This presentation includes forward-looking statements regarding Nektar’s proprietary drug candidates, the timing of the start and conclusion of ongoing or planned clinical trials, the timing and outcome of regulatory decisions, and future availability of clinical trial data. Actual results could differ materially and these statements are subject to important risks detailed in Nektar's filings with the SEC including the Form 10-Q filed on November 8, 2018. Nektar undertakes no obligation to update forward-looking statements as a result of new information or otherwise.
Dr. Arlene O. Siefker-Radtke

Dr. Siefker-Radtke is a professor in the department of Genitourinary Medical Oncology, Division of Cancer Medicine at the University of Texas MD Anderson Cancer Center. She also serves as the Clinical Co-leader of the Bladder Cancer Specialized Program of Research Excellence (SPORE) Executive Committee.

She has been practicing for 20 years since graduating from Johns Hopkins University, School of Medicine in 1996. She specializes in bladder cancer, and specifically the development of novel immuno-oncology and other targeted agents.
Today’s Speakers

Dr. Arlene O. Siefker-Radtke
Professor of Genitourinary Medical Oncology, Division of Cancer Medicine, The University of Texas MD Anderson Cancer Center

Dr. Jonathan Zalevsky
Chief Scientific Officer Nektar Therapeutics

Dr. Mary Tagliaferri
Chief Medical Officer Nektar Therapeutics
Today’s Agenda

• Arlene Siefker-Radtke M.D., MD Anderson Cancer Center
  • Background on Urothelial Cancer and Treatment
  • “NKTR-214 + nivolumab in first-line advanced/metastatic urothelial carcinoma (mUC): Updated results from PIVOT-02”

• Jonathan Zalevsky Ph.D., Nektar Therapeutics
  • Biomarker and Translational Medicine

• Mary Tagliaferri M.D., Nektar Therapeutics
  • Development Strategy in Urothelial Cancer

• Open to Q&A
Incidence of Urothelial Cancer

- Urothelial cancers encompass carcinomas of the bladder, ureters, and renal pelvis, which occur at a ratio of 50:3:1, respectively\(^1\)
- 9\(^{th}\) most common cancer worldwide (~430,000 diagnosed worldwide annually)\(^2\); 6\(^{th}\) most common cancer in US
  - Stage 1 at diagnosis (in situ)\(^3\) : 51%
  - Stage 2 at diagnosis (localized)\(^3\) : 34%
  - Stage 3/4 at diagnosis\(^3\) : 11%
- Tumor recurrence or progression occurs in more than half of patients\(^2\)
- ~75\% of all cases occur in men (4\(^{th}\) most common cancer in men)\(^2\)
- Peak incidence in the seventh decade of life\(^3\)

1. 2016 Cancer Network; 2. BMC Cancer 2016; 3. SEER 18 2008-2014, All Races, Both Sexes by SEER Summary Stage 2000 (3\% of cases are unknown stage of diagnosis)
Metastatic Stage IV Urothelial Cancer (mUC)

- ~20-40% of all patients with superficial bladder cancer will progress to more advanced stages including muscle-invasive bladder cancer (MIBC) with metastases\(^1\)
- Cisplatin-gemcitabine remains standard-of-care (SOC) for these patients (based upon eligibility)
- Metastatic stage IV patients have the worst prognosis with a 5-year survival rate of only 4.8\(^2\)
- In the community setting, over 50% of patients are not eligible for cisplatin therapies
- For those that are cisplatin-ineligible or refuse SOC, treatment options include:
  - Gemcitabine-carboplatin regimen
  - Single agent checkpoint inhibitor therapy

\(^1\) UNM Health Sciences Center; 2. SEER 18 2008-2014, All Races, Both Sexes by SEER Summary Stage 2000
Two anti-PD1/PD-L1 agents have approval in the 1L cisplatin-ineligible setting

Regulatory authorities have restricted 1L usage to patients whose tumors with high PD-L1 expression, CPS ≥ 10, or PD-L1 IC ≥ 5%.

The Agency took this action on June 19, 2018, due to decreased survival associated with the use of Keytruda (pembrolizumab) or Tecentriq (atezolizumab) as monotherapy compared to platinum-based chemotherapy in clinical trials to treat mUC patients who have not received prior therapy and who have low PD-L1 expression

The labels of both drugs have been revised to reflect the limitation in the indication:

- **KEYTRUDA** is indicated for the treatment of patients with locally advanced or metastatic urothelial carcinoma who are not eligible for cisplatin-containing therapy and whose tumors express PD-L1 (Combined Positive Score ≥ 10), or in patients who are not eligible for any platinum-containing chemotherapy regardless of PD-L1 status.

