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Midatech Pharma Plc

(MTP-NASDAQ)

MTP: Multiple Data Readouts Over the Next 12 Months…

Based on our probability adjusted DCF model that takes into account potential future revenues from GNP, Q-Sphera, and NI platform products along with revenues from Midatech Pharma US, MTP is valued at $6.50 per share. This model is highly dependent upon continued clinical and commercial success and will be adjusted accordingly based upon future clinical results and the company's execution.

Current Price (04/27/18)	$0.75
Valuation	**$6.50**

OUTLOOK

Midatech Pharma Plc (MTP) recently announced financial results for 2017 and provided a business update. We anticipate data readouts from three clinical programs (acromegaly/carcinoid, brain cancer treatment, and an autoimmune vaccine for diabetes) and three preclinical programs (liver cancer, childhood and adult brain cancer) over the next 12 months. The company's US commercial business was breakeven on an adjusted EBITDA basis in the second half of 2017. We forecast for the company's current cash position to be sufficient to fund operations into 2019.

SUMMARY DATA

52-Week High	**$2.90**
52-Week Low	**$0.74**
One-Year Return (%)	**-73.87**
Beta	**0.84**
Average Daily Volume (sh)	**8,978**
Shares Outstanding (mil)	**31**
Market Capitalization ($mil)	**$23**
Short Interest Ratio (days)	**N/A**
Institutional Ownership (%)	**0**
Insider Ownership (%)	**N/A**
Annual Cash Dividend	**$0.00**
Dividend Yield (%)	**0.00**
5-Yr. Historical Growth Rates	
Sales (%)	**N/A**
Earnings Per Share (%)	**N/A**
Dividend (%)	**N/A**
P/E using TTM EPS	**N/A**
P/E using 2018 Estimate	**-3.2**
P/E using 2019 Estimate	**-3.2**

Risk Level	**High**
Type of Stock	**Small-Value**
Industry	**Med-Drugs**

ZACKS ESTIMATES

Revenue
(In millions of £)

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2017	1.5 A	1.9 A	2.1 A	2.1 A	7.6 A
2018	2.2 E	2.2 E	2.3 E	2.3 E	9.0 E
2019					10.7 E
2020					10.8 E

Earnings per share
(In £)

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2017	-0.09 A	-0.10 A	-0.06 A	-0.07 A	-0.31 A
2018	-0.07 E	-0.07 E	-0.06 E	-0.07 E	-0.26 E
2019					-0.21 E
2020					-0.24 E

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WHAT'S NEW

Business Update

Midatech Pharma Plc (MTP) is a specialty pharmaceutical company with three novel drug delivery technologies. The technologies are designed to enable the targeted delivery, sustained release, or solubilized local delivery of existing therapeutic drugs.

The Q-Sphera sustained release (SR) technology platform, with numerous and distinct advantages over traditional polymer microsphere production, utilizes precisely and consistently manufactured monodispersed micro particles such that active drug compounds are released into the body in a tightly controlled manner over an extended period of time (e.g., weeks to months)

