ASCO Analyst & Investor Webcast

June 1, 2018

Forward Looking Statements

These slides and the accompanying oral presentation contain forward-looking statements and information relating to bluebird bio, its product candidate bb2121 and oncology research and development plans. The use of words such as “may,” “might,” “will,” “should,” “expect,” “plan,” “anticipate,” “believe,” “estimate,” “project,” “intend,” “future,” “potential,” or “continue,” and other similar expressions are intended to identify forward-looking statements. For example, all statements we make regarding the initiation, timing, progress and results of our preclinical and clinical studies and our research and development programs, our ability to advance product candidates into, and successfully complete, clinical studies, and the timing or likelihood of regulatory filings and approvals are forward looking. All forward-looking statements are based on estimates and assumptions by our management that, although we believe to be reasonable, are inherently uncertain. All forward-looking statements are subject to risks and uncertainties that may cause actual results to differ materially from those that we expected. These statements are also subject to a number of material risks and uncertainties that are described in our most recent quarterly report on Form 10-Q, as well as our subsequent filings with the Securities and Exchange Commission. Any forward-looking statement speaks only as of the date on which it was made. We undertake no obligation to publicly update or revise any forward-looking statement, whether as a result of new information, future events or otherwise, except as required by law.

Welcome

Nick Leschly, chief bluebird

bluebirdbio



trueblue

Making Hope
A Reality

bluemojo

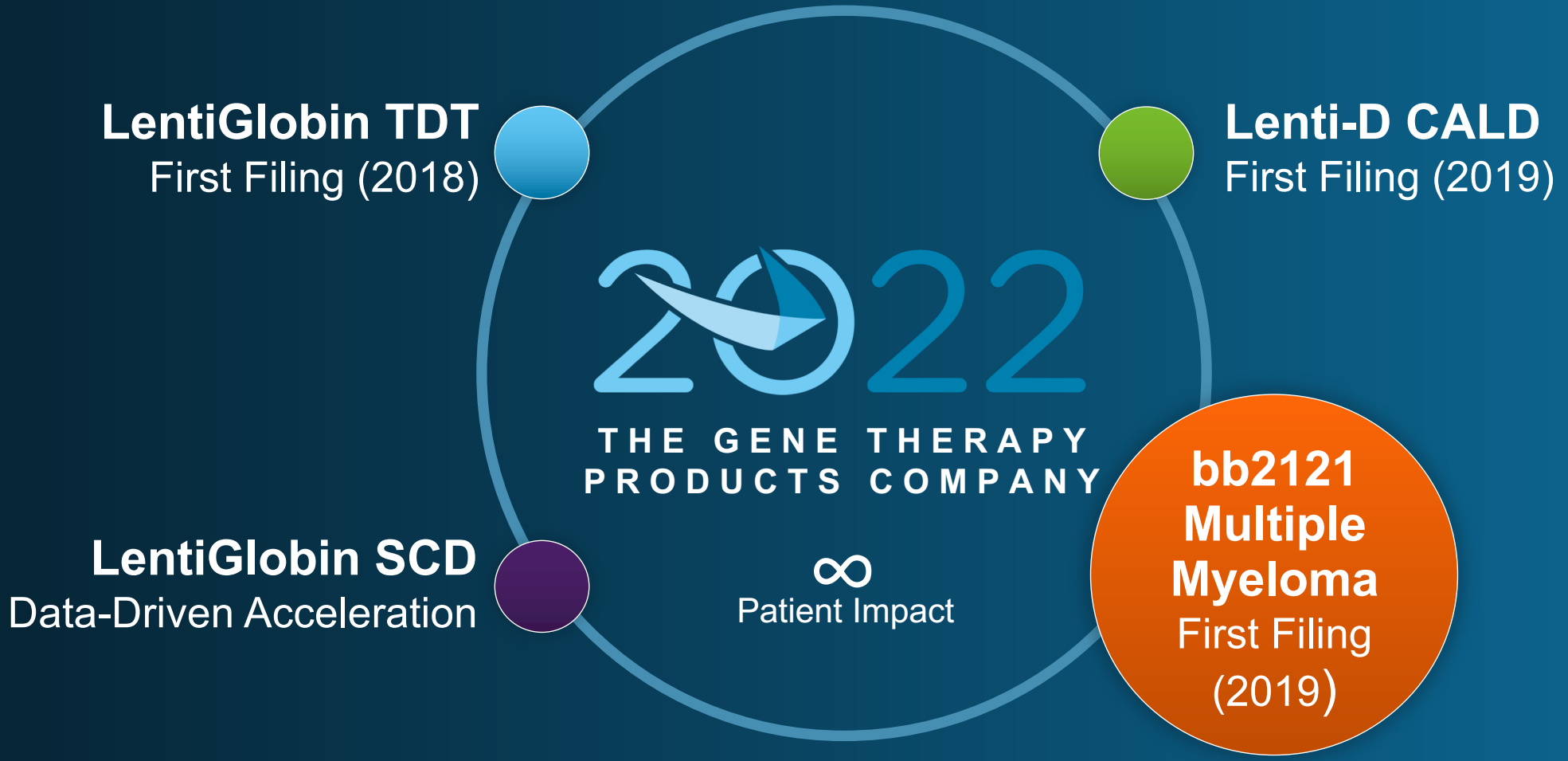






Path to Patients

Three Regulatory Filings Anticipated by End of 2019



2+ Products on the Market

2+ Programs Nearing Commercialization

4+ Additional Programs in the Clinic

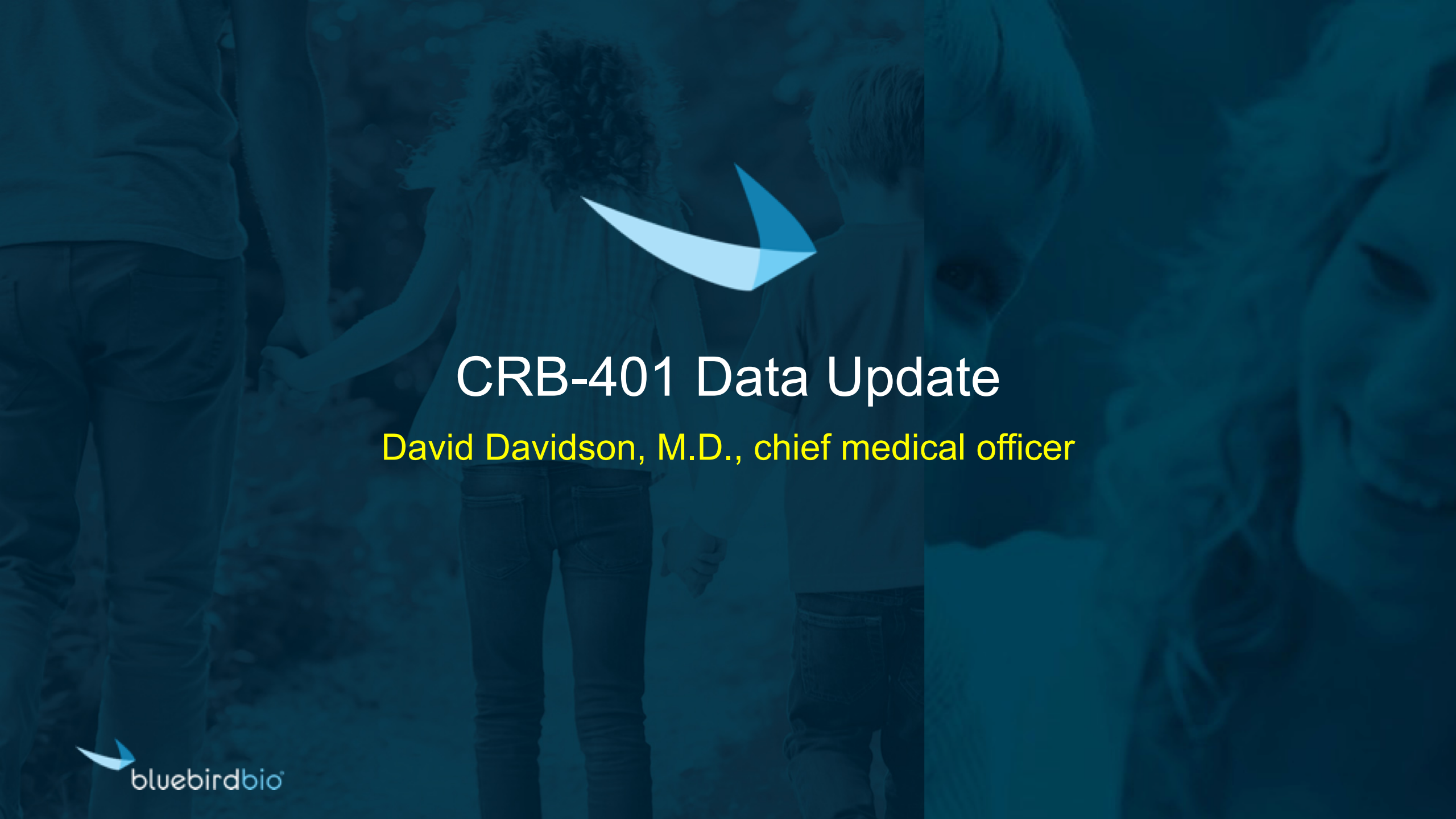
Key Questions for Today

What more have we learned about efficacy and durability of bb2121 in this heavily pretreated patient population?

What are the new learnings? BCMA expression? Dose response?

Is the safety profile still manageable?

Is the path to earlier lines progressing?



CRB-401 Data Update

David Davidson, M.D., chief medical officer

bluebirdbio

Baseline Demographics and Clinical Characteristics

Parameter	Escalation (N=21)	Expansion (N=22)
Median (min, max) follow-up, d	345 (46, 638)	87 (29, 184)
Median (min, max) age, y	58 (37, 74)	65 (44, 75)
Male, n (%)	13 (62)	16 (73)
Median (min, max) time since diagnosis, y	4 (1, 16)	6 (1, 36)
ECOG PS,[1] n (%)		
0	10 (48)	6 (27)
1	11 (52)	16 (72)
High-risk cytogenetics, n (%)		
del(17p), t(4;14), t(14;16)	8 (38)	9 (41)

ECOG, Eastern Cooperative Oncology Groups performance status; ISS, international staging system; NA, not available. [1]Data at screening presented.

