Cellmid Limited
First-in-Class mAb Oncology Program Will Rate the Stock; Lots of Room To Grow For Advangen; New Target Price of 8.4c

Summary - In the 10 months since our last update Cellmid has had several major announcements, trial results, Cxbladder launch and the Advangen Inc acquisition. In view of that we provide a company update and our fresh view on Cellmid going forward. Whilst the share price since our last report remained range bound between 3c – 5c, we believe that the company has moved to the next level and is currently significantly undervalued by investors. Cellmid now has (A) a first-in-class oncology program (anti-midkine monoclonal antibody) that we expect to go into clinic late 2014 / early 2015; (B) a global consumer healthcare brand for hair loss with successfully launched products in Australia and Japan; and (C) a royalty stream from the Cxbladder test that was launched in the US in 2013. Our price target of 8.4c (+1.2c vs. previous) include: 3.9c (+1.2c vs previous) for the consumer healthcare business; 1.7c (-1.3c vs. previous) for the LungDx test; and 2.8c (+1.3c) for the Cxbladder test. We do not currently include the oncology program into our model, but believe that this represents major upside for the share price and our current valuation in the next 12-18 months, once the program is at the clinical stage (first trial in humans).

Moving to oncology with anti-MK antibody is the right decision - We support management’s choice to progress with a cancer indication, rather than diabetics nephropathy. In our view, if the company is successful in moving into the clinic with the oncology program, the quality of that asset will put Cellmid in the same echelon as US biotechs that are developing first-in-class antibodies as cancer therapeutics (e.g. Onconova, Oncomed, Verastem). Even in the US, such companies represent a rare opportunity, as most of the industry R&D is focused on the same targets (e.g VEGF, VEGFR, EGFR, PI3K). In contrast, Cellmid is the first and only company to target midkine and will have significantly lower differentiation risks, easier clinical development and regulatory pathways (see pages 4-5 of the report).

There are only a few companies in Australia with first-in-class antibody programs that employ new mechanism of action, with Patrys (ASX: PAB) as the only other we are aware of. We believe that positive data from the midkine program will validate overseas interest and upside for investors.

Advangen and consumer healthcare - lots of room to grow - We currently value Cellmid’s consumer healthcare business at 3.9c (vs. 2.7c previously) as we include the Advangen Inc acquisition and update our estimates for its Australian subsidiary. In our view, investors underestimate the fact that Advangen has a global consumer health brand and with management taking all necessary steps to increase the brand equity, it’s just a matter of time until it becomes a very significant business. This represents substantial upside to the current share price, ahead with their commercial strategy. According to a recent industry report, the leading hair care brands are valued between $0.9B and $2.9B, and we see a big opportunity for Advangen in major markets given its therapeutic claims. We expect considerable increase in product sales in CY2014, CY2015. In our valuation we only consider Australia, China and Japan while note that all additional markets (rest of Asia, North America, EU) represent significant mark up to our valuation.

Update on diagnostics segment (see inside note for details) - Last quarter Pacific Edge completed the first commercial sales of its Cxbladder tests signalling the start of the royalty revenues to CDY. We are increasing our estimates of market share and valuation to 2.8c (+1.3c vs previously) given the better than expected reimbursement landscape for the test. We are a bit disappointed in Quest’s lack of action regarding the LungDx test. As a result we reduce our market penetration rates and postpone the launch to FY2015 to remain conservative. We Value LungDx at 1.7c (vs. 3c previously). We change our royalty rate on diagnostic business from 2% to 4% in line with the current industry standards. We believe that future molecular diagnostic partnership could add 2 cents per share per test.

Action and recommendation - with positive investors sentiment towards biotechnology sector and upside opportunities coming from each of Cellmid’s three business units (therapeutics, diagnostics, consumer healthcare) we reiterate our Speculative Buy recommendation and increase our target price to 8.4 cents.
BUSINESS OVERVIEW

First In Human Trial Should Rerate the Company

Opportunities in the Oncology Market? Why Cellmid Should Focus On Oncology?

Reason 1

According to a recent Deloitte report oncology has dominated in- and out-licensing activity among biotechnology companies throughout the last 6 years. In our view, any potential transaction between Cellmid and a larger partner in the therapeutic arena will allow the company to leverage their IP around midkine (MK) antibodies and will provide significant upside for investors.

Figure 1. Oncology Continues to Dominate Dealmakings. Source: Deloitte Development, 2013

Reason 2

The Deloitte report also provides evidence that oncology indications have a higher percent distribution of early product development stages for potential M&A transactions (Figure 2). In our view, concentrating midkine development on oncology indications significantly reduces the time towards a potential transaction between Cellmid and larger partner. As indicated, 15% and 36% of transactions in oncology happen at Phase I and Phase II stage of development respectively. In contrast, the rates for other therapeutic areas are 5% and 22% respectively. Cellmid will be moving into Phase I late 2014.

Figure 2. Cancer M&A Trends: 30% of Acquisitions are Early Stage Versus 15% for Non-Cancer. Source: Deloitte Development, 2013
Reason 3

The average upfront cash payment for oncology-focused licenses & JVs in major markets at the Phase I stage is US$28.5M, which exceeds current market capitalization of the Company. We believe that the quality of the midkine therapeutic program is on par with the licensed programs accounted in this data. In our view, there is a high probability of Cellmid striking a major partnership in the next 12-24 months, once the company is in the Phase I stage of the program.