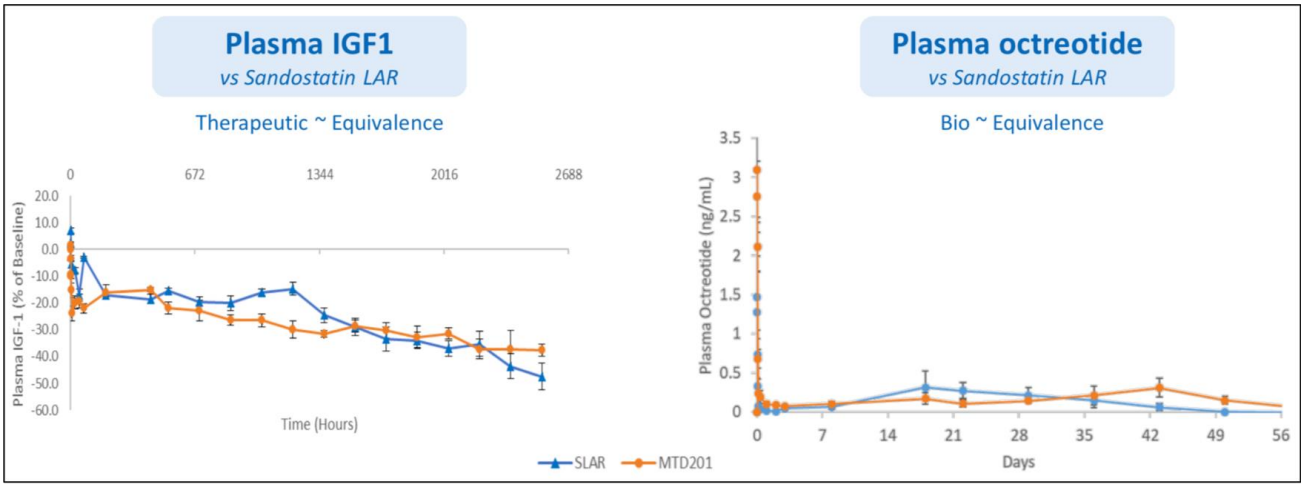
The gold nanoparticle (GNP) technology platform is based on GNP drug conjugates, which at 2 nm are among the smallest particles in biomedical use. They are composed of a core of gold atoms surrounded by a layer of carbohydrates and linkers for attachment of small molecules (e.g., chemotherapeutics, peptides, etc.) and targeting agents. The small size and multi-valency arrangement around the gold core underpin the ability to improve biodistribution and thus safety and efficacy of existing drugs.

The Nano Inclusion (NI) technology is utilized for potent small molecule chemotherapeutics that have minimal solubility at biological pH, which limits them to oral administration. When reformulated with the NI technology, the complexed molecules solubilize such that parenteral routes of administration can be employed. This enables local administration directly into the tumor.

Q-Octreotide (MTD201) Update

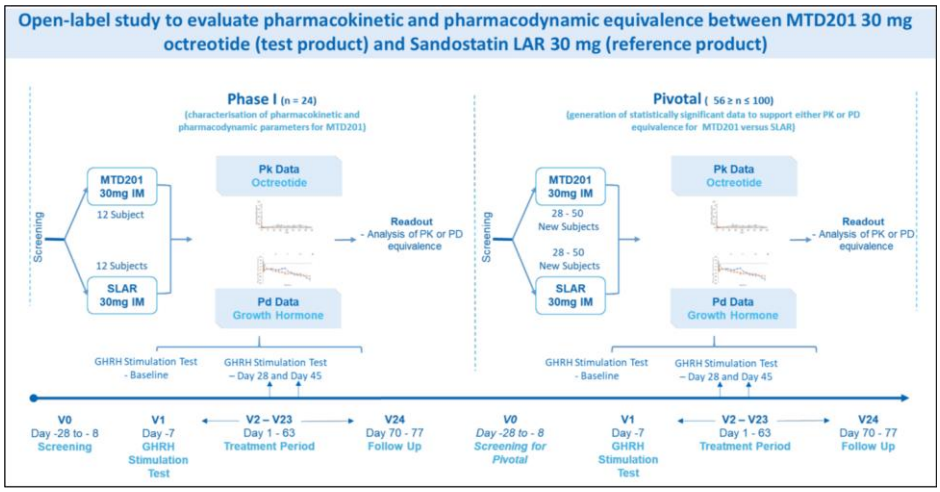
Midatech's lead development product, MTD201 (Q-Octreotide), is based on the company's Q-Sphera technology. The microspheres are small (approximately 25 µm), spherical particles that are designed for the sustained release of peptides and other small molecule drugs. Midatech's manufacturing process allows for high drug loading, precise control over particle size and morphology, and highly linear reproducible drug release kinetics. The particles can be injected using a fine gauge needle with clear benefit for the patient.

Octreotide is an octapeptide that mimics naturally occurring somatostatin, although it is a more potent inhibitor of growth hormone, glucagon, and insulin. Ultimately, the drug causes a normalization of growth hormone and/or insulin-like growth factor 1 (IGF-1). It is an existing, immediate- and sustained- release injection product used to decrease the production of growth hormone in people suffering from acromegaly and for the treatment of neuroendocrine (hormone secreting) tumors (NET). It is sold by Novartis under the brand name Sandostatin® and the sustained release version Sandostatin® LAR®. The following graphs show the therapeutic equivalence (based on IGF1 levels) and bioequivalence (based on plasma octreotide levels) for MTD201 and Sandostatin® LAR®.



