

WPD Pharmaceuticals

OCTOBER 2020 | BERUBICIN (WP744, WPD104)



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Company Overview

WPD Pharmaceuticals is a diverse biotech company that has 10 novel drug candidates with 4 in clinical development stage via its development partners. WPD drug candidates are in collaboration via its development partners with institutions including MD Anderson Cancer Center, Mayo Clinic, Emory University, Wake Forest University and leading hospitals and academic centers in Poland.

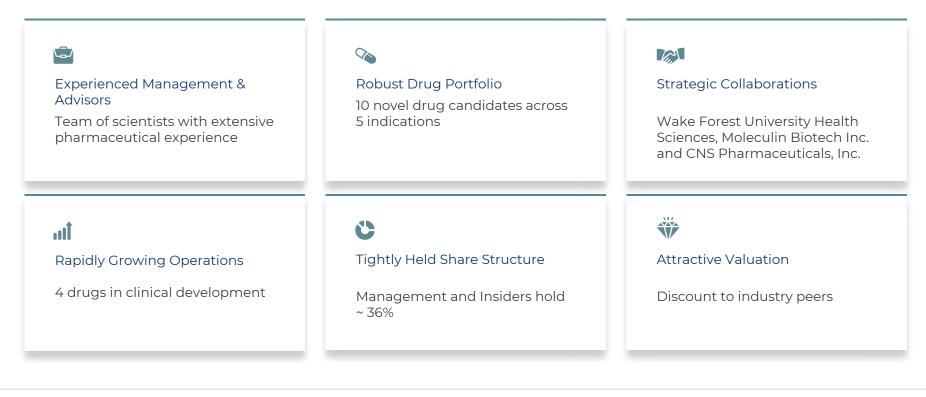
Alongside direct and indirect investment of \$71 million, over \$29 million of grant funding (total of \$100 million USD) has gone towards the development of our robust drug development pipeline with a focus on melanoma, brain cancer, leukemia and pancreatic cancer. Notably, add to this investment figure \$14 million USD in grants recently awarded to WPD Pharmaceuticals from The National Centre for Research and Development in Poland.

With a groundswell of multi-continental grant support and a diverse portfolio of potentially breakthrough drug technologies, WPD Pharmaceuticals, we believer, is now strategically positioned to enter the market with blockbuster potential.





Investment Highlights





	Discovery	Pre-Clinical	Regulatory	Clinical I / II
Brain Cancers		WPD101		Berubicin
				WP1066
Pancreatic Cancers		WP1122	WP1066	
		WP1234	WP1732	
Other Cancers	WPD103			Annamycin
				WP1220
Melanoma	WPD102			



Indications to Treat **Glioblastoma**



OVERVIEW

Berubicin (BER) (WP744, WPD104) is a new anthracycline proven to be able to reach brain tumors by crossing the blood brain barrier (BBB) (Inge et al., 2004). BER and other anthracyclines (such as Doxorubicin) mechanism of action is based on alkylation cytoplasm and destruction of the DNA structure, generation of free radicals, apoptosis induction and direct damage to the membrane of cancer cell (Wu et al., 2004). Moreover, the covalent, biologically inactive BER-DNA-topo II complex prevents the DNA strands from reconnecting, which leads to their fragmentation and thus leads to cell death (Figure 1). Also, Berubicin has strong cytotoxic effects on tumor cells with high MDR1/P-gp protein expression, which significantly limits the effectiveness of others chemotherapeutics (Brooks et al., 2007). Common side effects of anthracyclines, cardio and cytotoxicity, are not expressed by BER in relation to normal cells, as required by FDA preclinical tests (Sterba et al. 2013). These properties allow BER to be considered as a candidate for pediatric therapy when long-term effects of chemotherapeutic agents are of key importance. Regardless of CNS tumors, Berubicin could also be consider as a drug-candidate in other types of cancer (Federl et al., 2001).

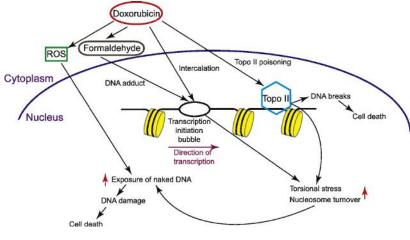


Figure 1. Representation of molecular mechanisms of anthracyclines (Doxorubicin) cytotoxic action in cancer cells. In cell nucleus Doxorubicin forms a complex by DNA through G bases in both of DNA strands and prevents Topo-II activity and DNA synthesis. In cell cytoplasm Doxorubicin generates ROS. Consequently, cell death is induced.