![Figure 3. Average and Median Upfront Cash Payments for Oncology-Focused Licenses & JVs in Major Markets 2008-2012, Discovery-Phase III (n=100). Source: Defined Health, 2013](image)

Reason 4 - First in Class Program

Once the clinical program for anti-MK starts, Cellmid will offer patients access to a new therapeutic option that utilizes novel signalling pathway (MK - Alk - Notch2). Xalkori (Crizotinib, an ALK inhibitor) is the only product approved that targets the same pathway.

Why It Is Important To Have First in Class Compound?

![Figure 4. The Concentration of Clinical Development Effort Around the Same Targets. Midkine Ab is first-in-class with no competition. Source: Defined Health, 2013](image)

In 2013, PhRMA a leader in healthcare analytics, released a report listing nearly 1,000 R&D projects in the industry’s pipeline for oncology against a whole range of cancers. Unfortunately for patients, the concentration of clinical development effort around the same targets (molecules) is extremely high. Eight targets are addressed by >20% of the projects, with each of these targets having more than 24 projects in clinical development (Figure 4 in blue, mTor to EGFR). Thus, clinical projects that target VEGF lead the list with 70 programs developed around this molecular factor. In addition to the clinical development congestion on these targets, there is a huge numbers of preclinical projects addressing the same targets (Figure 4 in red).
Reason for this "concentration" is that portfolio decision-making in large and small companies have a strong bias towards the programs and/or drugs that have a well established mechanism of action and have significant prior clinical research (in humans) completed, as a means to reduce biologic risk. Thus, most R&D portfolio prioritizations punish novel target programs due to low "confidence in mechanism", and therefore assuming them riskier than "precedented" targets.

In Contrast, in this Congested Environment We Like the Midkine Program

We agree with the view of industry key opinion leaders (KOLs) that "the concentration of development activity on these privileged targets feels way outside the norm, and it represents a lot of wasted investor's money".

We believe that for all of the "precedented" programs the differentiation risks have dramatically increased and we therefore see midkine program as a much better option for investors.

Differentiation risks include:

- Phase III development risk (e.g., active comparator in your drug class; refractory patients);
- Regulatory risks (e.g., higher bar for approval with other approved agents ahead);
- Reimbursement risks (e.g., why should payors pay for your drug);
- Marketing risks (e.g., how do you get market share).

It is extremely difficult to differentiate the 10th VEGF inhibitor to enter its clinical development program. However, this would not be the case for a midkine program.

Reason 5 - Cellmid’s First in Class Therapeutic Antibodies Will Target MK positive Patients

The cancer field has been undergoing some significant changes and challenges, especially in this era of premium-priced, targeted therapies. The challenges range from molecular stratification of patients to the increasing pushback from payers and large cancer centers themselves around the cost benefits of new therapies.

In our view, the use of molecularly targeted agents (i.e. MK antibody) directed to specific patient populations (i.e. patients overexpressing MK) can help overcome market access barriers by providing a stronger efficacy signal and hence meaningful clinical value.

Overview of CDY’s Midkine Oncology Program - Evidence for a Successful Outcome

Midkine clinical program is significantly de-risked.

In our view the risks around the clinical development of midkine are mitigated through extensive collaboration between Cellmid and partners on target development and validation by various means.

These include:

1. Early validation of midkine antibody effectiveness as an anti-cancer agent in several animal models of disease (Figure 5);
2. Understanding that pharmacology can duplicate the results demonstrated with the transgenic knock-out or knock-down models (Figure 6);
3. Demonstrating that multiple therapeutic modalities (i.e. molecular antibody, siRNA, small molecule inhibitors) achieve the same outcome in preclinical models (Figure 7);
4. Demonstrating that the biochemical pathway that midkine regulates is a valid target for oncology (Figure 8);
5. Diagnostics validation - numerous publications and clinical trials identify midkine as a strong predictive and prognostic indicator in numerous cancers (Figure 9);
6. The company is working towards the creation of a translational strategy with midkine expression levels as a biomarker for target enrolment of patients. In our view, this is an important bridge for the company from animals to the clinic.
Evidence 1 - Early Validation of MK-antibody in Animal Model

Inhibition of MK signalling by anti-MK mAb suppressed osteosarcoma growth both in vitro and in vivo. These results clearly indicate that approaches utilizing anti-MK mAb may be effective for osteosarcoma or other cancer treatment by inhibiting tumor growth.

In experiments shown below, sections of lungs obtained from tumor cell-injected mice were treated with control solution or anti-MK mAb and were stained for metastasis. The experiment confirmed that inhibition of MK function reduced the incidence of lung metastasis, which suggests that MK regulates tumor cell release in blood, engraftment, and proliferation in the lungs.

**Figure 5.** Treatment with anti-MK antibody prevents lung metastasis in animal model of osteosarcoma. *Source: Cancer Letters, 2011*

**Evidence 2 - MK knockout (KO) mice show lower tumor incidence**

MK knockout animals demonstrated lower tumour incidence and slower tumorigenesis in a neuroblastoma. Experiments described below addressed the involvement of endogenous midkine in the tumorigenesis on the background that have high frequency of sporadic tumors (MYCN mice line).

Results showed that wild type animals began to die from 6 weeks of age, and the peak of the deaths from tumor occurred at an age of 9 to 14 weeks. Around 30% of MYCN transgenic mice were free of tumor.

