**UNITED STATES**
**SECURITIES AND EXCHANGE COMMISSION**
**Washington, D.C. 20549**

**FORM 8-K**

**CURRENT REPORT**
**PURSUANT TO SECTION 13 OR 15(d) OF**
**THE SECURITIES EXCHANGE ACT OF 1934**

Date of Report (Date of earliest event reported): October 2, 2017

# DELMAR PHARMACEUTICALS, INC.

(Exact name of registrant as specified in its charter)

| **Nevada** | **000-54801** | **99-0360497** |
|---|---|---|
| (State or Other Jurisdiction of Incorporation) | (Commission File Number) | (I.R.S. Employer Identification Number) |

Suite 720-999 West Broadway
Vancouver, British Columbia
Canada V5Z 1K5
(Address of principal executive offices)

(604) 629-5989
(Registrant's telephone number, including area code)

Copies to:
Gregory Sichenzia, Esq.
Jeff Cahlon, Esq.
Sichenzia Ross Ference Kesner LLP
1185 Avenue of the Americas, 37th Floor
New York, New York 10036
Phone: (212) 930-9700
Fax: (212) 930-9725

(Former address, if changed since last report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions (see General Instruction A.2. below):

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (17 CFR §230.405) or Rule 12b-2 of the Securities Exchange Act of 1934 (17 CFR §240.12b-2).

Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

**Item 8.01 Other Events.**

On October 2, 2017, DelMar Pharmaceuticals, Inc. presented a poster at the American Association for Cancer Research (AACR) Special Conference: Addressing Critical Questions in Ovarian Cancer Research and Treatment. A copy of the poster is attached as Exhibit 99.1 hereto.

**Item 9.01 Financial Statements and Exhibits.**

(d) Exhibits.

| Exhibit Number | Description |
|---|---|
| 99.1 | Poster |

**SIGNATURES**

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

**DELMAR PHARMACEUTICALS, INC.**

Dated: October 4, 2017

By: /s/ Jeffrey Bacha
Name: Jeffrey Bacha
Title: Chief Executive Officer

# Distinct mechanism of action of DNA damaging agent dianhydrogalactitol (VAL-083) suggests combination therapy with PARP inhibitors

Jeffrey Bacha[1], Guangan He[2], Xiaolei Xie[2], Anne Steino[1], Dennis M. Brown[1] and Zahid H. Siddik[2]

[1]DelMar Pharmaceuticals, Inc., Vancouver, Canada and California, USA; [2]The University of Texas MD Anderson Cancer Center, Houston, TX

ABSTRACT # A01

## BACKGROUND

Ovarian cancer is initially treated with surgery. However, due to the advanced stage of most ovarian cancers at diagnosis, it is often impossible to surgically remove all tumor tissue. Thus, most women with ovarian cancer receive chemotherapy as an adjuvant treatment following surgery to treat residual disease. Chemotherapy in ovarian cancer typically consists of platinum(Pt)-based drugs combined with non-Pt agents. Unfortunately, most women with advanced ovarian cancer develop recurrent disease with progressively shorter disease-free intervals. Those whose tumors recur within 6 months of Pt-based therapy are considered Pt-resistant/refractory and have a very poor prognosis. The response rate to second line therapy is in the 10-15% range and OS is ~12-months[1]. Thus, **development of new chemotherapies and targeted agents to overcome chemotherapy resistance in ovarian cancer, particularly for Pt-resistant/refractory tumors is a significant unmet medical need.**

**VAL-083 is a DNA-targeting agent with a unique mechanism of action and proven efficacy and safety**

VAL-083 (dianhydrogalactitol) is a first-in-class, bi-functional DNA-targeting agent, with a mechanism of action that differs from other DNA-targeting and chemotherapeutic agents used in the treatment of ovarian cancer[2]

- *VAL-083 has shown efficacy in a variety of murine cancer models in NCI screens*[3]
- *VAL-083 demonstrated activity in historic clinical trials against gynecological cancers, including ovarian cancer*
- *Once weekly dose of 60-75 mg/m² was well tolerated*
- *Partial and complete responses to in recurrent ovarian cancer and cervical cancer were reported*
- *Combination of VAL-083+cisplatin demonstrated an ORR of 39% in patients with advanced recurrent and metastatic disease*
- *VAL-083 was recommended for further advanced studies in the treatment of ovarian cancer*[4,5]
- *VAL-083 has recently received orphan drug designations from the FDA for ovarian cancer, glioma, and medulloblastoma therapy.*

VAL-083 introduces irreversible interstrand DNA crosslinks (ICLs) at the N⁷-position of guanine , leading to persistent DNA DSBs and cancer cell death. These DNA DSBs, which form during the S phase, occur within 24h of treatment and the signaling persists for 24-72h after removal of VAL-083, ultimately leading to S/G2 phase cell cycle arrest and cell death through two parallel pathways: one **p53-dependent** and one **p53-independent**[6] (Figure 1).

