Biosceptre International Ltd.
Jonas Webb Building
Babraham Research Campus
Babraham, Cambridge CB22 3AT
United Kingdom
Phone: + 44 1223 496 090
http://www.biosceptre.com/

Company Description

Biosceptre International Ltd. ("Biosceptre" or "the Company") is an immune-oncology company that has identified a novel receptor cancer target—a variant of $P2X_7$ ($nfP2X_7$)—that exists in a range of cancers, including lung, breast, colorectal, and prostate, but is not found on healthy tissue. Because of this **specificity†**, drugs directed to the $nfP2X_7$ target may prove effective at treating cancers with high precision and minimal side effects. Accordingly, Biosceptre is progressing into pivotal clinical trials with a portfolio of three anticancer compounds: (1) BIL03s, a systemic domain antibody (dAb) to treat blood-based and solid cancers; (2) BIL06v, a **peptide** vaccine therapeutic that stimulates the patient's own immune system to target $nfP2X_7$ in cancers; and (3) BIL010t, a topical **antibody (Ab)** treatment targeting $nfP2X_7$ in **non-melanoma skin cancers**. In parallel, the Company has leveraged its proprietary position in $nfP2X_7$ research into a pipeline of discovery programs that could be out-licensed for use in cancer diagnostics and imaging as well as for veterinary programs.

Key Points

- Significant research and development (R&D) is underway in the area of targeted cancer therapies, as they are a cornerstone of **precision medicine**. To date, over 30 **monoclonal antibodies (mAbs)**, administered either alone or conjugated with a cytotoxic agent, have been approved by the U.S. FDA to treat cancer. Currently available targeted therapies are sold at a high price, yet are often still associated with poor efficacy and a relatively minor impact at improving quality of life. Should a new, targeted therapeutic prove effective while demonstrating an excellent safety and efficacy profile, it could capture a significant share of a market forecast to reach $125 billion by 2020.
- Biosceptre's highly specific molecular target has been identified on the cell surface of 20+ human cancer tissue types.
- The Company holds 13 issued U.S. patent families as well as a global intellectual property (IP) portfolio that offers protection out to 2032 and continues to file patent applications. This IP portfolio is believed to enable the Company to pursue its multi-modality approach with freedom to operate.
- The team leading Biosceptre's antibody development is highly experienced in commercial and research services as well as in developing therapeutic antibodies for use in trials, de-risking scale-up.
- To continue developing its current oncology product candidates, Biosceptre seeks to raise £25 million (~US$32.8 million) via its first institutional financing event.

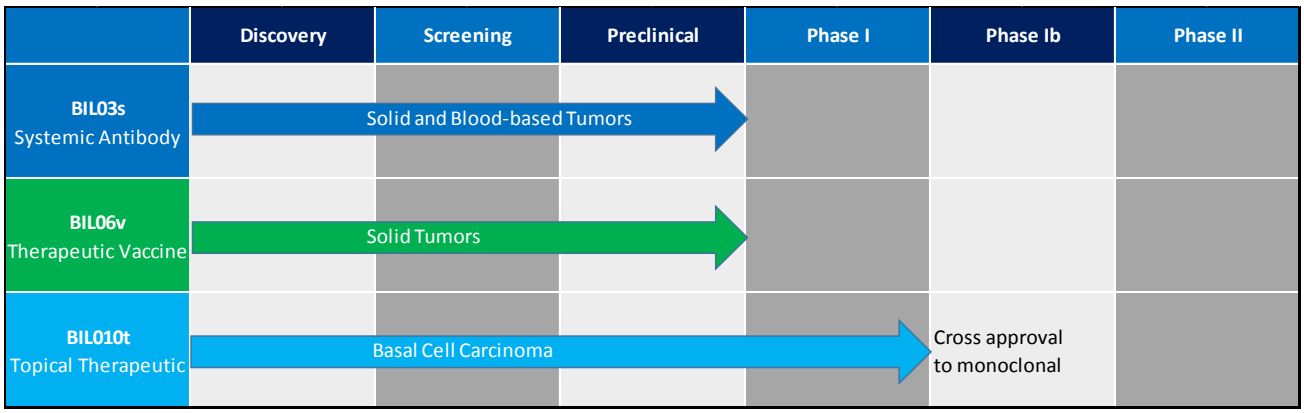


Table of Contents

Investor Highlights 3

Executive Overview 4

Intellectual Property 8

Milestones 10

Leadership 12

Core Story 16

Market Opportunities 16

Biosceptre's Technology Overview 23

Biosceptre's Product Development 30

Potential Competition 36

Historical Financial Results 41

Risks and Disclosures 43

Glossary 50

Investor Highlights

- ***Biosceptre is a clinical-stage immune-oncology company that has identified a novel target***—non-functional $P2X_7$ ($nfP2X_7$)—against which it is developing a pipeline of systemic and topical product candidates to treat a range of cancers.