- **TECENTRIQ** is indicated for the treatment of patients with locally advanced or metastatic urothelial carcinoma who:
  - Are not eligible for cisplatin-containing therapy, and whose tumors express PD-L1 (PD-L1 stained tumor-infiltrating immune cells [IC] covering ≥5% of the tumor area), as determined by an FDA-approved test, or
  - Are not eligible for any platinum-containing therapy regardless of PD-L1 status


1. Tecentriq (atezolizumab) [package insert]. South San Francisco, CA: Genentech, Inc.; 2018;
**PD-L1 Expression Prevalence in 1L mUC**

Approximately 70% of cisplatin-ineligible patients have tumors with low PD-L1 expression (regardless of testing methods) leaving a high unmet need for new therapies

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Assay</th>
<th>PD-L1 High Definition</th>
<th>Prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>PD-L1 high</td>
</tr>
<tr>
<td>ATEZO</td>
<td>VENTANA SP142</td>
<td>≥ 5% expression on tumor infiltrating immune cells</td>
<td>27%</td>
</tr>
<tr>
<td>PEMBRO</td>
<td>22C3 pharmDx</td>
<td>Combined positive score of ≥ 10*</td>
<td>30%</td>
</tr>
</tbody>
</table>

* CPS = (PD-L1 positive tumor cells, lymphocytes, macrophages) / number of viable tumor cells x 100

Sources: Product Inserts for atezolizumab and pembrolizumab

- Pembrolizumab and atezolizumab utilize a different PD-L1 assay with different definition of PD-L1 high and low
- Direct comparison between atezolizumab and pembrolizumab assay is not possible given differences in assays; however, both the pembrolizumab and atezolizumab assays are FDA validated assays for the 1L cisplatin-ineligible population
# Atezolizumab and Pembrolizumab in 1L Cis-ineligible Advanced Urothelial Cancer: PD-L1 Low Expressors

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Source</th>
<th>Data Cut-off</th>
<th>Published</th>
<th>N-size</th>
<th>PD-L1 Status</th>
<th>ORR</th>
<th>CR</th>
<th>PR</th>
<th>DoR</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ATEZO</strong></td>
<td>ASCO 2018</td>
<td>29 mo. (7/2017)</td>
<td>6/2018</td>
<td>(N=87)</td>
<td>&lt; 5%</td>
<td>22%</td>
<td>NA</td>
<td>NA</td>
<td>NE</td>
</tr>
<tr>
<td></td>
<td>Lancet 2017</td>
<td>17 mo. (7/2016)</td>
<td>1/2017</td>
<td>(N=39)</td>
<td>&lt; 1%</td>
<td>21%</td>
<td>NA</td>
<td>NA</td>
<td>NE (12.8-NE)</td>
</tr>
<tr>
<td></td>
<td>Package Insert</td>
<td>NR</td>
<td>12/2018</td>
<td>(N=87)</td>
<td>&lt; 5%</td>
<td>21.8%</td>
<td>6.9%</td>
<td>14.9%</td>
<td>NR (8.1,15.6+)</td>
</tr>
<tr>
<td><strong>PEMBRO</strong></td>
<td>ASCO 2018</td>
<td>Up to 24 mo. (11/2017)</td>
<td>6/2018</td>
<td>(N=110)</td>
<td>&lt; 10</td>
<td>21%</td>
<td>3%</td>
<td>18%</td>
<td>NE (1.4+,16.3+)</td>
</tr>
<tr>
<td></td>
<td>Lancet 2017</td>
<td>Up to 10 mo. (9/2016)</td>
<td>11/2017</td>
<td>(N=46)</td>
<td>&lt; 1</td>
<td>11%</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td></td>
<td>Package Insert</td>
<td>NR</td>
<td>12/2018</td>
<td>(N=260)</td>
<td>&lt; 10</td>
<td>21%</td>
<td>3%</td>
<td>18%</td>
<td>NE (1.4+,16.3+)</td>
</tr>
</tbody>
</table>

NE = Not estimable; NR = Not reached; NA = Data point not provided / mentioned in sources and papers.
Atezolizumab and Pembrolizumab in 1L Cis-ineligible Advanced Urothelial Cancer: All Patients (Combined High and Low PD-L1 Populations)

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Source</th>
<th>Data Cut-off</th>
<th>Published</th>
<th>N-size</th>
<th>ORR</th>
<th>CR</th>
<th>PR</th>
<th>DCR</th>
<th>DoR</th>
</tr>
</thead>
<tbody>
<tr>
<td>ATEZO</td>
<td>ASCO 2018</td>
<td>29 mo. (7/2017)</td>
<td>6/2018</td>
<td>(N=119)</td>
<td>24%</td>
<td>8%</td>
<td>16%</td>
<td>NA</td>
<td>NE (30.4-NE)</td>
</tr>
<tr>
<td></td>
<td>Lancet 2017</td>
<td>17 mo. (7/2016)</td>
<td>1/2017</td>
<td>(N=119)</td>
<td>23%</td>
<td>9.2%</td>
<td>13.4%</td>
<td>NA</td>
<td>NE (14.1-NE)</td>
</tr>
<tr>
<td></td>
<td>Package Insert</td>
<td>NR</td>
<td>12/2018</td>
<td>(N=119)</td>
<td>23.5%</td>
<td>6.7%</td>
<td>16.8%</td>
<td>NA</td>
<td>NR (3.7,16.6+)</td>
</tr>
<tr>
<td>PEMBRO</td>
<td>ASCO 2018</td>
<td>Up to 24 mo. (11/2017)</td>
<td>6/2018</td>
<td>(N=370)</td>
<td>29%</td>
<td>7%</td>
<td>22%</td>
<td>NA</td>
<td>NR (1.4+,17.8+)</td>
</tr>
<tr>
<td></td>
<td>Lancet 2017</td>
<td>Up to 10 mo. (9/2016)</td>
<td>11/2017</td>
<td>(N=370)</td>
<td>24%</td>
<td>5%</td>
<td>19%</td>
<td>47%</td>
<td>NR (9-NR)</td>
</tr>
<tr>
<td></td>
<td>Package Insert</td>
<td>NR</td>
<td>12/2018</td>
<td>(N=370)</td>
<td>29%</td>
<td>7%</td>
<td>22%</td>
<td>NA</td>
<td>NR (1.4+,17.8+)</td>
</tr>
</tbody>
</table>