In contrast, transgenic mice possessing homozygous deletion of the midkine gene (midkine -/-) exhibited the suppressed phenotype (Fig. 6). Their tumor deaths were delayed for 1 to 2 weeks and more than 40% of them were tumor-free.

**Figure 6.** The suppression of tumor incidence and progression in midkine-knockout mice. *Source: Cancer Research, 2013*
Evidence 3 - Midkine Clinical Program is Extensively Validated by Other Therapeutic Approaches Targeting Midkine

<table>
<thead>
<tr>
<th>TOOLS</th>
<th>EXPERIMENTS</th>
<th>REFERENCES</th>
</tr>
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<tbody>
<tr>
<td>Oligodeoxynucleotide</td>
<td>Intratumor injection to CMT-93 (mouse rectal carcinoma) xenograft</td>
<td>Takei et al., 2001</td>
</tr>
<tr>
<td>Morpholino oligomer</td>
<td>Intratumor injection to PC-3 (prostate carcinoma) and SW620 (colon carcinoma) xenografts</td>
<td>Takei et al., 2005</td>
</tr>
<tr>
<td>siRNA</td>
<td>Intratumor injection to PC-3 xenograft</td>
<td>Takei et al., 2006</td>
</tr>
<tr>
<td>Oligonucleotide</td>
<td>Intravenous injection to in situ hepatocellular carcinoma model</td>
<td>Dai et al., 2007</td>
</tr>
<tr>
<td>MK-TRAP midkine-binding peptide derived from (LRP1)</td>
<td>MK-TRAP-transfected CMT-93 xenograft</td>
<td>Chen et al., 2007</td>
</tr>
<tr>
<td>Polyclonal antibody</td>
<td>Anchorage-independent colony formation of G401 (Wilms’ tumor) and CMT-93</td>
<td>Chen et al., 2007</td>
</tr>
<tr>
<td>Oligonucleotide-loaded nanoparticle</td>
<td>Intravenous injection to in situ hepatocellular carcinoma model</td>
<td>Dai et al., 2009</td>
</tr>
<tr>
<td>siRNA</td>
<td>Intratumor injection to T98 (glioma) xenograft</td>
<td>Lorente et al., 2011</td>
</tr>
<tr>
<td>Monoclonal antibody</td>
<td>Intraperitoneal injection to 143B (osteosarcoma) xenograft</td>
<td>Suysyoshi et al., 2012</td>
</tr>
<tr>
<td>RNA aptamer</td>
<td>Intratumor injection to TNB1 and YT-nu (neuroblastomas)</td>
<td>Kishida et al., 2013</td>
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</table>

In regard to the use of midkine as a molecular target in cancer therapy, several molecular tools have been established to target midkine, and have been shown to exert therapeutic effects on xenografted tumors derived from several kinds of cancer (Figure 7). These tools can be mainly classified into three groups:

1) **RNAi-based nucleotides.** Oligodeoxynucleotide, morpholino oligomer, and siRNA were all shown to efficiently suppress the growth of xenografted tumors.

2) **Small peptides or antibodies.** The midkine-binding peptide (MK-TRAP) was utilized to neutralize the secreted midkine protein. MK-TRAP expression in G401 (Wilms’ tumor) cells resulted in growth inhibition in cell culture. In addition, MK-TRAP-expressed CMT-93 cell-derived xenograft tumors have been shown to exhibit suppressed growth in vivo. Finally, a recent report indicated the growth inhibition of xenografted 143B cells (osteosarcoma) by intraperitoneal injection of monoclonal antibody (see above Figure 5).

3) **RNA aptamers.** RNA aptamers, which specifically recognize and directly bind to particular proteins, are considered nucleic acid analogs to antibodies. They form a particular three-dimensional structure and recognize a specific target in the same way as antibodies. Intratumor injection of the RNA aptamer against midkine into neuroblastoma cell-derived xenografted tumors has been shown to induce significant growth suppression. The tumor volume and weight of treated tumors were approximately 25% of the values in control tumors.

**Figure 7.** Cancer therapies targeting midkine. Source: British Journal of Pharmacology, 2013
Evidence 4 - Midkine is a Part of ALK-Notch2 Signalling Pathway - A Well Validated Oncology Target

Figure 8.Midkine signalling in tumor cells.
Source: British Journal of Pharmacology, 2013

What Science Suggests?

Notch2 and ALK are two main factors that appear to mediate the role of midkine as a tumorigenic factor (Figure 8).

- Previous research showed that MK and ALK (anaplastic lymphoma kinase) play indispensable roles in drug resistance of select cancers and suggest that MK functions upstream of ALK while not necessarily through a direct ligand receptor relationship.

- Notch2 was reported as a functional receptor of midkine in neuroblastoma cells. Although MK-Notch2 signalling induced the expression of Hes1, a canonical target gene of Notch family members, there might be other MK-Notch2-specific target genes involved in the tumorigenesis and tumor growth.

In summary, it appears that midkine function in tumorgenesis involves Notch2 and ALK signalling that recently became the hot spot in biotech.

Because of the marked clinical efficacy of ALK inhibitors, ALK is now a promising target for some tumours. Indeed, crizotinib (Xalkori), an ALK inhibitor, has recently been approved by the Food and Drug Administration for the treatment of lung cancer harbouring ALK rearrangement. Launched in late 2011, the drug generated $120 million in worldwide sales in first-half 2013 and could generate peak sales of more than $1.5 billion (assuming potential patient populations with a similar gene alteration in several cancer types can be identified).