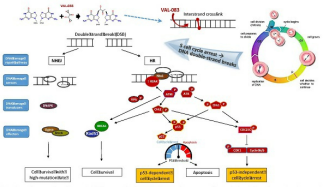


***FIGURE 1.*** *Mechanisms of action of VAL-083 induced chemotherapeutic cytotoxicity. Apoptosis can be induced through either p53 dependent or p53 independent pathways. BRCA1 dysfunction, which is common in ovarian cancer, increases the cytotoxic potential of VAL-083.*

This unique mechanism of action suggests that **VAL-083 may be efficacious in treating patients whose tumors are refractory to current standard of care ovarian cancer therapies, including Pt-based and PARP inhibitors**, either as a single agent or as a component of combination therapy regimens.

**References**

1. Naumann RW, et al. Drugs 2011; 71:1397–1412.
2. Zhai B, et al. Cancer Res. July 2017: 77(13), abstract #2483.
3. Scherf U, et al. Nature Genetics 2000; 24: 236-244.
4. Stehman FB, et al. Gynecol Oncol 1983; 15(3):381-390.
5. Slavik M, et al. Am J Clin Oncol (CCT) 1982; 5:483-86.
6. Peng C, et al. Acta Pharmacol Sin. 2017 Apr;38(4):561-570.

## RESULTS

**VAL-083 maintains anti-tumor activity independent of p53 status and is able to overcome Pt-resistance**

The $IC_{50}$ for VAL-083 in the cisplatin-resistant cell-lines 2780CP-16, OVCAR-10, Hey and OVCA-433 were 4 to 7-fold greater than for A2780; while the corresponding $IC_{50}$ values for cisplatin in these models were 10 to over 25-fold greater. These results demonstrate that there is only partial cross-resistance between cisplatin and VAL-083, further suggesting distinct modes of action for the two drugs.

***TABLE 1:*** VAL-083 cytotoxic activity in and characteristics of panel of ovarian cancer cell lines.

| Ovarian Cancer Cell Lines | A2780 | 2780CP | OVCAR-10 | HEY | OVCA-433 |
|---|---|---|---|---|---|
| Histology | Unknown | Unknown | Adenocarcinoma | HGSOC | HGSOC |
| p53 mutation | WT | V172F | V172F, G266R | P72R | P72R |
| Cisplatin sensitivity/resistance | Sensitive | Resistant | Resistant | Less sensitive | Resistant |
| VAL-083 $IC_{50}$ µM (SE) | 0.54 (0.046) | 2.2 (0.289) | 3.6 (0.173) | 2.1 (0.289) | 2.3 (0.058) |
| Cisplatin $IC_{50}$ µM | 0.22 | 12.0 | 9.0 | 3.1 | 10.2 |

The dependence on p53 status was investigated in isogenic models with (HCT-116$^{p53+/+}$) or without (HCT-116$^{p53-/-}$) p53 knockout. Loss of p53 increased resistance to cisplatin and oxaliplatin by 3 and 6-fold, respectively, whereas the increase in resistance to VAL-083 was <2-fold. This further suggests a cytotoxic mechanism for VAL-083 that is less dependent on wild-type p53 compared to Pt-based chemotherapy.

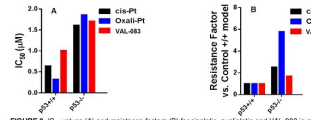


***FIGURE 2.*** *$IC_{50}$ values (A) and resistance factors (B) for cisplatin, oxaliplatin and VAL-083 in molecularly engineered isogenic models of HCT-116 with (p53+/+) or without (p53-/-) p53.*

**VAL-083 cytotoxic activity is independent of chemo-resistance mechanisms implicated in resistance to Platinum and PARPi therapy**

To explore the dependence of mismatch repair (MMR) and non-homologous end-joining (NEJH) DNA repair mechanisms, VAL-083 activity was investigated in human cancer cell lines HCT116, LoVo, M059K and M059J. MMR-deficiency is implicated in Pt-resistance, and NHEJ-deficiency is implicated in resistance to PARP inhibitors (PARPi). VAL-083 was equactive against cancer cells that are proficient and deficient in these DNA-repair mechanisms, suggesting a distinct mechanism and an ability to overcome treatment resistance to Pt-based and PARPi chemotherapy.