NE = Not estimable; NR = Not reached; NA = Data point not provided / mentioned in sources and papers
Bempegaldesleukin* (NKTR-214) + nivolumab in first-line advanced/metastatic urothelial carcinoma: Updated results from PIVOT-02

Arlene Siefker-Radtke¹, Mayer Fishman², Arjun V. Balar³, Giovanni Grignani⁴, Adi Diab¹, Jianjun Gao¹, Mary Tagliaferri⁵, Alison Hannah⁵, Erin Karski⁵, Jonathan Zalevsky⁵, Ute Hoch⁵, Ahsan Rizwan⁵, EJ Liao⁵, Mehmet A. Bilen⁶

1. University of Texas MD Anderson Cancer Center, Houston, TX;
2. H. Lee Moffit Cancer Center & Research Institute, Tampa, FL;
3. Perlmutter Cancer Center at NYU Langone Health, New York, NY;
4. Candiolo Cancer Institute - FPO, IRCCS, Candiolo, Italy;
5. Nektar Therapeutics, San Francisco, CA;
6. Winship Cancer Institute of Emory University, Atlanta, GA
About Bempegaldesleukin (NKTR-214)

- Bempegaldesleukin (NKTR-214) is a CD122-preferential IL-2 pathway agonist that has been shown to increase tumor-infiltrating lymphocytes, T cell clonality and increase PD-1 expression\(^1,2\)

- Bempegaldesleukin combined with checkpoint inhibitor nivolumab has been shown to convert PD-L1 non-expressors to expressors (PD-L1 negative <1% to PD-L1 ≥1%)\(^2\)

- PIVOT-02 is a multicenter, Phase 1/2 study evaluating bempegaldesleukin plus nivolumab and includes a cohort of patients with locally advanced or metastatic UC who are cisplatin-ineligible or cisplatin-eligible who have refused SOC

Bempegaldesleukin + Anti-PD-1 Combination Highly Efficacious in Mouse Model of Bladder Cancer

C3H mice, N=7/group; SC implant of MBT-2; bempegaldesleukin, 0.8 mg/kg IV, q9dx3; Anti-PD-1, 200 µg IP, BIWx3W; * p < 0.05 vs Vehicle; ** p < 0.05 vs anti-PD-1
Ongoing PIVOT-02 Study: 1L mUC Cohort

Primary endpoints:
- Safety and tolerability per CTCAE v4.03
- ORR per RECIST v1.1 assessed every 8 (±1) weeks
- Per protocol, efficacy evaluable is defined as patients with ≥1 post-baseline scan

Secondary and exploratory endpoints:
- Duration of response, OS, PFS, clinical benefit rate, PK
- ORR by immune related RECIST (irRECIST)

Biomarker endpoints (subset of patients in each cohort):**
- Absolute lymphocyte count and blood immuno-phenotyping
- Baseline and on-treatment biopsies (3 weeks) were collected in patients, when clinically feasible

Preliminary data presented have a cut-off of Dec 3, 2018

ECOG PS: Eastern Cooperative Oncology Group performance score; mUC: Locally advanced or metastatic UC; ORR: overall response rate; OS: overall survival; PFS: progression free survival; PK: pharmacokinetics; RECIST: response evaluation criteria in solid tumors; RP2D: recommended phase 2 dose

**Patients submitted tissue during screening and underwent tumor biopsy during week 3 of treatment

DOSE ESCALATION ACROSS A RANGE OF SOLID TUMORS

bempegaldesleukin 0.003 mg/kg q2w + nivolumab 240 mg q2w

bempegaldesleukin 0.006 mg/kg q3w + nivolumab 240 mg q2w

Recommended Phase 2 dose
bempegaldesleukin 0.006 mg/kg q3w + nivolumab 360 mg q3w

DOSE EXPANSION

1L mUC expansion cohort

Other tumor types being evaluated in separate expansion arms (ongoing)

Key mUC Inclusion Criteria
- Unresectable locally advanced or metastatic disease
- Cisplatin-ineligible
- Cisplatin-eligible who refused SOC
- ECOG 0-1

- 41 mUC patients enrolled and received at least one dose of bempegaldesleukin + nivolumab
- 27 patients were efficacy evaluable defined as having at least one post-baseline scan (26/27 Stage IV metastatic UC)

**Patients submitted tissue during screening and underwent tumor biopsy during week 3 of treatment

DOSE ESCALATION ACROSS A RANGE OF SOLID TUMORS

bempegaldesleukin 0.006 mg/kg q2w + nivolumab 240 mg q2w

bempegaldesleukin 0.009 mg/kg q3w + nivolumab 360 mg q3w

Recommended Phase 2 dose
bempegaldesleukin 0.006 mg/kg q3w + nivolumab 360 mg q3w

DOSE EXPANSION

1L mUC expansion cohort

Other tumor types being evaluated in separate expansion arms (ongoing)
# PIVOT-02: Baseline Patient Characteristics in 1L mUC