No Notch2 antibodies / drugs targeting this receptor have being approved to date though OncoMed Pharmaceuticals is considered to be the front runner in clinical development (currently in Phase Ib/II, company has Market Cap $1B). Since midkine works upstream of both ALK and Notch2 it could potentially offer a better therapeutic modality for cancer patients.
Evidence 5 - Midkine is a Well Proven Predictive and Prognostic Indicator in Numerous Cancers

The use of midkine as a diagnostic and/or prognostic marker in various cancers has been extensively covered in medical literature with hundreds of peer-reviewed publications published to date. In our view this represent a strong validation factor for the use of anti-midkine antibody as anti-cancer agent. Below we provide a summary of Cellmid’s current collaborations in the diagnostic area (not including partnerships with Pacific Edge and Quest Diagnostics).

<table>
<thead>
<tr>
<th>Indication</th>
<th>Project</th>
<th>Collaborators</th>
<th>Goals</th>
</tr>
</thead>
<tbody>
<tr>
<td>General</td>
<td>Latex bead assay clinical validation</td>
<td>Fujikura Kosei</td>
<td>1. Develop validated latex bead MK assay using CDY mAbs 2. Clinical validation of MK</td>
</tr>
<tr>
<td>Metastatic colorectal cancer</td>
<td>Disease recurrence</td>
<td>Not disclosed</td>
<td>1. Assess MK vs CEA for disease re-occurrence 2. Serum vs plasma analysis</td>
</tr>
<tr>
<td>Hepatocellular carcinoma (HCC)</td>
<td>Early detection</td>
<td>Not disclosed</td>
<td>1. Evaluate MK for detecting early clinical HCC in at-risk patients (Hep C positive) 2. MK vs AFP, AFP-L3, DCP in HCC diagnosis</td>
</tr>
<tr>
<td>Prostate cancer</td>
<td>Urine cancer detection</td>
<td>Not disclosed</td>
<td>1. Assess uMK in PC detection (= MK RNA) 2. Determine if MK differentiates aggressive PC</td>
</tr>
<tr>
<td>Bladder cancer</td>
<td>Urine cancer detection</td>
<td>Dr. Anna Nordin</td>
<td>1. Assess MK as a marker of androgen independent PC 2. Assess MK ELISA for urine MK determinations</td>
</tr>
<tr>
<td>Glioblastoma (GBM)</td>
<td>THB resistance in GBM</td>
<td>Not disclosed</td>
<td>1. Evaluate MK as a biomarker for THB resistant GBM</td>
</tr>
<tr>
<td>Colon cancer</td>
<td>Early detection/ screening</td>
<td>Abcodia Inc.</td>
<td>1. Evaluate MK as biomarker for pre-symptomatic detection of CRC</td>
</tr>
<tr>
<td>General</td>
<td>To assess midkine levels in kidney disease (KD)</td>
<td>Not disclosed</td>
<td>1. MK assessment in all KD admissions, including acute and chronic</td>
</tr>
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</table>

Importantly, we believe that Cellmid’s validated MK ELISA test is ready to become the companion diagnostic for anti-MK antibody therapy. Having an appropriate companion biomarker test has become vital for any therapeutic, but especially so for oncology drugs.

Regulators and clinicians now demand that only patients who are likely to respond are treated, and the treatment needs to be appropriately monitored for response and relapse. The MK ELISA can perform all of these roles as it is not only validated but extensively tested (see below).

Recently announced data on MK ELISA

The company has recently completed its two year long CK3000 program investigating normal serum concentrations of midkine (MK) in the largest ever study of healthy volunteers involving 574 individuals. Of these apparently healthy subjects 96.3% had serum MK concentrations under 1000pg/mL, with 90.7% below 500pg/mL.

MK levels above1000pg/mL were considered to be abnormal and were investigated further. For these 21 individuals (3.7% of all subjects) elevated MK showed no correlation with age, sex, smoking or alcohol intake, and nor did any of the 21 subjects have elevated CRP, HbA1c or high LDL. Liver and kidney function tests were also normal.

6 of these 21 patients had accessible patient records at Kumamoto Hospital and were followed up more closely. 4 of these 6 subjects had in the past been admitted to the hospital for cancer (glioblastoma, osteosarcoma), autoimmune disease (rheumatoid arthritis) and an acute inflammatory condition.

We expect Phase I to start late 2014 / early 2015

Phase I/IIa Clinical Study Planned

The company is planning to start IND enabling animal studies 1Q14 with data available 2H2014. With pre-IND meeting planned for the 3Q2014, we expect the company to move into first human trials towards the end of 2014 or early 2015.

This Phase I program will be a dose escalating study that will enrol 12 advanced or end stage cancer patients with prior chemotherapy. We expect MK ELISA to be used for patients screening in the trial enrolment. According to management the study should be completed in 4Q2015.
Consumer Healthcare Business; Advangen is a Global Brand and Worth 3.9c per Share

Recent market research indicates that the global beauty industry continues to do well, outgrowing other segments of consumer healthcare. With the increasing wealth of women in developing economies, not surprisingly, the sales of beauty products in these countries are growing.