Heavily Pretreated Patient Population

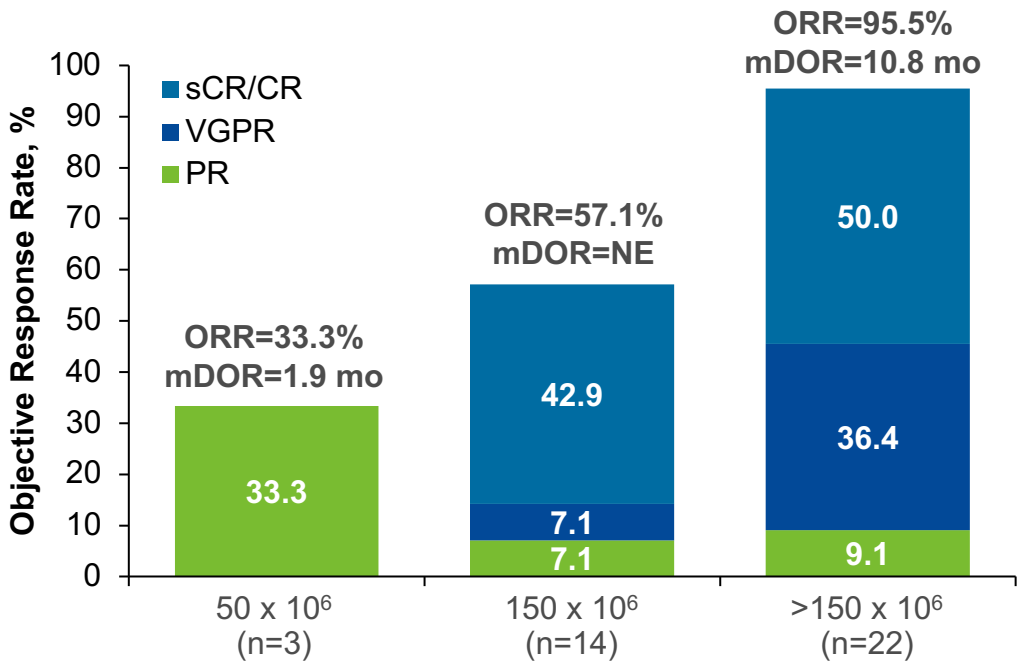
Parameter	Escalation (N=21)	Expansion (N=22)
Median (min, max) prior regimens	7 (3, 14)	8 (3, 23)
Prior autologous SCT, n (%)	21 (100)	19 (86)
0	0	3 (14)
1	15 (71)	14 (64)
>1	6 (29)	5 (23)

	Escalation (N=21)		Expansion (N=22)	
Parameter	**Exposed**	**Refractory**	**Exposed**	**Refractory**
Prior therapies, n (%)				
Bortezomib	21 (100)	14 (67)	22 (100)	16 (73)
Carfilzomib	19 (91)	12 (57)	21 (96)	14 (64)
Lenalidomide	21 (100)	19 (91)	22 (100)	18 (82)
Pomalidomide	19 (91)	15 (71)	22 (100)	21 (96)
Daratumumab	15 (71)	10 (48)	22 (100)	19 (86)
Cumulative exposure, n (%)				
Bort/Len	21 (100)	14 (67)	22 (100)	14 (64)
Bort/Len/Car/Pom/Dara	15 (71)	6 (29)	21 (96)	7 (32)

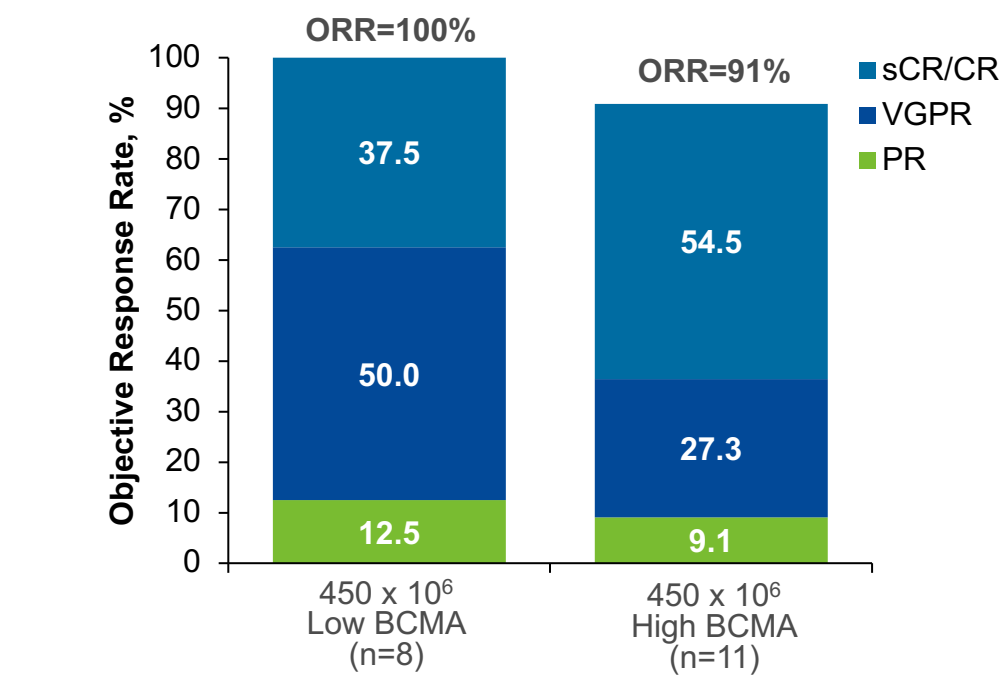
SCT, stem cell transplant. Data cut-off: March 29, 2018.