Source: Midatech Pharma Plc

Midatech will be performing a two-phase clinical trial: a first in human proof of concept phase in 24 healthy volunteers, followed by a pivotal confirmatory phase in an additional 56-100 healthy volunteers. The company is hoping to show interchangeability with Sandostatin® LAR® either pharmacokinetically (PK Data on octreotide levels in the blood) and/or pharmacodynamically (PD Data on growth hormone levels), thus potentially offering patients an alternative treatment for NETs, carcinoid syndrome, and acromegaly. Since it would take a significant amount of time to recruit enough acromegaly patients to conduct the PD portion of the study, Midatech developed a novel study design in healthy volunteers who will be administered growth hormone releasing hormone (GHRH), which will cause an increase in growth hormone thus mimicking disease in healthy subjects. The level of growth hormone will then be monitored and compared between groups administered MTD201 or Sandostatin® LAR®. The regulatory authorities have agreed to this trial design. We anticipate the trial initiating in the second quarter of 2018 with topline results in late 2018/ early 2019. Assuming positive clinical results, the company plans to file for approval under the 505(b)(2) pathway, potentially as early as 2020. An outline of the trial is given below.



Source: Midatech Pharma Plc

MTX110 Update

MTX110 is being developed for the treatment of diffuse intrinsic pontine glioma (DIPG), and uses the company's NI technology, which allows for the solubilized local delivery of potent therapeutics directly to the tumor. The active compound is the poorly soluble hydroxamic acid drug panobinostat, a histone deacetylase inhibitor (HDACi), which until recently could not be formulated for parenteral administration. Midatech's NI technology enabled the aqueous solubility of this class of small molecule cancer therapeutic, which expands parenteral delivery options that in turn are expected to improve the safety and efficacy of the treatment. Midatech in-licensed the drug panobinostat for use in treating DIPG for an upfront payment of $1 million and potential future milestone payments. Panobinostat was developed by Novartis and approved in 2015 for the treatment of multiple myeloma.

DIPG

DIPG is a highly infiltrative brainstem high grade glioma that occurs mostly in children. The tumors are aggressively infiltrative such that cancer tissue typically cannot be differentiated from normal brain tissue. The overall median survival of children with DIPG is approximately 9 months and remains unchanged despite decades of clinical trial research. The only standard of care is palliative focal radiotherapy, but this has minimal effect on survival and essentially all children die of this disease. Surgical resection is unavailable due to the location of the tumor in the brainstem. New therapeutic strategies are urgently needed. Approximately 1,000 individuals worldwide are diagnosed with DIPG each year.

Panobinostat

Panobinostat (Farydak®) is a potent, nonselective histone deacetylase inhibitor. It was selected as a potential treatment for DIPG following the screening of 83 drugs against 14 patient-derived DIPG cell cultures (Grasso *et al.*, 2015). Panobinostat was effective against 12/16 patient-derived DIPG cell cultures. Although effective in both *in vitro* and *in vivo* models, panobinostat does not cross the blood-brain barrier effectively thus necessitating an alternate means of delivery. Direct delivery of MTX110, the soluble form of panobinostat, bypasses the blood brain barrier and ensures adequate drug exposure to tumor cells. MTX110 molecular targeting and intratumoral delivery provides significant potential for treatment of DIPG.