Australian Business

Cellmid’s consumer healthcare business is focused on commercialization of hair care / hair loss products. These products contain FGF-5 inhibitors sourced from botanical extracts. FGF-5 was shown to shorten hair growth cycle in numerous animal studies and its inhibition provides therapeutic benefits. In Australia, Cellmid received a TGA listing for the évolis® hair growth tonics in February 2012 providing validation of the clinical performance and safety of the product by the regulatory body of Australia. We view the TGA listing as a good marketing tool in the domestic market as it supports évolis® therapeutic claims. Advangen’s hair loss prevention products will not require a prescription and will be sold as over the counter medicines in pharmacies.

Advangen’s évolis® product range was launched in June 2012. The list of pharmacies includes some of the largest pharmacy chains such as Priceline, Terry White and National Pharmacies. Frostbland Pty Ltd was appointed as an exclusive distributor for the pharmacy and drug store market in Australia and New Zealand.

Acquisition of Advangen Inc (Japan) Brings Global Brand

With the acquisition of Advangen Inc in May 2013 Cellmid has taken control of global rights to the FGF-5 inhibitor hair growth technology. Key facts to consider (that favour acquisition):

- Cellmid got the rights to several established Japanese brands and access to a mature Japanese market with 700K units (Advangen, Japan) of product sold since launch in 2007;
- In addition, the company got the exclusive right to manufacture, market and distribute its products in China, Taiwan, South Korea, Singapore and Malaysia. This region is considered among the largest hair loss markets globally;
- Importantly, with the Advangen Inc. (Japan) acquisition Cellmid has taken over potentially lucrative Chinese import permits to the Lexilis® and Jo-Ju® brands;
- Early evidence of the market size in Asia and market demand - The Japanese distribution agreement for 30K units with Natural Garden Co Ltd. In January 2014 the company signed a Chinese distribution agreement for its hair loss brands with Beijing Huana Likang Biotechnology Co.

Advangen Revenue and Profit Estimates

Currently we only estimate sales from the Australian China and Japan (see next page). Whilst the rest of Asia, US and Europe represent larger opportunities, we do not include sales from these regions into our model until we get more clarity from the company on the path forward and more information on regulatory requirements.

Since the first sales of Advangen’s products in Japan, more than 700,000 bottles of the product have been sold in the established Japanese hair growth market alone. Advangen commenced sales of its first product in Japan in 2007, so the annual volume were exceeding 100K units per year. We estimate peak sales at 100K units per year in Japan.

For the distribution in China we estimate moderate uptake of the products through Huana Likang direct marketing campaigns. We have a conservative view with 30K units in peak sales from this partner until more clarity on this distribution channel.

See details on our modelling assumptions next page (Figure 10).
Molecular Diagnostics – Valued at 4.5c per Share

Midkine is a Part of Cxbladder – Pacific Edge Successfully Launched the Test in 2013

In 2010 Cellmid entered into a non-exclusive license agreement with Pacific Edge Biotechnology Limited (PEB) for the use of Cellmid’s midkine technology in PEB’s bladder cancer test. Cellmid is eligible to receive milestone payments in addition to royalties on product sales which we estimate to be 4%. We change our royalty rate on diagnostic business from 2% to 4%, in line with the current industry standards.

The test provides general practitioners and urologists with a quick, cost effective and accurate measure of the presence of a bladder cancer, and provides urologists with the opportunity to reduce their reliance on the need for invasive tests. The non-invasive nature of Cxbladder should be more compelling for the patient and will likely lead to overall higher compliance to the monitoring regimen.

Clinical Evidence Suggests Cxbladder Will Have Market Leading Performance

The Cxbladder clinical study met its primary clinical end point of identifying bladder cancer significantly more accurately than other commercially available tests benchmarked in the trial. Cxbladder demonstrated 82% sensitivity at 85% specificity. Impressively, Cxbladder showed 100% sensitivity in detecting late stage bladder cancer (all stages other than Ta).

In our view, Cxbladder has sufficient performance to challenge urine cytology as the routine adjunct to cystoscopy. In addition, based on its ability to distinguish between high and low risk tumors Cxbladder could potentially be used to prioritize primary care patients for urgent cystoscopic evaluation.

Current Diagnostic Options for Bladder Cancer

Cytology is the most common test used by general practitioners to triage patients with haematuria. If cytology indicates the possibility of cancer, the patient is referred to a urologist for cystoscopy (invasive and expensive) to confirm the diagnosis. Cytoscopy cost is in the region of $600 - $1,000. Cxbladder is designed to potentially replace cytology and to also be used as an adjunct to cystoscopy.

Recent Updates on Cxbladder Commercialization

• Pacific Edge USA’s completed custom built laboratory for high throughput testing with the design capacity to process up to 4,000 tests per week that could support $115M US in revenues assuming the current test price at $550;

• Direct marketing of Cxbladder to Large Urology Group (“LUG”) practices by Pacific Edge’s sales force commenced 1 July 2013 (e.g. 10% of US urologists have aggregated themselves into business units (of up to 100 urologists);

• Sales territories designed and mapped by third party consultants—19 sales territories established which cover 60% of the U.S. market. Lead territories, based on volume of expected sales (Pittsburg and Cleveland), are in the immediate vicinity of PED USA’s laboratory in Hershey, PA;
Recent Update on Cxbladder Commercialization (continued)

- In October 2013 Pacific Edge has completed the first commercial sales of Cxbladder tests signifying the start of the commercial revenue for the company in the US. The tests were ordered by US based clinicians and processed in Pacific Edge USA’s custom laboratory in Hershey Pennsylvania;