Tumor Response: Dose-related and Independent of Myeloma BCMA Expression Levels

Tumor Response By Dose[1]



Tumor Response By BCMA Expression[1]



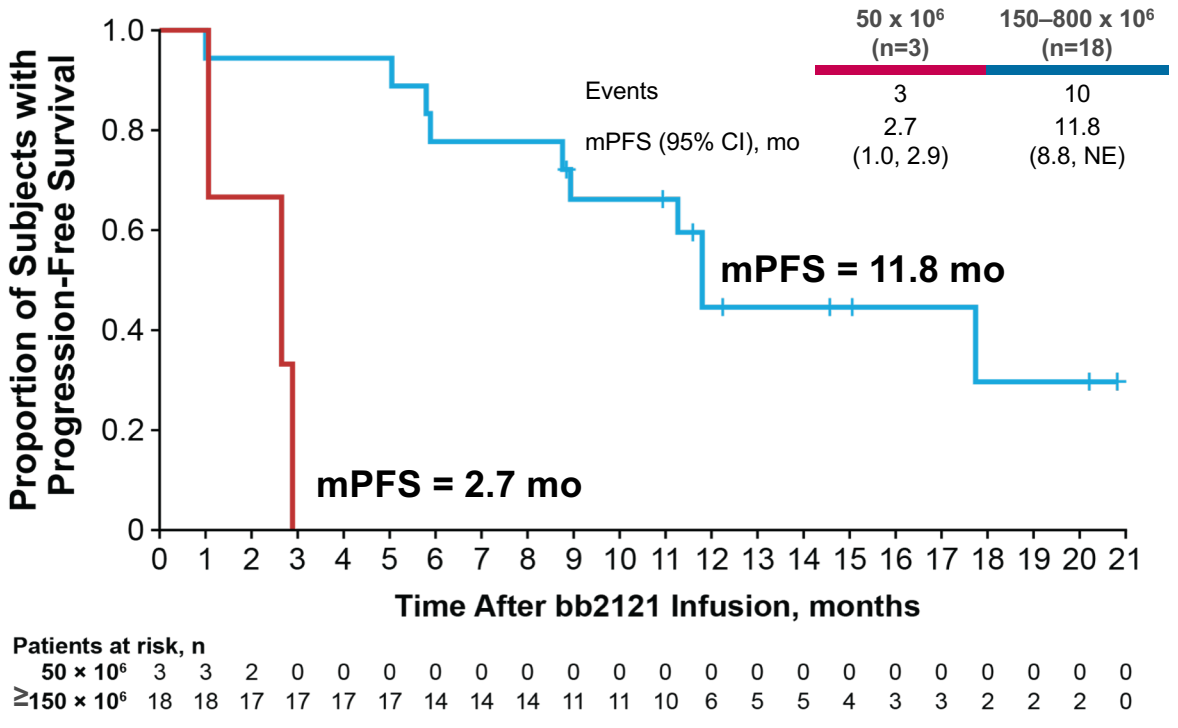
- 80.6% ORR across active dose cohorts (150-800 x 10^6)

CR, complete response; mDOR, median duration of response; ORR, objective response rate; PD, progressive disease; PR, partial response; sCR, stringent CR; VGPR, very good partial response. Data cut-off: March 29, 2018. [1]Patients with ≥2 months of response data or PD/death within <2 months. ORR is defined as attaining sCR, CR, VGPR, or PR, including confirmed and unconfirmed responses. Low BCMA is <50% bone marrow plasma cells expression of BCMA; high BCMA is defined as ≥50%.

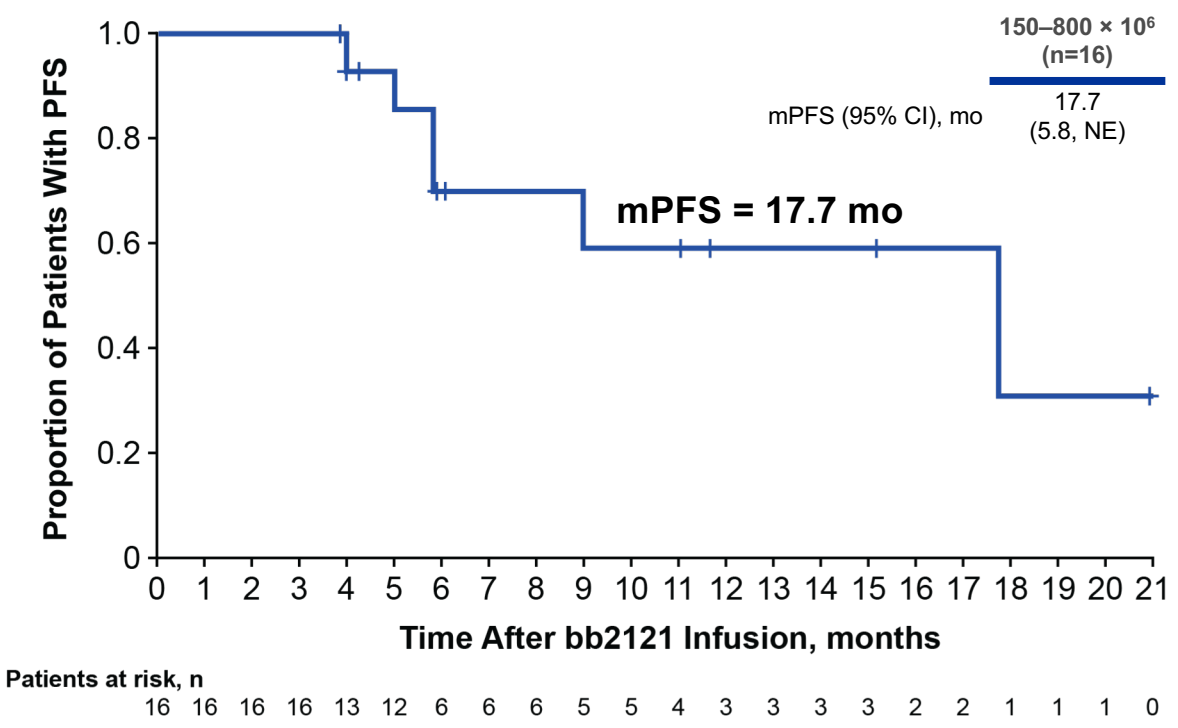
Hitting the Mark for Progression Free Survival