<table>
<thead>
<tr>
<th>n, %</th>
<th>All Patients (N=41)</th>
<th>Efficacy Evaluable (n=27)*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age, median (range) in years</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Population</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cisplatin Ineligible</td>
<td>27 (66%)</td>
<td>16 (59%)</td>
</tr>
<tr>
<td>Renal impairment</td>
<td>19 (70%)</td>
<td>12 (75%)</td>
</tr>
<tr>
<td>Hearing Loss</td>
<td>4 (15%)</td>
<td>2 (13%)</td>
</tr>
<tr>
<td>Peripheral neuropathy, grade ≥2</td>
<td>4 (15%)</td>
<td>1 (6%)</td>
</tr>
<tr>
<td>Missing</td>
<td>1 (4%)</td>
<td>1 (6%)</td>
</tr>
<tr>
<td>Cisplatin Eligible (refused SOC)</td>
<td>14 (34%)</td>
<td>11 (41%)</td>
</tr>
<tr>
<td><strong>Sex</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>29 (71%)</td>
<td>20 (74%)</td>
</tr>
<tr>
<td>Female</td>
<td>12 (29%)</td>
<td>7 (26%)</td>
</tr>
<tr>
<td><strong>PD-L1 Status</strong>^a</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive [≥ 1% TC]</td>
<td>13 (32%)</td>
<td>12 (44%)</td>
</tr>
<tr>
<td>Negative [&lt;1% TC]</td>
<td>13 (32%)</td>
<td>11 (41%)</td>
</tr>
<tr>
<td>Not evaluable^b</td>
<td>2 (5%)</td>
<td>-</td>
</tr>
<tr>
<td>Not available^b</td>
<td>13 (32%)</td>
<td>4 (15%)</td>
</tr>
<tr>
<td><strong>Locally Advanced Disease</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Metastatic Disease (Stage IV)</td>
<td>40 (98%)</td>
<td>26 (96%)</td>
</tr>
<tr>
<td>Lymph node only^c</td>
<td>16 (39%)</td>
<td>11 (41%)</td>
</tr>
<tr>
<td>Visceral (non-nodal metastases)^d</td>
<td>24 (59%)</td>
<td>15 (56%)</td>
</tr>
<tr>
<td><strong>ECOG Performance Score</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>18 (44%)</td>
<td>13 (48%)</td>
</tr>
<tr>
<td>1</td>
<td>22 (54%)</td>
<td>14 (52%)</td>
</tr>
<tr>
<td>Not available</td>
<td>1 (2%)</td>
<td>-</td>
</tr>
<tr>
<td><strong>Prior systemic neoadjuvant therapy</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prior systemic adjuvant therapy</td>
<td>5 (12%)</td>
<td>4 (15%)</td>
</tr>
<tr>
<td>Previous Cystectomy</td>
<td>5 (12%)</td>
<td>2 (7%)</td>
</tr>
</tbody>
</table>

All pts (N=41) received at least one dose of bempegaldesleukin and nivolumab

^a PD-L1 status evaluated using the 28-8 PharmDx assay; TC: tumor cells

^b Pts with PD-L1 assessment N/E: biopsy sample collected but tissue not evaluable; Pts with PD-L1 assessment N/A: 4 pts no available biopsy samples for analysis due to physician waivers; 9 pts pending biopsy sample analysis.

^c Defined as disease metastasized to lymph node (LN) only (includes only pts with LN disease or LN + primary site of disease)

^d Defined as disease metastasized outside of lymph nodes (excludes pts with LN disease or LN + primary site of disease)

*Efficacy-evaluable defined per protocol as patients with at least one post-baseline scan. As of 12/3/2018, 1 pt was excluded for non-eligibility (no target lesion), and 3 pts discontinued prior to first scan (1 due to pt decision; 1 due to clinical progression; 1 due to death from disease). 10 pts pending first scan in database.
## PIVOT-02: Treatment-Related Adverse Events (TRAE) in 1L mUC

<table>
<thead>
<tr>
<th>Patients experiencing at least one TRAE</th>
<th>N=41 (n, %)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Most Common TRAEs Grade 1 or 2 occurring in &gt;15% of the population^a</td>
<td>36 (88%)</td>
</tr>
<tr>
<td>Flu-like symptoms^b</td>
<td>29 (71%)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>23 (56%)</td>
</tr>
<tr>
<td>Rash^c</td>
<td>19 (46%)</td>
</tr>
<tr>
<td>Pruritus</td>
<td>13 (32%)</td>
</tr>
<tr>
<td>Decreased appetite</td>
<td>11 (27%)</td>
</tr>
<tr>
<td>Nausea</td>
<td>9 (22%)</td>
</tr>
<tr>
<td>Patients experiencing at least one Grade 3 TRAE</td>
<td>6 (15%)</td>
</tr>
<tr>
<td>Flu-like symptoms^b,e</td>
<td>2 (5%)</td>
</tr>
<tr>
<td>Hypotension^e</td>
<td>1 (2%)</td>
</tr>
<tr>
<td>Drug reaction with eosinophilia and systemic symptoms^d</td>
<td>1 (2%)</td>
</tr>
<tr>
<td>Encephalopathy^d,f</td>
<td>1 (2%)</td>
</tr>
<tr>
<td>Hypereosinophilic syndrome^f</td>
<td>1 (2%)</td>
</tr>
<tr>
<td>Myasthenic syndrome^d</td>
<td>1 (2%)</td>
</tr>
<tr>
<td>Complete atrioventricular block^d,g</td>
<td>1 (2%)</td>
</tr>
<tr>
<td>Myocarditis^g</td>
<td>1 (2%)</td>
</tr>
<tr>
<td>Myositis^g</td>
<td>1 (2%)</td>
</tr>
<tr>
<td>Patients experiencing at least one Grade 4 or 5 TRAE</td>
<td>0</td>
</tr>
<tr>
<td>Patients who discontinued due to a TRAE</td>
<td>4 (10%)</td>
</tr>
</tbody>
</table>