- ***The oncology market has seen a significant transformation away from cytotoxic and anti-hormonal therapies toward more targeted therapies***. Targeted cancer therapies are drugs or other substances that block the growth and spread of cancer by interfering with specific molecules involved in tumor growth and progression—Biosceptre's products fall into this class. In 2013, IMS Health, Inc. estimated that targeted therapies represented 46% of global oncology sales, up from 11% a decade ago. In clinical development, the oncology drug pipeline has expanded by over 60% during the past decade, with approximately 90% of the focus on targeted agents.

- ***The $nfP2X_7$ receptor is a broadly occurring cancer target that has been identified on the surface of 20+ human cancer types***, including lung, breast, colorectal, and prostate cancers. $nfP2X_7$ has a significant positive attribute among cancer targets in that it is not expressed on the cell surface of normal, healthy tissue, minimizing the potential for side effects.

- ***Biosceptre is developing three proprietary clinical candidates addressing the $nfP2X_7$ target***: (1) BIL03s, a domain antibody (dAb) for systemic treatment of solid and blood-based cancers; (2) BIL06v, a peptide-protein conjugate vaccine therapeutic that stimulates the patient's own immune system to target $nfP2X_7$ in cancers; and (3) BIL010t, a topical antibody (Ab) treatment targeting $nfP2X_7$ in non-melanoma skin cancers. The Company has completed one clinical trial for BIL010t that has demonstrated favorable human safety data and indicative efficacy data that supports BIL010t and other products in the Company's pipeline.

    - While BIL010t represents the most advanced-stage candidate in the Company's pipeline (Phase I complete), Biosceptre believes that the other candidates in its pipeline (BIL03s and BIL06v) hold greater market potential.

- ***In parallel, through a series of collaborations, Biosceptre has a pipeline of external development programs*** where the Company seeks out-licensing agreements to develop cancer diagnostics and imaging technologies, as well as veterinary programs, which can benefit from the Company's proprietary position with $nfP2X_7$.

- ***The Company holds broad intellectual property (IP)***, with 13 granted U.S. patents and a global portfolio with protection through 2032. Biosceptre has secured IP protection on the $nfP2X_7$ target until 2022 with additional protection covering therapeutic intervention until at least 2035 (with further patents in development).

- ***The Company's scientific team is highly experienced in product development***. Its scientific advisory board is led by Sir Gregory Winter, a founder of Cambridge Antibody Technology, Domantis, and cofounder of Bicycle Therapeutics; and Professor Terrence Rabbitts, a professor of molecular biology at the University of Oxford. Sir Gregory Winter has also recently agreed to join the Company's Board of Directors. The Company's CSO, Dr. Shaun McNulty, has over 20 years of experience in major pharma and biotech drug discovery. Clinicians supporting the Company's trials include Professor Gavin Marx (chair of the Section of Oncology at the Sydney Adventist Hospital [Aus.]), Professor Nick Pavlakis (head of medical oncology, Royal North Shore [Aus.]), and Dr. Bob Li (attending physician at Memorial Sloan Kettering [U.S.]). Biographies are provided on pages 12-15.

- ***Biosceptre seeks funding of £25 million (~US$32.8 million) for continued development of its oncology products***. Funds are intended to cover the costs of Phase I trials for both BIL03s and BIL06v, with data collected in these two trials to include indicative efficacy signals. Funds are also earmarked to cover the costs of a Phase II trial for BIL010t, the planning work for Phase II trials for BIL03s and BIL06v, and the costs of advancing the preclinical portfolio to the selection of one or more further clinical candidates for development (approximately 8% [£2 million] of the funds sought are intended for this purpose). Lastly, funding may support an increase in infrastructure ahead of any potential initial public offering ([IPO] currently planned for the second half of 2017) and out-licensing activity for diagnostic and veterinary programs.

Executive Overview

Biosceptre International Ltd. ("the Company" or "Biosceptre") is a closely held, UK-based, biotech research and development company that has identified a novel receptor and oncology target, termed nfP2X$_7$, and is developing a product pipeline directed at this receptor to treat a range of cancers. The nfP2X$_7$ target has been shown to be highly specific to cancer cells, with the Company having demonstrated no cross-reactivity against normal tissue in humans—a feature that could prove disruptive within the field of immunotherapy oncology. Further, nfP2X$_7$ occurs across a broad range of cancers, including lung, breast, colorectal, and prostate tumors.