- mPFS of 11.8 months at active doses (≥150 x 10^6 CAR+ T cells) in 18 subjects in dose escalation
- mPFS of 17.7 months in 16 responding subjects from all study cohorts who are MRD-negative

PFS at Inactive (50 x 10^6) and Active (150–800 x 10^6) Dose Levels[1]



PFS in MRD-Negative Responders
Escalation and Expansion Cohorts



Data cut-off: March 29, 2018. Median and 95% CI from Kaplan-Meier estimate. NE, not estimable.
[1]PFS in dose escalation cohort.

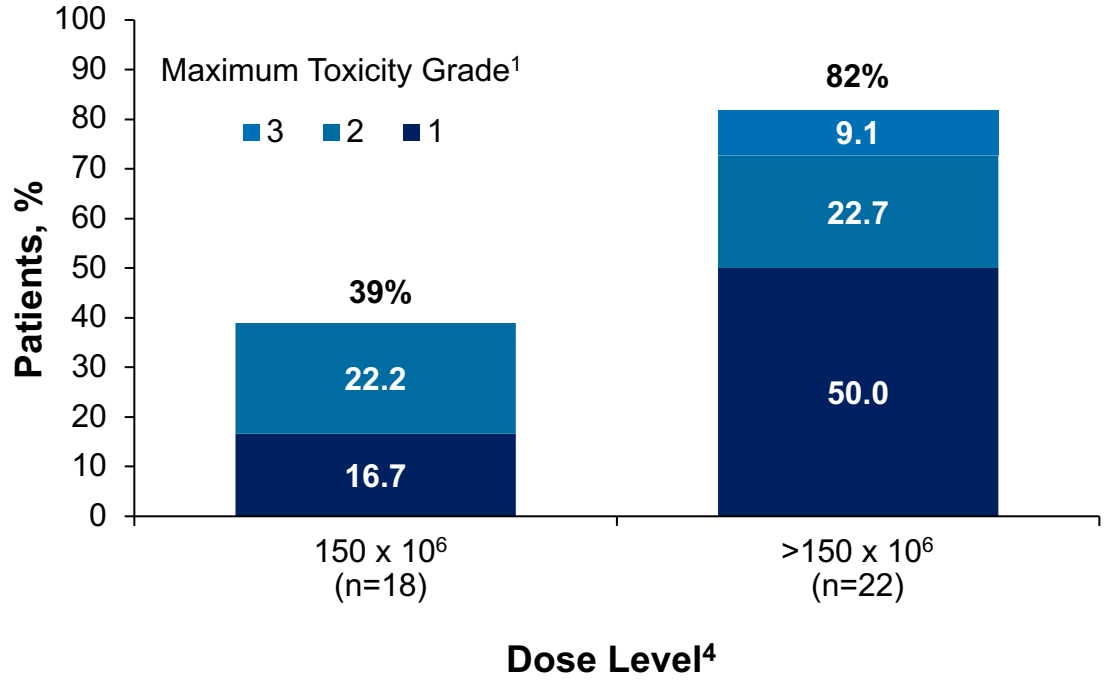
PFS progression-free survival; MRD, minimal residual disease.
Includes patients treated with <50 x 10^6 CAR T cells who were MRD-negative at >1 postbaseline time point

bb2121 Continues to be Generally Well-Tolerated; No New Safety Signals

CAR T Treatment-Emergent Adverse Events
All Infused Patients (N=43)

TEAE, n (%)	Overall	Grade ≥3
Cytokine release syndrome[1]	27 (63)	2 (5)
Neurotoxicity[2]	14 (33)	1 (2)
Neutropenia	35 (81)	34 (79)
Thrombocytopenia	26 (61)	22 (51)
Anemia	24 (56)	19 (44)
Infection[3]		
Overall	26 (61)	9 (21)
First Month	10 (23)	2 (5)