---

^a All AE’s Grade 1 or 2 except for two events of Grade 3 flu-like symptoms
^b Includes preferred terms: chills, influenza like illness, pyrexia, influenza
^c Includes preferred terms: erythema, rash, rash erythematous, rash generalized, rash macular, rash maculo-papular, rash maculovesicular, rash papular, rash pruritic, rash pustular, rash vesicular, exfoliative rash
^d AE leading to treatment discontinuation
^e One event of flu-like symptoms and hypotension occurred in same pt
^f Encephalopathy and hypereosinophilic syndrome occurred in same pt
^g Complete atrioventricular block, myocarditis, and myositis occurred in same pt
**PIVOT-02: RECIST v1.1 Objective Response Rate in 1L mUC**

<table>
<thead>
<tr>
<th>Efficacy Evaluable Patients, n</th>
<th>Total Efficacy Evaluable±</th>
<th>PD-L1 &lt;1%</th>
<th>PD-L1 ≥1%</th>
<th>PD-L1 Unknown</th>
</tr>
</thead>
<tbody>
<tr>
<td>ORR* (CR+PR)</td>
<td>27</td>
<td>11</td>
<td>12</td>
<td>4</td>
</tr>
<tr>
<td>CR</td>
<td>5 (19%)</td>
<td>2 (18%)</td>
<td>3 (25%)</td>
<td>0</td>
</tr>
<tr>
<td>PR</td>
<td>8 (30%)</td>
<td>3 (27%)</td>
<td>3 (25%)</td>
<td>2 (50%)</td>
</tr>
<tr>
<td>DCR (CR+PR+SD)</td>
<td>19 (70%)</td>
<td>8 (73%)</td>
<td>9 (75%)</td>
<td>2 (50%)</td>
</tr>
<tr>
<td>SD</td>
<td>6 (22%)</td>
<td>3 (27%)</td>
<td>3 (25%)</td>
<td>0</td>
</tr>
<tr>
<td>PD</td>
<td>8 (30%)</td>
<td>3 (27%)</td>
<td>3 (25%)</td>
<td>2 (50%)</td>
</tr>
</tbody>
</table>

ORR for efficacy evaluable cis-ineligible population (n=16) is 44%  
CR: complete response; DCR: disease control rate; PD: progressive disease; PR: partial response; SD: stable disease;  
*As of data cut-off date of 12/3/2018, ORR by primary investigator assessment included 4 unconfirmed responses: two patients with uPR and one patient with uCR pending confirmatory scan and one patient with uPR discontinued for AE after first scan with no confirmatory scan. Since 12/3/2018, 3 of 4 patients have had scans confirming responses (including CR)  
±Efficacy Evaluable defined per protocol as patients with at least one post-baseline scan. As of 12/3/2018, 1 pt was excluded for non-eligibility (no target lesion), and 3 pts discontinued prior to first scan [1 due to pt decision; 1 due to clinical progression; 1 due to death from disease]; 10 pts pending first scan in database
### PIVOT-02: RECIST v1.1 Objective Response Rate by Assay in 1L mUC

<table>
<thead>
<tr>
<th>% TC Cells*</th>
<th>Combined Positive Score (CPS)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>PD-L1 &lt;1%</td>
<td>CPS Score &lt;1</td>
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<td>Efficacy Evaluable Patients, n</td>
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<tr>
<td>ORR (CR+PR)</td>
<td>5 (45%)</td>
</tr>
<tr>
<td>CR</td>
<td>2 (18%)</td>
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<tr>
<td>PR</td>
<td>3 (27%)</td>
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<tr>
<td>DCR (CR+PR+SD)</td>
<td>8 (73%)</td>
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<tr>
<td>SD</td>
<td>3 (27%)</td>
</tr>
<tr>
<td>PD</td>
<td>3 (27%)</td>
</tr>
</tbody>
</table>

*CPS* Calculated using 28-8 assay

*Calculated using 28-8 assay*
PIVOT-02: RECIST v1.1 Objective Response Rate by Assay in 1L mUC

<table>
<thead>
<tr>
<th>Efficacy Evaluable Patients, n</th>
<th>% TC Cells*</th>
<th>Combined Positive Score (CPS)*</th>
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<tr>
<td></td>
<td>PD-L1 &lt;1%</td>
<td>PD-L1 ≥1%</td>
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<tr>
<td>ORR (CR+PR)</td>
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<td></td>
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<tr>
<td>11</td>
<td>5 (45%)</td>
<td>6 (50%)</td>
</tr>
<tr>
<td>12</td>
<td>6 (50%)</td>
<td></td>
</tr>
<tr>
<td>CR</td>
<td>2 (18%)</td>
<td>3 (25%)</td>
</tr>
<tr>
<td>1 (10%)</td>
<td>4 (31%)</td>
<td>2 (15%)</td>
</tr>
<tr>
<td>1 (10%)</td>
<td>4 (31%)</td>
<td>2 (15%)</td>
</tr>
<tr>
<td>PR</td>
<td>3 (27%)</td>
<td>3 (25%)</td>
</tr>
<tr>
<td>3 (27%)</td>
<td>3 (25%)</td>
<td></td>
</tr>
<tr>
<td>DCR (CR+PR+SD)</td>
<td>8 (73%)</td>
<td>9 (75%)</td>
</tr>
<tr>
<td>3 (27%)</td>
<td>3 (25%)</td>
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</tr>
<tr>
<td>SD</td>
<td>3 (27%)</td>
<td>3 (25%)</td>
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<tr>
<td>3 (27%)</td>
<td>3 (25%)</td>
<td></td>
</tr>
<tr>
<td>PD</td>
<td>3 (27%)</td>
<td>3 (25%)</td>
</tr>
</tbody>
</table>