- Pacific Edge signed an agreement with FedMed in October, a national preferred provider network in the United States, to make Cxbladder. The commercial relationship with FedMed provides FedMed’s contracted insurance carriers, third party administrators, health and welfare funds, and self-insured health plans with access to Cxbladder. More than 40 million Americans have access to FedMed’s National Provider Network of over 550,000 physicians, 4,000 hospitals and 60,000 ancillary care providers nationwide;

- Building a relationship with the CMS is a key target for Pacific Edge in 2014. CMS is the US federal agency which administers Medicare and Medicaid and will reimburse Pacific Edge for all Medicare / Medicaid patients who utilise Cxbladder. Approximately 115 million U.S. citizens are covered by Medicare and Medicaid. Pacific Edge has already conducted preliminary discussions and is expecting to complete negotiations in August 2014;

We Value Cxbladder at 2.8 cents per share

We are increasing our estimates of market share given better than expected reimbursement landscape for the test. We use a price of $550 per test which is on the lower side of the range provided by PEB. Using penetration rates of 0.5% - 9% in FY2014 – FY2022 and using PEB’s market size model we estimate revenues of $5.3M - $140.9M from the test in FY2014 – FY2022 respectively.

Using a royalty rate of 4% (vs 2% previously) we forecast $211K - $5.6M in royalties to Cellmid in FY2014 – FY2022 respectively. We use a 10% discounting rate according to our valuation grid (Figure 15, see page 14).

Our new valuation for Cxbladder is 2.8c (+1.3c vs previous) as we view a better commercial opportunity for the test. Higher penetration and royalty rates will provide an upside to our current estimates and CDY valuation.

Midkine is a Part of Highly Expected Lung Cancer Diagnostic Test

With the exception of the prostate specific antigen (PSA) test for prostate cancer, screening technology for early detection of other major cancers has not been within reach of the diagnostics sector until recently. For lung cancer a non-invasive IVD-based test that would allow detection with high accuracy and at an early stage, would be very attractive, considering the many issues with current, mainly in vivo-based (invasive) procedures (i.e. lung biopsy).

In 2009 Cellmid licensed midkine as a biomarker for the early diagnosis, prognosis and disease monitoring of lung cancer to be used in Celera’s proprietary biomarker panel. The terms of the license are not publically disclosed but involve upfront and milestone payments and royalties on product sales. Celera Corporation is now a part of Quest Diagnostics (NYSE: DGX). We estimate first commercial launch of the test in FY2015 as a Laboratory Developed Tests (LTD) that will be regulated under Clinical Laboratories Improvement Amendment and thus do not require FDA approval. Under the license agreement Cellmid will receive milestone payments in addition to single digit royalties. We estimate a 4% royalty to Cellmid from future sales of the test. An earlier launch will represent upside to our valuation.

The test showed 85% sensitivity and 83% specificity in clinical settings, and compared well with CT (computer tomography) scanning. CT is the current gold standard screening method and has a much lower specificity. According to Celera the specificity rate for CT is about 75%.
Considering the associated risks of CT scans and morbidity associated with invasive follow-up diagnostics, it is expected that Celera’s test will be at least an adjunct screening method and will assist in further clarifying the diagnosis in patients who have tested positive during their CT screening (Figure 13, Post-CT). This patient population is estimated to be 1.7 million. In addition, the test could be used in pre-CT serving as a filter to identify high risk individuals whose malignant state could be checked through test. That would provide an upside to our sales estimates.

Market Size (US only) and Our Revenue Model for Celera’s Test

The high risk group (for developing lung cancer) consists of current and past cigarette smokers. Currently cigarette smokers make up 24% of adults in the US (or 47.5 million people) and past smokers comprise another 24.1 million adults. This group is greater than twenty times more likely to develop lung cancer than non-smokers. However according to medical literature, there are currently about only 7 million people in the US who would meet the eligibility criteria for the National Lung Screening Trial (NLST) and thus would be eligible for regular CT screening.

The rate of positive screening tests in NSLT was determined at 24.2% with low-dose CT. We thus estimate that there is about 1.75 million people who could test positive upon CT imaging (in clinical settings there could be up to 96% of false-positives after first scan). We use this number as a target population for Celera’s lung cancer diagnostic product.

We currently do not have information on the pricing of Celera’s lung cancer test and thus using a conservative estimate of $1,000 per test given the $1,000 - $4,000 range for LDT test in the US with some high complexity tests fetching in excess of $4,000 per test.

We Value LungDx at 1.7 cents (~1.3 cents from previous valuation) as Quest is Not in a Hurry to Launch the Test

We are a bit disappointed in Quest’s lack of action regarding the LungDx test. As a result, we reduce our market penetration rates and postpone the lunch to FY2015 to remain conservative. Using market penetration rates of 1% - 5% in FY2015 – FY2022, we estimate revenues from the test of $18.6M - $114.4M in FY2015 – FY2022 respectively. Using a royalty rate of 4% (Midkine is 1 out of 6 biomarkers in the test), we forecast $743K - $4.6M in royalties to Cellmid in FY2015 – FY2022 respectively. Higher penetration and royalty rates, as well as price per test will provide an upside to our current estimates and CDY valuation.

We increase our discount rate for LungDX to 15% according to our valuation grid (Figure 15, see page 14) as we see more uncertainties associated with LungDx commercialization.
Summary on Quest's LungDX

While we are still awaiting the annual update from Quest on the readiness of LungDX test to become commercial, we remain confident that the launch of the test is on the way and expect it in FY2015 as latest.