Cytokine Release Syndrome By Dose Level



- No grade 4 CRS events
- No fatal CRS or neurotoxicity events

- Patients with a CRS event, 63%

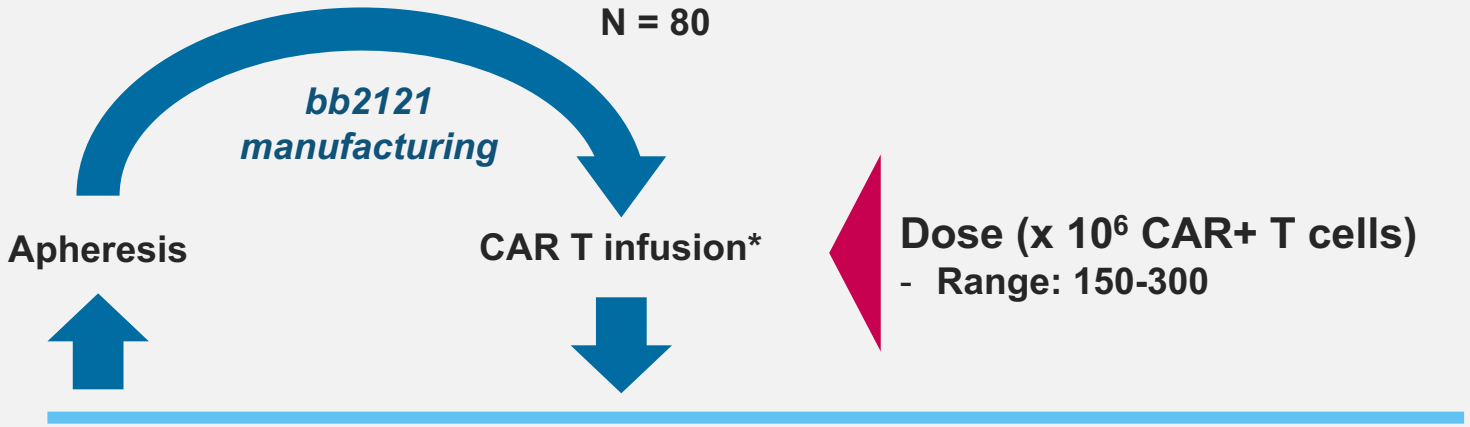
Data cut-off: March 29, 2018. NE, not estimable.[1]CRS uniformly graded per Lee et al., *Blood* 2014;124:188-195. [2]Events occurring in first 28 d and including dizziness, bradyphrenia, somnolence, confusional state, nystagnmus, insomnia, memory impairment, depressed level of consciousness, neurotoxicity, lethargy, tremor and hallucination. [3]Includes the SOC Infections and Infestations. Events observed in >10% include upper respiratory tract infection and pneumonia. [4]3 patients were treated at the 50 x 10^6 dose level for a total of 43 patients.

bb2121-MM-001: bb2121 Registration-Enabling Trial (KarMMa)

KarMMa

Relapsed and refractory MM

- ≥3 prior treatment regimens with ≥ 2 consecutive cycles each (unless PD was best response)
- Received prior IMiD®, PI and anti-CD38
- Refractory (per IMWG) to last treatment regimen



Endpoints

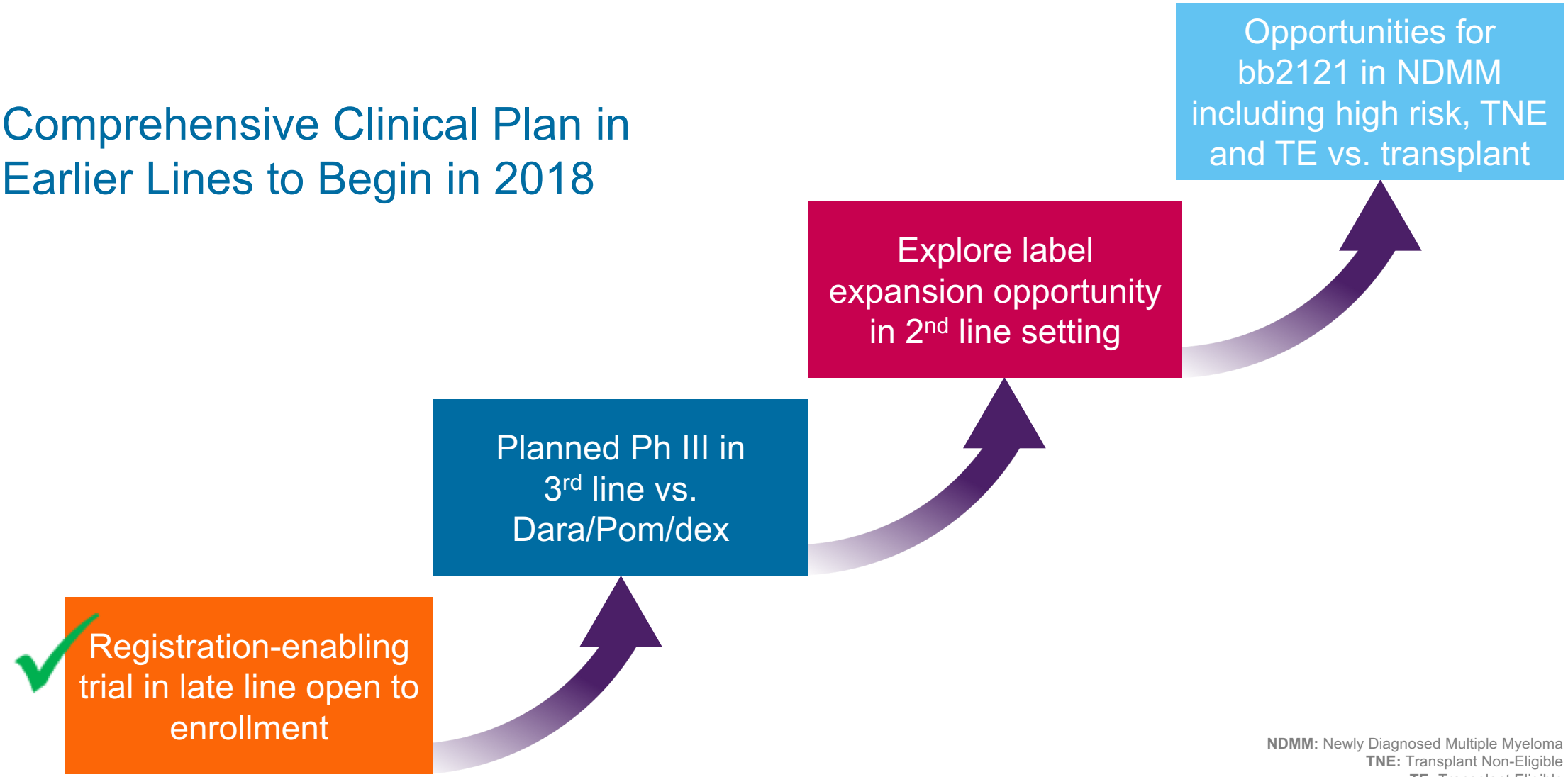
Primary: ORR

Key Secondary: CR, TTR, DOR, PFS, TTP, OS, Safety, bb2121 expansion and persistence, MRD (genomic and flow assays)