*Calculated using 28-8 assay
PIVOT-02: Best Overall Response in 1L mUC at RP2D

Overall Response Rate

- ORR by RECIST*: 13 (48%)
- ORR by irRECIST: 14 (52%)

Responses noted across all disease locations

- Visceral non-nodal metastases (n=15): 8 (53%)
- Nodal metastases (n=11): 5 (46%)

*As of data cut-off date of 12/3/2018, ORR by primary investigator assessment included 4 unconfirmed responses: two patients with uPR and one patient with uCR pending confirmatory scan and one patient with uPR discontinued for AE after first scan with no confirmatory scan. Since 12/3/2018, 3 of 4 patients have since had scans confirming responses (including CR)
PIVOT-02: Target Lesion Change Over Time in 1L mUC at RP2D

1L metastatic urothelial cancer (n=27 Efficacy Evaluable)

- Median duration of Follow-Up (months): 5.1
- Median Time to Response (months): 2
- Patients with Ongoing Responses: 11/13 (85%)
- Median % reduction from baseline in responders: 78%
- Median % reduction from baseline, all efficacy evaluable patients: 32%

In patients with RECIST response, no patients discontinued due to relapse. Two patients discontinued for TRAE.

*NR = Not reached
SITC 2018: Stage IV IO-Naïve 1L Melanoma Cohort with CR Rate of 24% (SITC 2018)

Overall Response Rate
- Confirmed ORR (CR+PR): 20 (53%)
- CR: 9 (24%)
- DCR (CR+PR+SD): 29 (76%)
- PD-L1 negative (n=14): 6 (43%)
- PD-L1 positive (n=19): 13 (68%)
- PD-L1 unknown (n=5): 1 (20%)
- LDH > ULN (n=11): 5 (45%)
- Liver metastases (n=10): 5 (50%)

High level of concordance in ORR between independent central radiology (53%) and investigator-assessed 19/38 (50%).

Per protocol, efficacy evaluable is defined as patients with ≥ 1 post baseline scan. 3 patients discontinued prior to 1st scan due to an unrelated TEAE [n=1] and Patients Decision [n=2]. One patient not represented in plot had target lesions per protocol by investigator assessment but did not have target lesions at baseline by independent central radiology; patient achieved SD based on non-target lesions during the study. #: Best overall response is PD. *: Best overall response is SD. + Best overall response is PR with -100% reduction of target lesions. §: Best overall response of CR is unconfirmed; PR confirmed.
Case Study: Pseudoprogression in Urothelial Cancer Patient with 64% Tumor Reduction from Baseline at Week 40

- One documented case of pseudoprogression was observed in a 70-year-old male with disease that included left external iliac lymph nodes (target lesion) and bilateral pulmonary nodules (non-target lesions) at baseline.
- Initial tumor assessment (week 9) revealed 23% increase in target lesions; biopsy of progressing lesions revealed lymphocytic infiltrate on IHC staining.
- Patient continued on treatment; the following scan (week 20) revealed a 28% decrease in target lesions from baseline.
- The week 24 scan revealed a 48% reduction in target lesions from baseline and patient met criteria for PR by irRECIST.
- Patient continues on study treatment; most recent week 40 scan showed 64% decrease from baseline.

Serial CT Scans Consistent With Pseudoprogression with Tumor Reduction Developing by Week 20
Case Study: Near Complete Response in Urothelial Carcinoma Patient with Co-existing Angiosarcoma

- 67 y/o male with stage 4 urothelial cancer reported a history of “waxing and waning” nodule along his right cheek for 1 year.

- For his urothelial cancer, he started on bempegaldesleukin+nivolumab, and within days of starting his therapy reported rapid growth in the skin nodule. After being referred to dermatology, the biopsy was consistent with an angiosarcoma.

- Upon discussion with our angiosarcoma expert, these are often ARID1A positive (mutation testing pending). By cycle 8 of the combination therapy, the angiosarcoma had visually cleared.