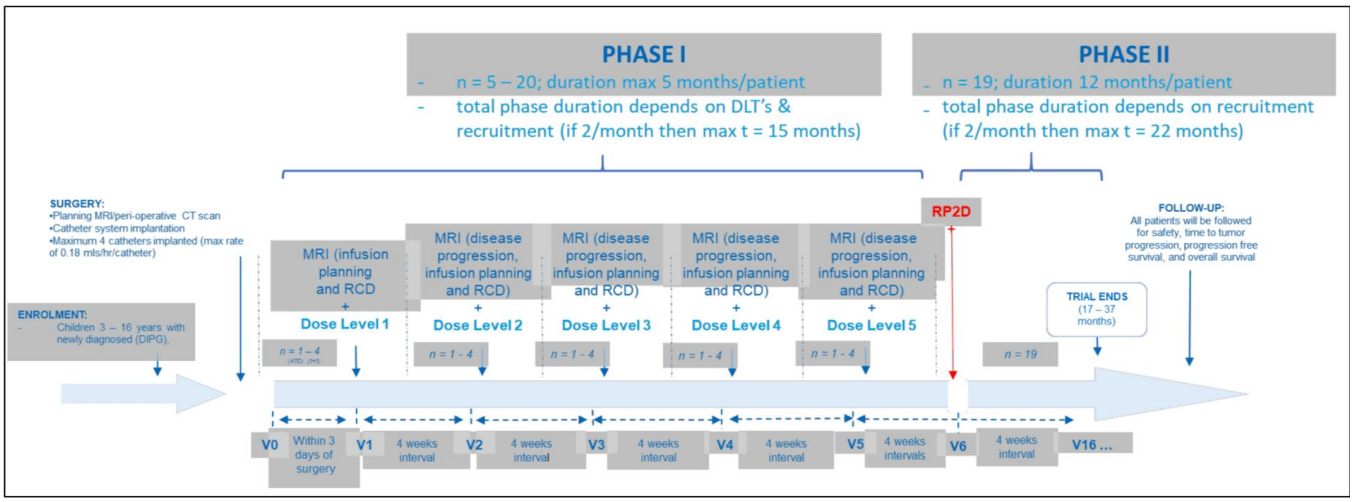
Convection-Enhanced Delivery

One of the many difficulties in treating tumors of the central nervous system is getting enough drug into the tumor for a sufficient time to allow for a therapeutic effect. Many drugs do not effectively pass through the blood-brain barrier, and for these compounds direct injection into the tumor is commonly used. However, even with direct administration, limited diffusion of drug through the tumor and brain interstitium means only a small volume of tissue surrounding the injection site is effectively treated.

Convection-enhanced delivery (CED) is a method used to deliver drugs into the brain through a pressure gradient in order to saturate the extracellular fluid compartment (Bobo *et al*., 1994). In contrast to diffusion, which depends entirely upon a concentration gradient to distribute the molecules, the use of hydraulic pressure in CED allows for homogenous distribution over large distances by displacing the interstitial fluid. Since being shown to be safe for the delivery of drugs to the brainstem (Sandberg *et al*., 2002), CED has been tested in a number of adult malignant gliomas, however there are no completed CED trials for DIPG with a few clinical trials ongoing (Zhou *et al*., 2017).

Clinical Trial

On January 16, 2018, Midatech announced that FDA approved the investigational new drug (IND) application to initiate a clinical trial of MTX110 in patients with DIPG. We anticipate the first patient being dosed soon with topline results available at the end of 2019. The efficacy endpoint for the Phase II component will be Overall Survival (OS) at 12 months, conducted at the recommended Phase 2 dose. In order for the study to be positive, 12/19 patients in the Phase II portion of the study would need to survive to at least one year. To date, MTX110 has been used on a compassionate use basis to treat five patients, where the drug was well tolerated. Treating DIPG represents a potential $50-$100 million worldwide opportunity based on the available patient population and potential for orphan drug pricing.



Source: Midatech Pharma Plc

MTD119 Update

MTD119 is the company's lead development product utilizing the GNP technology. It is being developed for the treatment of hepatocellular carcinoma and utilizes mertansine (DM1) as a cytotoxic agent. DM1 is a derivative of maytansine that is currently utilized in the approved antibody-drug conjugate (ADC) therapy Kadcyla®. In preclinical models, Midatech has reported the GNP-conjugation allows otherwise lethal doses of mertansine to be administered with peak reduction in tumor growth more than 6x greater than the current standard of care, sorafenib (Nexavar®). The company has initiated an IND-enabling program to study drug metabolism, pharmacokinetics, dosing, and toxicity of MTD119 that is expected to complete early 2019. If successful, this will be followed by a first in human study set to initiate in the second half of 2019.