In 2013 Quest announced the sale of its HemoCue and OralDNA businesses (both Point-of-Care tests) and realigned their business strategy focusing on esoteric growth (refers to tests performed at reference laboratories that use rigorous testing and that exceed what most hospitals and basic labs can do, i.e. LungDX) through disease focus and laboratory information services.

We view LungDX as a strong fit with Quest’s corporate strategy and expect the company to launch the test in the next 12 months. Alternatively, we could see Quest divesting this asset in the same time frame which would indicate an upside to our current view.

Future Molecular Diagnostic Partnership Could Add 2 cents or More Per Share Per Test

According to PwC, M&A and partnership deal values in the diagnostic space jumped to exceptional levels during the last two years. Interestingly, partners were not only existing players in the diagnostics sector, but also private equity, life sciences research groups, clinical laboratories, and medical technology players. New entrants also included pharmaceutical companies in search of companion diagnostic products. According to EvaluatePharma consulting group, in-vitro diagnostics will be the industry’s top segment by 2018, pulling in sales of $54.5B and outstripping old standbys like cardiac devices and imaging technologies.

The surge and diversity of these deals encourages our belief in the growth prospects of Cellmid’s highly validated diagnostic pipeline and more future out licensing deals. We believe Cellmid will be eligible for similar economics in each new deal, adding 2 cents per current share price per deal or more. That could include both in-vitro diagnostics and companion diagnostics applications.
Intellectual Property

We view Cellmid’s almost exclusive midkine patent portfolio as a core asset to the company’s present and future business. Strong IP rights on midkine as a biomarker or therapeutic agent are crucial for future partnerships. Midkine’s current patent portfolio includes 20 patent families and 77 patents of which 51 granted (see list below)

2 Patent Family Entitled: Composition comprising midkine or pleiotrophin protein and method of increasing hematopoietic cells (2 patents granted Exp 2017/2018)
3 Patent Family Entitled: Drugs containing as the active ingredient midkine or inhibitors thereof (9 patents granted Exp 2018/2020)
4 Patent Family Entitled: Preventives or remedies for ischemic disease (7 patents granted Exp 2018)
5 Patent Family Entitled: Mass secretion/expression system of true MK family protein (1 patent granted Exp 2019)
8 Patent Family Entitled: Monoclonal antibody against human MK (1 patent granted Exp 2020)
9 Patent Family Entitled: New method for preparing antisense oligonucleotide (1 patent granted Exp 2022)
10 Patent Family Entitled: Method for diagnosing rheumatism (1 patent granted Exp 2022)
11 Patent Family Entitled: Preventive for adhesion following abdominal surgery (2 patents granted Exp 2024)
12 Patent Family Entitled: Arthritis-associated gene and use thereof in examining arthritis (1 patent granted Exp 2024)
13 Patent Family Entitled: Method for treatment or prevention of disease associated with functional disorder of regulatory T cell (1 patent granted Exp 2026)
15 Patent Family Entitled: Composition for treating or preventing myocardial disorder or heart failure (1 patent granted Exp 2025)
16 Patent Family Entitled: Nitric oxide synthase activator (under examination Exp 2027)
17 Patent Family Entitled: Pharmaceutical composition for vascular occlusive disease (under examination Exp 2026)
18 Patent Family Entitled: Therapeutic agent for occlusive peripheral vascular disease, and use thereof (Filed Exp 2027)
19 Patent Family Entitled: Method of treatment or prevention of hair loss or for the enhancement of hair growth (awaiting filing Exp 2031)
20 Patent Family Entitled (PCT application): Antibody recognizing N-domain of midkine (Filed Exp 2032)
Risk Analysis

We believe there are several risks to Cellmid’s share price and our price target. Our price target includes future royalty streams from lung and bladder cancer diagnostic products (A$0.045). Our valuation of diagnostic products relies on timely market entry, commercial success of these tests, and their reimbursement levels in US. In addition, Advangen is commercializing hair loss prevention products that contribute A$0.039/sh in our price target. There are upside and downside risks associated with that product line.

Downside

Commercial Risk: Significant portion of CDY’s forecasted revenues come from royalties on lung cancer and bladder cancer tests paid by Quest Diagnostics and Pacific Edge. If the sales numbers for these tests materially differ from our forecast, our price target could be impacted as well as the stock price. The same argument is valid for the Advangen business unit. Lower than forecasted sales from Advangen’s Australian and Japanese business could negatively affect the share price.

In addition, future therapeutics and diagnostics developed by the company may require development partners and the company may be delayed or unsuccessful in seeking out such partners. The company has multiple product development programs to ensure that this risk is mitigated.

Reimbursement Risks (on Partnered Tests): Medicare reimbursement could decline. We do believe that Medicare reimbursement for the clinical lab fee schedule (important for diagnostics reimbursement) is likely to decline in the future, given recent chatter regarding co-payments and additional market basket reductions. Conversely, material inflation in the annual market basket adds upside to our forward estimates.

 Intellectual Property Risks: The patent positions of biotechnology companies can be highly uncertain, and the company could face the risk in obtaining and defending its key product patents. Failure to protect midkine patents could negatively impact the stock price.

Technical Risks: associated with the development of the company’s products which may cause a delay in development or failure to complete development programs. To mitigate this risk, the company has a diverse portfolio of assets at various stages of development and with multiple revenue opportunities.