- Patient had an unknown PD-L1 status for his UC. His UC has an ARID1A mutation (in addition to FGFR3, POLE, and TSC1). By cycle 8 of the combination therapy, this patient has achieved a near complete response in UC. The patient continues on therapy.
On-Treatment PD-L1 Conversion (PD-L1 Negative to Positive)

- 13 paired tissue samples were evaluated for changes in PD-L1 expression (28-8 Assay)
- 7 of 10 (70%) patients who were PD-L1 negative at Baseline converted to PD-L1 positive by Week 3
- 3 of 3 patients who were PD-L1 positive at Baseline remained PD-L1 positive

Patient with Urothelial Carcinoma

Baseline: PD-L1 Negative

Week 3: PD-L1 Positive

* 1 patient with NE; ^ 1 patient with PD, 1 patient with NE.
2019 ASCO-GU

**RECIST Responses Observed Independent of PD-L1 Status and CD8+ Infiltrate**

- All patients with available baseline PD-L1 Status and CD8 TIL (N=22) were included in the analysis. Five patients from the 27 efficacy evaluable patients did not have sufficient biomarkers to be included in the analysis (4 were not available for PD-L1 and 1 was not evaluable for CD8 TIL). +2 patients with SD

- 22 baseline tissue samples* were evaluated for PD-L1 expression (28-8 IHC pharmDx Assay) and CD8 (Agilent CD8/144B antibody) positive cells and correlation with response

- Similar responses observed across patients regardless of baseline CD8+ TILs

- 4/8 patients with both low CD8+ TIL and no PD-L1 expression achieved responses

---

*All patients with available baseline PD-L1 Status and CD8 TIL (N=22) were included in the analysis. Five patients from the 27 efficacy evaluable patients did not have sufficient biomarkers to be included in the analysis (4 were not available for PD-L1 and 1 was not evaluable for CD8 TIL). +2 patients with SD
Conclusions

• Bempegaldesleukin (NKTR-214) and nivolumab in 1L metastatic urothelial carcinoma was well tolerated and demonstrated promising clinical benefit in patients who were either cisplatin-ineligible or cisplatin-eligible who refused SOC
  • ORR in cisplatin-ineligible was 44%; ORR in refused SOC was 55%
  • Therapy demonstrated deep responses with CR rate of 19% (median 78% tumor shrinkage among responders)
  • No relapses observed among responders

• Responses were observed regardless of baseline PD-L1 expression
  • ORR in PD-L1 positive patients was 50% and PD-L1 negative was 45%

• Bempegaldesleukin + nivolumab demonstrated conversion of PD-L1 status from negative at baseline to positive on treatment
  • 70% (7/10) of matched biopsies converted

• These data support the potential benefit of this combination in patients with urothelial cancer
  • Phase 2 study of bempegaldesleukin and nivolumab in progress to further evaluate efficacy and safety in the 1L cisplatin-ineligible population of patients whose tumors have low expression of PD-L1 (PIVOT-10, NCT 03785925)
Biomarker and Translational Medicine
Jonathan Zalevsky, Chief Scientific Officer
Introduction

- Compare and contrast pharmacodynamics and mechanistic biomarkers between the 1L MEL and 1L UC tumor types after treatment with bempegaldesleukin and nivolumab from PIVOT-02
  - Serial analysis of lymphocyte counts in whole blood
  - Tumor biopsy at baseline and 3 weeks post treatment
    - CD8 TIL infiltration
    - PD-L1 conversion from negative to positive
    - Differential gene expression
    - TCR repertoire changes
  - Correlation of baseline biomarkers with response
Continuous Mobilization of Lymphocytes After Every Treatment Cycle

- Bempegaldesleukin provides rapid activation of the immune system
- Effect of lymphocyte mobilization is consistent and maintained with successive treatment cycles
- Lymphocyte effects observed to similar extent across all IL tumor types shown here from PIVOT-02 (n=180)
Similar TIL Increase After Bempegaldesleukin + Nivolumab in 1L MEL and 1L UC

**IHC for CD8 was obtained by standard methods. All 1L MEL and 1L UC patients with matched Baseline and Week 3 biopsy (N=8) were included in the analysis.**

Fold change was calculated from the Week 3 / Baseline values and is plotted with mean ± SEM.

Source: Diab SITC 2018
Similar TIL Increase After Bempegaldesleukin + Nivolumab in 1L MEL and 1L UC

Even though 1L UC has much lower CD8 TIL at Baseline, bempegaldesleukin + nivolumab effectively increases CD8 TIL infiltrate with same proportion as in 1L MEL.

IHC for CD8 was obtained by standard methods. All 1L MEL and 1L UC patients with matched Baseline and Week 3 biopsy were included in the analysis. Fold change was calculated from the Week 3 / Baseline values and is plotted with mean ± SEM.
Bempegaldesleukin + Nivolumab Promotes Favorable Anti-Tumor Gene Expression Changes in 1L MEL and 1L UC Tumors

- Differential gene expression patterns were similar between 1L MEL and 1L UC cohorts after treatment with bempegaldesleukin + nivolumab in PIVOT-02
  - T cell activation and co-inhibitory receptors
  - Gene associated with cytotoxic effector functions
  - PD-1 and PD-L1 genes
  - CD8 and CD4 Th1 associated genes
  - No induction of Th2 or Th17 or immunosuppressive genes

*Red dots indicate genes which are statistically significant (p-value<=0.05 when applying t-test (one-tailed)) and are over 2 fold higher (in linear space when comparing geometric means) Black dashed lines show 2-fold increase/decrease, red dashed line shows threshold for statistical significance.
Bempegaldesleukin Drives New T Cell Clones into the Tumor Microenvironment in 1L MEL and 1L UC

- All patients evaluated demonstrated new clones at Week 3 that were not present at Baseline.
- New TIL fraction and proportional abundance driven by bempegaldesleukin and with similar results in 1L MEL and 1L UC.
- Results indicate that therapy promotes new priming and T cell trafficking into the tumor.