On February 28, 2018, Midatech announced that the European Medicines Agency (EMA) granted Orphan Drug Designation (ODD) for MTD119. The ODD program is intended to assist in the development of drugs for the treatment of diseases or disorders that affect fewer than 5 in 10,000 people in the EU. In addition to development assistance, drugs granted approval under the ODD program are conferred with 10 years of market exclusivity.

Liver Cancer

Hepatocellular carcinoma (HCC) is the most common form of primary liver cancer, with over 700,000 individuals affected worldwide, and is the third leading cause of cancer death in the world (ACS). HCC is relatively rare in the U.S. (approximately 35,000 individuals in the U.S. will be diagnosed with HCC in 2017) and other countries where hepatitis infections are not widespread, as most cases of HCC are due to hepatitis infection (both hepatitis B and C). Most cases of liver cancer in countries with low hepatitis rates are due to metastasis of other primary tumors.

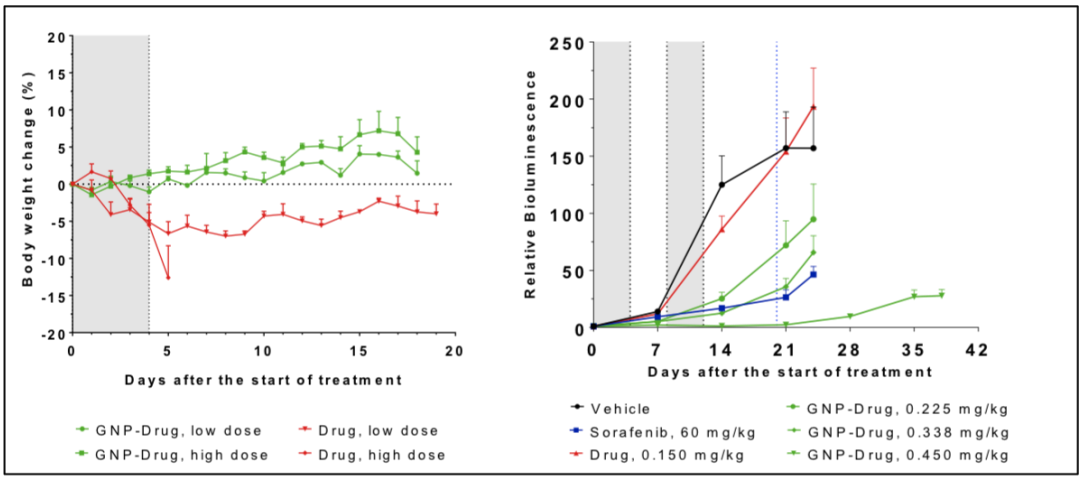
Survival time for patients with HCC is entirely dependent on how advanced the disease is when first diagnosed. If found early, liver transplantation offers a potential curative therapy, with 5-year overall survival of 75% and a tumor recurrence rate of less than 15% (Mazzaferro *et al*., 1996). Patients with small tumors and little underlying cirrhosis are eligible for surgical resection. Additional treatment options include local ablative therapies such as radio-frequency ablation (RFA), trans-arterial chemo-embolization (TACE), percutaneous ethanol ablation, and radioembolization.

There is no cure for advanced HCC; thus, there exists a significant unmet need for an effective therapy. The current standard of care for advanced HCC is sorafenib, which was approved based upon the results of two randomized, double blind, placebo controlled clinical trials where survival was extended by between 2 – 3 months (Llovet *et al*., 2008, Cheng *et al*., 2009). Sales of Nexavar® totaled $942 million in 2017, with approximately 80% of those revenues derived from the treatment of HCC (EvaluatePharma).

For patients refractory to sorafenib, the FDA recently approved regorafenib (Stivarga®) based on the outcome of a Phase 3 clinical trial of 573 patients with HCC that had progressed after treatment with sorafenib (Bruix *et al*., 2017). Similar to sorafenib, regorafenib was shown to extend median overall survival by 2.8 months compared to placebo.