Exploratory: BCMA expression/loss, T cell immunophenotype, GEP in BM, HEOR

Advancing bb2121 into Earlier Lines of Multiple Myeloma

Comprehensive Clinical Plan in Earlier Lines to Begin in 2018



NDMM: Newly Diagnosed Multiple Myeloma
TNE: Transplant Non-Eligible
TE: Transplant Eligible

Closing

Nick Leschly, chief bluebird

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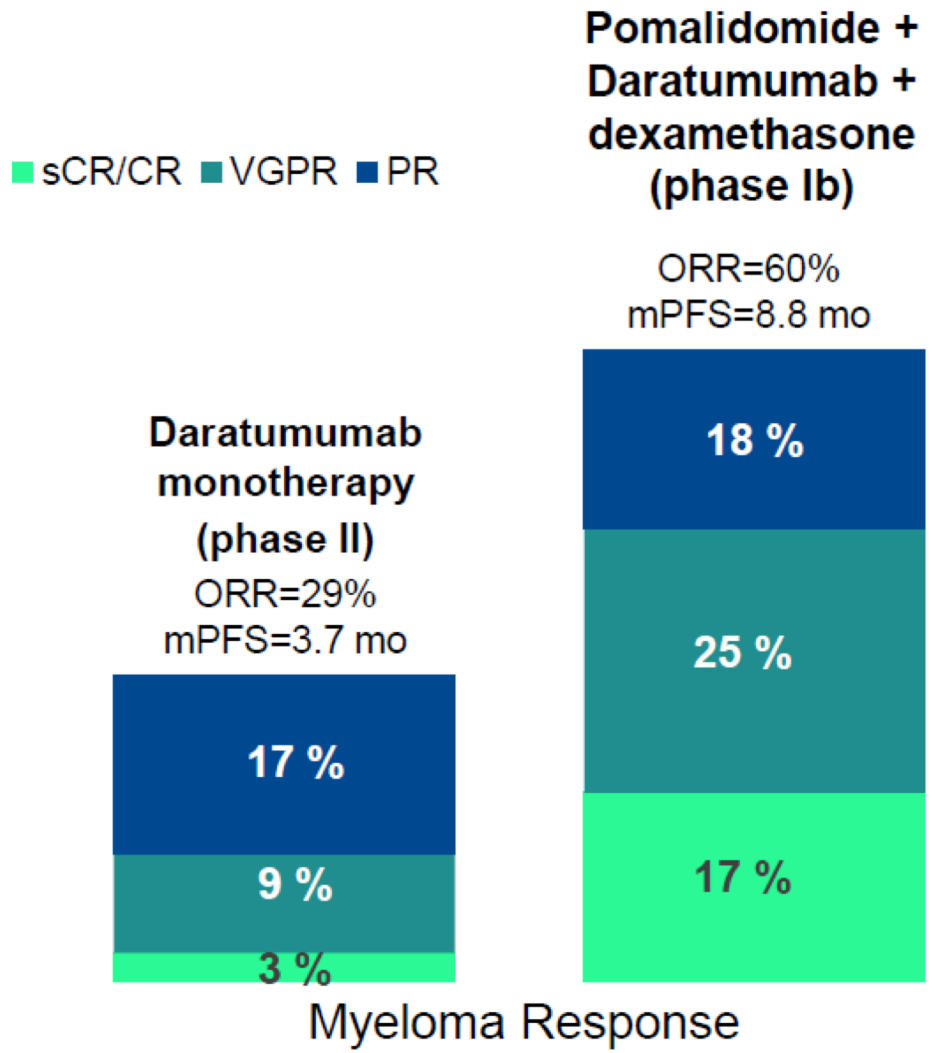
Response to Current Standard of Care in Late Line RRMM

Current standard of care in RRMM after two or more lines of therapy:

	Dara	PDd	bb2121
Phase	II	I	I
N	106	103	43
Eligibility	≥ 3 prior lines Pom allowed Dara-naive	≥ 2 prior lines Pom-naïve Dara-naive	≥ 3 prior lines Pom allowed Dara allowed
Median prior lines	5	4	7