Tumor biopsy was processed to nucleic acid and used for TCR repertoire analysis using immunoSEQ. Matched Baseline and Week 3 samples are reported as % productive frequency. TCR Clones more abundant at Baseline are shown in red and clones more abundant at Week 3 are shown in blue. Dark grey dots are not significant between timepoints and light gray dots are excluded for low abundance. The gray dashed line lists frequency equality and the red dashed line identifies the population used for statistical comparison. New T Cell infiltrates are shown in the oval.
RECIST Responses Observed Independent of PD-L1 Status and CD8+ Infiltrate in 1L MEL and 1L UC

37% of melanoma patients were PD-L1 negative

61% of UC patients were CPS <10 (Low expressor of PD-L1)

Source: Diab SITC 2018

+2 patients with SD
Conclusion

- Overall similar biomarker and translational medicine results for the combination of bempegaldesleukin + nivolumab in 1L MEL and 1L UC
- Results and activity of the combination are qualitatively similar even though UC has a much lower CD8 TIL infiltrate than MEL
- Supports the concept that the systemic immune activation by bempegaldesleukin and inhibition of local immunosuppressive mechanisms in the tumor by nivolumab can be a broadly applicable IO regimen
Clinical Development Plan
Mary Tagliaferri, Chief Medical Officer
## Nektar-BMS Collaboration: First Set of Registrational Trials Being Implemented

<table>
<thead>
<tr>
<th>Patient Population</th>
<th>Study Design</th>
<th>Number Patients</th>
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<tr>
<td>1L metastatic melanoma</td>
<td>Bempegaldesleukin+Nivo vs. Nivo</td>
<td>764</td>
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<tr>
<td><strong>RCC</strong></td>
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<td>1L metastatic RCC (intermediate/poor risk)</td>
<td>Bempegaldesleukin+Nivo vs. Physicians Choice TKI</td>
<td>600</td>
<td>Q4 2018</td>
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<tr>
<td>1L metastatic RCC (intermediate/poor risk)</td>
<td>Bempegaldesleukin+Nivo+Ipi vs. Nivo+Ipi</td>
<td>820</td>
<td>Q2 2019</td>
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<td>1L metastatic RCC</td>
<td>Bempegaldesleukin+Nivo+TKI vs. Nivo+TKI</td>
<td>330</td>
<td>Q1 2019</td>
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<td><strong>Bladder</strong></td>
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<tr>
<td>1L metastatic cis-ineligible urothelial cancer (PD-L1 negative patients)</td>
<td>Bempegaldesleukin+Nivo (chemo sparing) with gem/carbo reference arm</td>
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<td>Muscle-invasive bladder cancer</td>
<td>Peri-adjvant bempegaldesleukin + Nivo vs Nivo vs Surgery</td>
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<td>2L metastatic NSCLC (post CPI/chemo)</td>
<td>New cohort of bempegaldesleukin + Nivo in PIVOT-02</td>
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<td>1L metastatic NSCLC</td>
<td>Bempegaldesleukin+Nivo regimens</td>
<td>&gt;700</td>
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<tr>
<td>2L/3L metastatic NSCLC (post CPI)</td>
<td>Bempegaldesleukin+Nivo regimens</td>
<td>&gt;600</td>
<td>Q2 2019</td>
</tr>
</tbody>
</table>
PIVOT-10: Phase 2 1L Metastatic Cis-ineligible Urothelial Cancer (PD-L1 Negative Patients) Trial Design (AA)

Population
- Untreated metastatic or unresectable urothelial cancer
- Cisplatin-ineligible
- Low PD-L1 expression (CPS ≤ 10)

Stratification factors
- Liver metastases (yes vs. no)
- ECOG PS (0 or 1 vs. 2)

Open-Label Treatment

Arm A (Treatment Arm)
- Bempegaldesleukin 0.006mg/kg q3W
- Nivolumab 360 mg
  (n=110)

Arm B (Reference Arm)
- Gemcitabine 1000 mg/m² on Days 1 & 8
- Carboplatin target AUC 4.5 on Day 1
  Cycle = 21 days
  (n=55)

Follow-up for safety, RECIST 1.1 progression, and survival

Endpoints
- Primary
  - ORR by BICR
- Secondary
  - PFS by BICR
  - OS in population
  - mDOR by BICR
  - Safety/tolerability

Randomization 2:1 N=165
(Cross-over with progression)
Phase 3 Confirmatory Trial 1L Muscle Invasive Bladder Cancer in Cis-ineligible Patients Trial Design

**Population**
- Muscle invasive, resectable urothelial cancer
- Stage T2-T4a
- Cisplatin-ineligible
- PS 0-1

**Stratification factors**
- Stage (T2 vs T3/4a)
- PD-L1

**Pre-Surgical Treatment**

**Arm A**
- Bempegaldesleukin 0.006 mg/kg q3W + Nivolumab 360 mg q3W x 3 cycles

**Arm B**
- Nivolumab 360 mg q3W x 3 cycles

**Arm C**
- No induction treatment

**Post-Surgical Treatment**

**Radical Cystectomy (All Arms)**
- Bempegaldesleukin 0.006 mg/kg q3W + Nivolumab 360 mg q3W x 9 months
- Nivolumab 360 mg q3W x 9 months

**Follow-up**
- Follow-up visits, monitor for reference and survival, follow-up until death

**Co-Primary Endpoints**
- EFS
- pCR
Q&A Session