HCC Targeted GNP

A GNP construct for targeting HCC was developed based on a gold nanoparticle core covered with a combination of carbohydrate galactose ligands and the potent tubulin inhibitor DM1 (mertansine), which inhibits microtubule assembly and disrupts mitosis in malignant cells. Preclinical models have shown a clear impact of the GNP technology on the safety and efficacy of DM1. In preclinical safety models, doses achieved with MTD119 (GNP bound DM1) were up to three times higher than those achieved with DM1 alone. The below left figure shows mice treated with DM1 alone at 150 µg/kg tolerated the drug very poorly (as exhibited by weight loss), whereas mice treated with GNP-DM1 at 450 µg/kg tolerated the drug very well (increasing weight during the study). The MTD119 construct was then tested in preclinical efficacy models, where it was tested in animals implanted with human liver tumor cells. The below right figure shows the superiority of MTD119 versus the current standard of care sorafenib, as well as versus DM1 alone. The only group of animals that completed the study was the one treated with high dose MTD119; mice treated with sorafenib or DM1 alone did poorly and did not complete the study. These findings likely reflect the impact the GNP technology has on DM1, including altered biodistribution, targeted efficacy, and reduced off target side effects. Moving forward the focus will be on evaluating and optimizing alternative dosing regimes, and looking to maximizing the therapeutic window for MTD119.



Source: Midatech Pharma Plc

Immunotherapy Programs

Midatech currently has three immunotherapy programs in development in immuno-oncology and autoimmune disease. The compounds use the GNP technology to deliver peptides to antigen presenting cells and depending upon which peptides are utilized it can result in stimulating an immune response (in the case of immuno-oncology) or dampen an immune response (in the case of autoimmune disease).

The most advanced immunotherapy program is MTX102, which is being developed as a therapy for the autoimmune disease Type 1 diabetes. MTX102 contains a self-peptide that is designed to generate a tolerogenic response and direct T cell phenotypes from pathogenic to regulatory. Following multiple preclinical and toxicology studies conducted between 2012 and 2015, the company initiated a Phase 1 clinical trial in 2016 in the UK and Sweden and we anticipate results from that study in 2019.

MTR111 and MTR116 are immuno-oncology programs designed for the treatment of adult brain cancer and DIPG, respectively. Each of those compounds contains peptides specific for that particular cancer. Upon administration, the drugs elicit increased cytotoxic T cell and T helper cell mediated immune responses targeted to these tumor biomarkers. Preclinical studies are currently ongoing and we anticipate data from those studies in the second half of 2018.

Management Changes

On March 15, 2018, Midatech announced current CEO Dr. Jim Phillips will retire at the end of May 2018 and Dr. Craig Cook, who is currently serving as the Chief Operating Officer and Head of Research and Development, will be appointed CEO following a three-month transition period. Dr. Cook joined Midatech in 2014 and has more than 20 years of experience in the biotechnology and pharmaceutical industry at companies such as Johnson & Johnson, Eli Lilly, Novartis Pharma, and Serono Biotech. Dr. Steve Damment, who has been with Midatech since 2015, will succeed Dr. Cook as the Head of Research and Development.

Financial Update

On April 23, 2018, Midatech reported financial results for 2017. Total gross revenues for the twelve months ending Dec. 31, 2017 were £12.1 million, compared to £9.2 million in 2016, while total revenues were £7.6 million in 2017 compared to £6.9 million in 2016. Total revenue is statutory revenue (total gross revenues after deducting for product returns, discounts, rebates, and other incentives) plus grant income. U.S. product revenues increased 28% in 2017 compared to 2016 to £6.7 million. The U.S. commercial business was breakeven on an EBITDA basis during the second half of 2017. Net loss in 2017 was £16.1 million, compared to £20.2 million in 2016, with total cash burn of £4.2 million.

During 2017, the company reclassified certain operating costs to better reflect the true nature of business activity, which included a reclassification of costs for 2015, 2016, and 2017. The company has three broad categories of costs: research and development costs; distribution costs, sales and marketing; and administration costs. Previously, certain costs were allocated to administration costs and those have now been reclassified as either research and development costs or distribution costs, sales and marketing. The reclassification for 2016 and 2015 are shown below.

