cohort data readout & Phase 2 start	

Ongoing discussions with regulators

Right of first negotiation for GSK oncology assets

Novartis has a right of first negotiation (ROFN) that is triggered upon our decision to seek a partner or divest certain oncology assets or if we propose to seek a marketing authorization for such oncology assets, on an asset by asset basis.

NVS does not have an “opt-in” or a “call” option related to GSK’s oncology pipeline.

GSK’s obligation is to negotiate in good faith. GSK would only enter into a transaction if it believes that is in the best interests of its shareholders.

The ROFN does not oblige GSK to sell to, or partner with, NVS. The ROFN is not an obligation to consummate a transaction with NVS. Under the ROFN, we are able to continue to develop and commercialise assets on our own.

The ROFN extends for 12.5 years from closing of the original GSK/Novartis transactions; i.e. September 2027.

Not intended to provide a complete summary of all the terms of the ROFN. The contractual terms of the ROFN are available at https://www.sec.gov/Archives/edgar/data/1131399/000119312516510261/d32974dex410.htm

Q&A