Competition Risks: therapeutics or diagnostics competing with the company’s products may be developed by others reducing the potential market. The company can do little to prevent competition. However, it operates in the pharmaceutical development sector where competitive products are often successfully marketed together.

Upside

Better-Than-Expected Sales: If molecular diagnostics or hair loss prevention products sales are better than we forecast, it could positively impact the share price.

Diagnostics: Future molecular diagnostic partnership could add 2 cents per share per test.

Oncology: We do not currently include the oncology program into our model, but point out that this represent a major upside for the share price and our current valuation in the next 12-18 months, once the program is at clinical stage (in humans).
Directors and Management

Dr David King, Chairman

Dr David King brings a depth of corporate governance, capital markets and listed company board experience to Cellmid. He has previously held positions as Executive Director, Chief Executive Officer and Managing Director in a number of private and listed companies. An expert in high growth companies Dr King has a track record in starting business ventures and developing them into attractive investment and/or take-over targets. His experience in successful start-up businesses has been instrumental in CDY’s recent acquisition of the Midkine intellectual property portfolio.

Dr King is a Fellow of the Australian Institute of Company Directors, a Fellow of the Australian Institute of Geoscientists and the Australian Institute of Mining & Metallurgy (Chartered Professional, Management) and holds degrees in physics and geophysics and a PhD in Seismology from the Australian National University.

Maria Halasz, Managing Director and CEO

Maria Halasz has been involved with biotechnology companies for 19 years; initially working in executive positions in biotechnology firms, then managing investment funds and later holding senior positions in corporate finance specialising in life sciences. Prior to joining Cellmid Ms Halasz had been an adviser to an independent sector based research firm in life sciences and managed Direct Capital Group Pty Ltd, a specialist biotechnology fund. She has also been a venture partner at the Emerging Technology Fund of venture capital firm Allen & Buckeridge. Since taking over as Chief Executive and Managing Director of Cellmid Ms Halasz has led the restructure of the business, the acquisition of the Midkine intellectual property portfolio and the recapitalisation of the company. Ms Halasz is a Member of the Australian Institute of Company Directors and holds a science degree in Microbiology and an MBA.

Graeme Kaufman, Non-Executive Director

Graeme brings over 45 years’ experience in biotechnology spanning technical, commercial and financial areas. Having worked for 34 years at CSL Limited, Australia’s largest biopharmaceutical company, he held senior positions including Production Director, General Manager Finance and General Manager Biosciences. Graeme holds BSc & MBA with Melbourne University.

Martin Rogers, Non-Executive Director

Mr Rogers has a strong science background, which includes degrees in science and chemical engineering and is currently a member of the management committee of the National Breast Cancer Foundation. Mr Rogers also has strong expertise in the corporate sector, with a focus on the incubation and development of new business ideas. He has previously been involved in the origination of a number of new business concepts and the establishment of internal ventures and external partnerships, including finance concept origination in the corporate banking sector for institutions such as Macquarie Bank.

Darren Jones, Head of Product Development

Darren Jones has worked in the Australian biotechnology industry for over 10 years, with particular responsibilities for developing promising therapeutic antibody candidates from discovery, screening, preclinical testing and humanising through to clinical trials. In addition to his considerable technical expertise in all aspects of the development of antibody therapeutics, he has extensive expertise in intellectual property management and strategic business planning. Prior to working in the biotechnology sector Mr Jones worked as a research scientist at the University of Technology and at St Vincent’s Hospital, Sydney in the fields of immunology, cancer and HIV. Darren has a BSc from the University of Sydney and a MSc degree from the University of Technology, Sydney.
Nicholas Falzon, Company Secretary and Financial Controller

Nicholas Falzon has been working with Cellmid for over four years and was appointed as Financial Controller and Company Secretary on the 6th October 2010. As a partner at Lawler Partners, Nicholas works with a number of listed and unlisted companies advising them on all aspects of their financial management. His special area is R & D Tax Concessions and he has been successful in applying for substantial tax offsets for Cellmid in the past.

Emma Chen - Advangen General Manager

With more than 12 years’ experience in the hair growth industry Emma Chen has recently been appointed as VP-Business Development by Advangen International Pty Ltd to broaden the Australian distribution network and increase sales for our évolis® and Advangen products in pharmacies and in the hair salon/beauty market.

Prior to Cellmid, Emma served as a Chief Executive Officer at Ashley & Martin from 1998 until 2008. Throughout her tenure Emma built Ashley & Martin into one the most recognised and trusted brands in the hair growth industry and established a highly profitable, premium medical clinic network in the process. Prior to this, Emma was involved in launching the first generic minoxidil brand, Hair A-Gain, in Australia in 1997 (by South Pacific Pharmaceuticals).
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Care has been taken to define the level of risk to return associated with a particular company.

Our recommendation ranking system is as follows:

**Buy**
Companies with 'Buy' recommendations have been cash flow positive for some time and have a moderate to low risk profile. We expect these to outperform the broader market.

**Speculative Buy**
We forecast strong earnings growth or value creation that may achieve a return well above that of the broader market. These companies also carry a higher than normal level of risk.

**Hold**
A sound well managed company that may achieve market performance or less, perhaps due to an overvalued share price, broader sector issues, or internal challenges.

**Sell**
Risk is high and upside low or very difficult to determine. We expect a strong underperformance relative to the market and see better opportunities elsewhere.

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