	2016 *reclassified* £'000	2016 *original* £'000	2015 *reclassified* £'000	2015 *original* £'000
Research and development costs	7,796	6,684	8,710	5,920
Distribution costs, sales and marketing	12,510	9,523	605	374
Administrative costs	5,123	9,222	4,908	7,929
	25,429	25,429	14,223	14,223

Source: Midatech Pharma Plc

The company exited 2017 with approximately £13.2 million in cash and cash equivalents. Earlier this year, the company announced a four-year senior secured loan agreement with MidCap Financial for up to $15 million. The company has received the first tranche of $7 million, with the issuance of additional funds being contingent upon clinical development milestones for MTD201 and MTX110. We estimate the company has sufficient capital to fund operations into 2019.

Valuation

Midatech's three proprietary drug delivery technologies (Q-Sphera for sustained release of already marketed products, Midacore gold nanoparticles (GNP) for targeted delivery, and Nano Inclusion (NI) for local delivery) help differentiate it from other specialty pharmaceutical companies and the potential quick path to market for MTD201 and MTX110 could deliver additional revenues beginning in just a few years. The company is further differentiated through its U.S. based sales force, which will allow the company to capture the full value of any approved products without the need to partner with a larger pharmaceutical company for sales in the U.S. We're pleased to see the company's commercial operations continuing to grow in line with our expectations, as well as achieving break even status in the second half of 2017. Our valuation for Midatech, which is derived from expected future cash flows from the commercial group, MTD201, MTX110, and MTD119, is $6.50 per share.

PROJECTED FINANCIALS

Midatech Plc
Income Statement

Midatech Pharma Plc (in millions of £)	2017 A	1H E	2H E	2018 E	2019 E	2020 E
Midatech Pharma US	£6.8	£4.0	£4.2	£8.2	£10.2	£10.3
MTX110 - DIPG Glioma	£0.0	£0.0	£0.0	£0.0	£0.0	£0.0
MTD201 - Acromegaly	£0.0	£0.0	£0.0	£0.0	£0.0	£0.0
MTD119 - Liver cancer	£0.0	£0.0	£0.0	£0.0	£0.0	£0.0
MTR103 - Glioblastoma	£0.0	£0.0	£0.0	£0.0	£0.0	£0.0
Grants & Collaborative Revenue	£0.8	£0.4	£0.4	£0.8	£0.5	£0.5
Total Revenues	**£7.6**	**£4.4**	**£4.6**	**£9.0**	**£10.7**	**£10.8**
Cost of Sales	£0.9	£0.6	£0.7	£1.3	£1.5	£1.5
Research & Development	£10.2	£6.0	£6.0	£12.0	£13.0	£14.0
Distribution Costs, Sales and Marketing	£9.4	£4.6	£4.7	£9.3	£10.0	£11.0
Administrative Costs	£3.1	£2.0	£2.1	£4.1	£4.2	£4.4
Impariment of Intangible Assets	£1.5	£0.0	£0.0	£0.0	£0.0	£0.0
Other Expenses	£0.0	£0.0	£0.0	£0.0	£0.0	£0.0
Operating Income	-£17.6	-£8.8	-£8.9	-£17.7	-£18.0	-£20.1
Non-Operating Expenses (Net)	£0.25	-£0.1	-£0.1	-£0.20	-£0.1	-£0.1
Pre-Tax Income	-£17.3	-£8.9	-£9.0	-£17.9	-£18.1	-£20.2
Income Taxes Paid	-£1.3	-£0.6	-£0.6	-£1.2	-£1.0	-£1.0
Net Income	**-£16.1**	**-£8.2**	**-£8.4**	**-£16.6**	**-£17.1**	**-£19.2**
Net Margin	-	-	-	-	-	-
Exchange Gain/Losses	-£1.2	£0.0	£0.0	£0.0	£0.00	£0.00
Total Comprehensive Gain/Loss	**-£17.3**	**-£8.2**	**-£8.4**	**-£16.6**	**-£17.1**	**-£19.2**
Net Loss per Share	**-£0.31**	**-£0.14**	**-£0.13**	**-£0.26**	**-£0.21**	**-£0.23**
YOY Growth	-	-	-	-	-	-
Basic Shares Outstanding	51.3	61.0	65.0	63.0	80.0	85.0

Source: Zacks Investment Research, Inc. *David Bautz, PhD*

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