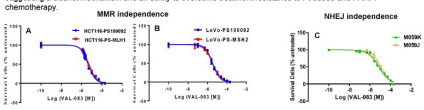


***FIGURE 3.*** *Cytotoxicity of VAL-083 (72 hr) in two pairs of human isogenic colorectal cancer cell lines: (A) MMR-proficient HCT116-PS-MLH1/ MMR-deficient HCT116-PS100092 and (B) MMR-proficient LoVo-PS-MSH2/MMR-deficient LoVo-PS100092, established by lentiviral infection. (C) VAL-083 cytotoxicity (72 hr) in isogenic glioblastoma cell lines: NHEJ-proficient M059K and NHEJ-deficient M059J. N=3.*

**VAL-083 displays synergy or superadditivity with PT-based and PARP inhibitor chemotherapy**

The combination of VAL-083 with either cisplatin or oxaliplatin in the human H460 (WT p53) NSCLC model demonstrated significant superadditivity (ps0.05) and synergism (CI<1) for both combinations. This cytotoxic effect of VAL-083 in combination with either platinum drug was observed also in A549 (WT p53) and H1975 (mutant p53) NSCLC cells, independently of p53 status (not shown). Data, where applicable, are shown as mean ± SE; N=7

***TABLE 2.*** The combination of VAL-083 with either cisplatin or oxaliplatin

| Cytotoxic Level (Fa) | Concentration (µM) VAL-083 | Concentration (µM) Cisplatin | CI |
|---|---|---|---|
| ED75 | 0.42 | 0.38 | 0.92 |
| ED90 | 0.92 | 0.85 | 0.91 |
| ED95 | 1.58 | 1.45 | 0.90 |

| Cytotoxic Level (Fa) | Concentration (µM) VAL-083 | Concentration (µM) Oxaliplatin | CI |
|---|---|---|---|
| ED75 | 0.29 | 0.21 | 0.86 |
| ED90 | 0.51 | 0.37 | 0.82 |
| ED95 | 0.73 | 0.54 | 0.81 |

**VAL-083 cytotoxicity is increased in BRCA1 dysfunctional ovarian cancer cells and VAL-083 displays superadditivity with PARP inhibitors (PARPi) olaparib, talazoparib and veliparib**

VAL-083 activity was increased (IC50 decreased) when BRCA1 was impaired. This suggests increased activity in ovarian cancer with dysfunctional BRCA1 and further suggests the potential for synergy with PARPi. VAL-083 in combination with PARPi olaparib, talazoparib or veliparib was superadditive in BRCA1-proficient ovarian cancer cells. Studies of VAL-083 in combination with PARPis in BRCA1-deficient ovarian cancer cells are ongoing.

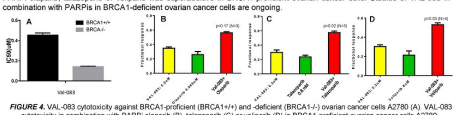


***FIGURE 4.*** VAL-083 cytotoxicity against BRCA1-proficient (BRCA1+/+) and -deficient (BRCA1-/-) ovarian cancer cells A2780 (A). VAL-083 cytotoxicity in combination with PARPi olaparib (B), talazoparib (C) or veliparib (D) in BRCA1-proficient ovarian cancer cells A2780 .

## CONCLUSIONS & FUTURE DIRECTIONS

- **VAL-083 exhibits a distinct mechanism of action from Pt-based chemotherapy or PARP inhibitors, and may offer an alternative to Pt- and PARP inhibitor-based chemotherapy for recurrent or relapsed ovarian cancer patients**
- **An IND for phase 1/2 trial in Recurrent Platinum-Resistant Ovarian Cancer, VAL-083 REPROVe Trial, has been allowed by FDA**
- **Data suggesting synergy or super-additivity for VAL-083 plus Pt-based agents and PARP inhibitors supports future combination clinical trials**

### VAL-083 REPROVe Trial (NCT03281681)

**Phase 1-2 Trial in Recurrent Platinum-Resistant Ovarian Cancer**

- IND for VAL-083 in ovarian cancer has been allowed by US FDA
- Planned enrollment: Up to 24 patients with platinum-resistant ovarian cancer
- *Primary endpoint:* Demonstration of overall response rate (ORR) benefit compared to historical control, as determined using RECIST v1.1.
- If successful: Trial will be expanded to approximately 60 patients
- *Secondary endpoints:* Safety & tolerability, efficacy via CA-125 biomarker measurement, progression free survival, duration of response, overall survival, pharmacokinetics and evaluation of symptoms using the FOSI index

Link to REPROVe trial on clinicaltrials.gov