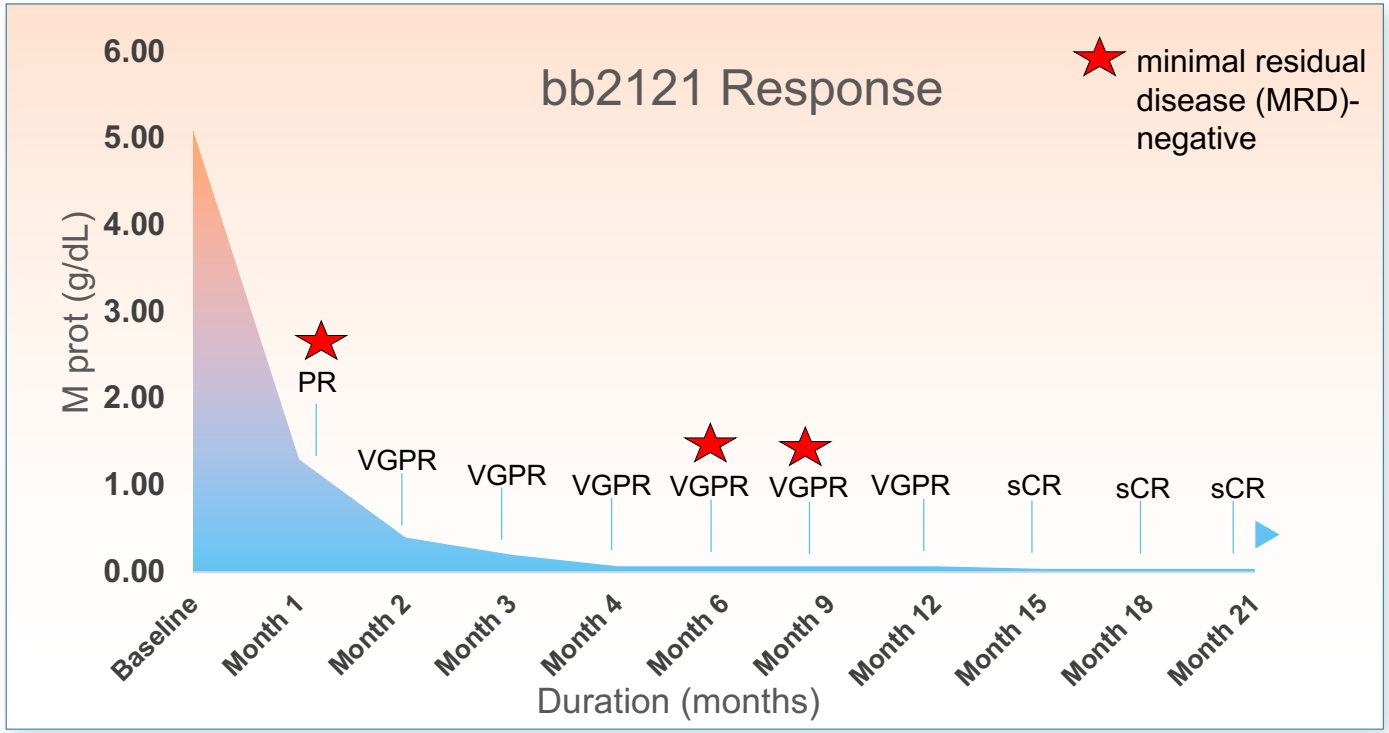
PDd=Pomalidomide + Daratumumab +dexamethasone.
Pom=Pomalidomide; Dara=Daratumumab



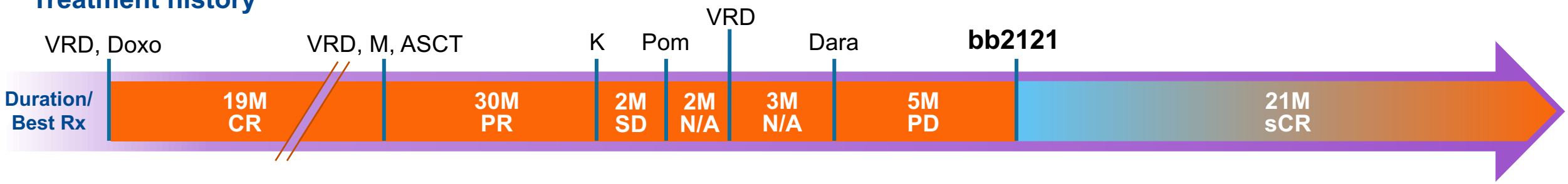
Chari, A. Blood 2017

bb2121 Patient Case: 21 Months in sCR

General Information	
Age & Gender	52 year old Male
Dose group	150x10^6
Tumor Burden	High
High Risk Cytogenetics (based on FISH)	No
Number of prior regimens	6
Initial diagnosis	May, 2010
BCMA% (prescreen, baseline)	60, 75



Treatment history



KEY ASCT: autologous stem cell transplant, R: Revlimid, M: melphalan, d: dexamethasone, V: Velcade, K: Kyprolis, P/Pom: Pomalyst, Vor: vorinostat, Dara: daratumumab, Doxo:Doxorubicin

Key Takeaways

Efficacy?	• 95.5% ORR in doses above 150M cells. • 50% CR rate at doses above 150M cells.
Durability?	• 11.8 months median PFS in dose-escalation active doses. • 17.7 months median PFS in MRD(-) patients with response (escalation and expansion).
BCMA? MRD?	• Consistent responses across BCMA expression levels. • 16/16 responding, MRD-evaluable patients were MRD negative.
Safety?	• No new safety signals (G3/G4 CRS or Neurotox).
Path forward?	• KarMMa on track. Earlier line development plan advancing.

Stay Tuned…

EHA

TDT
NORTHSTAR-2 STUDY
Updated data

SCD
HGB-206
Updated data

MM
CRB-401
Encore data presentation

EHA Conference Call: June 15, 8:00 am ET

2H**

TDT
EMA filing

TDT
NORTHSTAR-3 STUDY
First clinical data in TDT and β^0/β^0 genotypes

MM
Initiate 3rd line study*

SCD
Update on development and registration strategy

MM
CRB-402
First bb21217 clinical data

CALD
Starbeam STUDY
Updated data

*Celgene Responsibility, **Anticipated Clinical Data Updates


Q&A
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