OVERVIEW

Clinical utility of anthracyclines is limited by cumulative, doserelated progressive myocardial damage that may lead to chronic heart failure, reduced quality of life or death. Moreover, anthracyclines induce MDR proteins expression, thus relapsed tumors are chemoresistant.

Currently available anthracyclines do not cross the blood-brain barrier, thus could not be used in brain cancer therapy

Berubicin is a new anthracycline proven to be able to reach brain tumors by crossing the blood brain barrier (BBB) (Inge et al., 2004).

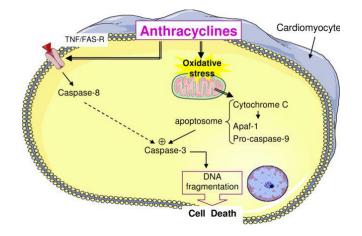


Figure 2. Schematic representation of antharcyclines-(Doxorubicin)-induced cardiotoxicity.



PRECLINICAL DEVELOPMENT

In preclinical research, Berubicin (WP744) cytotoxic action was verified in numerous cell lines, representing various cancer types (melanoma, breast, pancreatic, liver cancer, GBM and others) and in all tested models showed significantly lower IC50 value (the half maximal inhibitory concentration) in comparison to DOXO. Furthermore, in chemoresistant Pgp/MDR1-positive cells (MCF-7/DOX and MCF-7/VP16), resistant to DOXO-treatment, Berubicin still effectively induced cell death. Available results illustrate the unique potential of Berubicin as an anticancer drug.

> Invest New Drugs. 2007 Apr;25(2):115-22. doi: 10.1007/s10637-006-9018-3. Epub 2006 Oct 28.

The 4'-O-benzylated doxorubicin analog WP744 overcomes resistance mediated by P-glycoprotein, multidrug resistance protein and breast cancer resistance protein in cell lines and acute myeloid leukemia cells

Tracy A Brooks ¹, Kieran L O'Loughlin, Hans Minderman, Brian N Bundy, Laurie A Ford, Michael R Vredenburg, Ralph J Bernacki, Waldemar Priebe, Maria R Baer



CLINICAL DEVELOPMENT

WPD Pharmaceuticals conducts research related to the development of the WPD104 molecule - berubicin, as a novel drug in glioblastoma multiforme (GBM) therapy for children and adult patients, as a part of the project "New approach to glioblastoma treatment addressing the critical unmet medical need". The main goal of the project is to implement multicenter pediatric phase I clinical trial ("First In Children") to determine maximum tolerated dose (MTD) and phase Ib and phase II clinical trials in adults, in order to confirm the efficacy of berubicin, an innovative drug to eliminate brain cancer cells that are resistant to temozolomide – a standard chemotherapeutic. The project also provides for preclinical testing to determine the prospective use of berubicin with temozolomide and with other compounds developing by the WPD Pharmaceuticals as a candidates for anticancer drugs.



CLINICAL DEVELOPMENT

In the Phase I trial, 44% of patients experienced a statistically significant improvement in progression-free survival. This 44% disease control rate was based on 11 patients (out of 15 evaluable patients) with stable disease, plus responders. **One patient experienced a durable complete response, which is defined by National Cancer Institute as disappearance of all signs of cancer in response to treatment. This clinical trial was conducted in 2006 and the patient remained cancer free for over 13 years.**

Importantly, no serious side-effects were observed and Berubicin appeared to be well-tolerated. Hematologic toxicity was transient and did not limit Berubicin treatment.

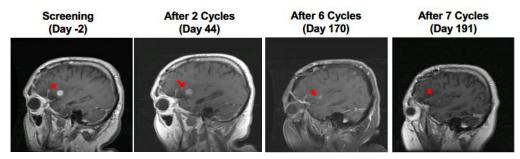


Figure 3. MRI scan of GBM-patient with durable complete response after 7 cycles of Berubicin treatment.



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FUNDING

On January 31, 2019, WPD received notice that it had been awarded a conditional grant in the amount of 22,033,066 PLN (CDN\$7,625,287 as at July 22, 2019) from the European Union's Regional Development Fund ("EURDF") under the Smart Growth Operational Program 2014-2020, Sectoral Program InnoNeuroPharm, Priority Axis I: Support R&D carried out by enterprises, Measure 1.2: Sectoral R&D Programs, implemented under the National Center for Research and Development, for development of its drug Berubicin hydrochloride, which is utilized via injection as a novel drug in GBM therapy for children and adult patients.





Corporate **Overview**

WPD Pharmaceuticals Inc.

CSE: WBIO

Capital Structure				
Issued and Outstanding	111,520,388			
Warrants	3,949,997			
Fully Diluted	115,470,385			
Management and Insider holdings	36%			





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CSE:WBIO

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