The Company is developing three proprietary clinical candidates addressing the nfP2X$_7$ target: (1) BIL03s, a domain antibody (dAb) for systemic treatment of solid and blood-based cancers; (2) BIL06v, a peptide vaccine therapeutic that stimulates the patient's own immune system to target nfP2X$_7$ in cancers; and (3) BIL010t, a topical antibody treatment targeting nfP2X$_7$ in non-melanoma skin cancers. The Company believes that each candidate holds considerable potential in treating cancer, either individually or in combination with other treatments. Biosceptre's intellectual property (IP) portfolio and expertise may further represent a key competitive advantage for applying and licensing its products and technologies across a range of therapeutic, diagnostic, and veterinary uses.

The Science Behind nfP2X$_7$

P2X$_7$ is a ligand-gated receptor on the surface of cells that performs multiple complex signaling roles. In healthy tissues, P2X$_7$ can play a key role in pathways involved in cell death as well as important cellular functions, such as proliferation and migration. P2X$_7$ can form an ion channel of three identical protein subunits, which together respond to extracellular **adenosine triphosphate (ATP)** and, on prolonged stimulation, a large pore. Biosceptre has discovered that in many cancers, P2X$_7$ becomes modified, causing it to lose the ability to form a pore but not other key functions. This enables cancer cells to express the receptor without experiencing ATP-induced **apoptosis**. The non-functional P2X$_7$ (nfP2X$_7$) receptor has been shown by Biosceptre to be involved in the proliferation and survival of cancer cells. ***This conformationally distinct state, defined as nfP2X$_7$,*** presents a new target for oncology therapy. nfP2X$_7$ can be targeted on its own or in combination with other oncology therapeutics acting on other pathways and targets.

Biosceptre's founder, Dr. Julian Barden (biography on page 13), has demonstrated that nfP2X$_7$ is widely expressed on cancer cells but not on normal tissue. He has shown that it is present in over 20 types of cancer (which accounts for approximately 95% of all cancers diagnosed). Biosceptre has more recently determined that nfP2X$_7$ also has a role in cancer cell survival *in vitro* across a broad range of cell lines. In nfP2X$_7$, **epitopes** are exposed that are not normally visible in P2X$_7$, as they are normally inaccessible inside the **trimer** structure of P2X$_7$ found in normal tissues. Biosceptre has developed antibodies that precisely target this epitope on the nfP2X$_7$ pore as it occurs on cancer cells. The presence of the nfP2X$_7$ form of P2X$_7$ on many cancer cell lines and tissues indicates that Biosceptre's pipeline has potential against many forms of cancer, including solid tumors, which is supported by *in vivo* efficacy data.

Market Size

According to the World Health Organization (WHO), there were approximately 14.1 million new cancer cases diagnosed worldwide as of 2012, with over 8.2 million attributable deaths and 32.6 million people living with the disease within five years of being diagnosed (Source: WHO). These numbers are expected to rise significantly over time. The Division of Cancer Prevention and Centers for Disease Control and Prevention (CDC) estimates that by 2025, 19.3 million new cancer cases will be diagnosed each year. However, despite the ever-increasing need for treatment, existing therapies often lead to poor efficacy despite their high cost and offer a relatively low impact on a patient's quality of life. Yet, in the U.S., the Food and Drug Administration (FDA) has approved over 30 therapeutics in the form of monoclonal antibodies (mAbs) alone or mAbs conjugated with a cytotoxic agent to treat cancer. Should a new therapeutic prove effective, which demonstrates excellent safety and a broad efficacy profile, it would likely capture a significant share of this cancer therapeutics market—a global market that reported $100 billion in annual sales in 2014 and could reach $147 billion by 2018 (Source: IMS Institute for Health Informatics, a unit of drug data provider IMS Health).

Targeted therapies encompass the highest-selling class of cancer therapeutics, and sales of targeted mAbs specifically have been consistently growing for the past decade. At current growth rates, sales of existing mAbs plus revenue from new products approved in the coming years may drive worldwide mAb sales to approximately $94 billion by 2017 and nearly $125 billion by 2020 (Source: the National Institutes of Health, U.S. Library of Medicine).

Pipeline

Biosceptre has established a solid IP portfolio surrounding nfP2X$_7$, where its IP represents a platform for oncology immunotherapy across a range of therapeutic modalities. Initial research has demonstrated that drugs directed to nfP2X$_7$ hold the potential to treat multiple cancers while circumventing the toxicity experienced with many marketed cancer drugs. In addition to existing clinical-stage candidates targeting nfP2X$_7$, Biosceptre is developing a second generation of products utilizing innovative targeting approaches to further improve delivery and efficacy. Figure 1 depicts the Company's therapeutic pipeline targeting nfP2X$_7$ as well as provides an overview of its discovery programs. Further descriptions of its more advanced clinical candidates are provided on pages 23-35.

Figure 1
PRECLINICAL AND CLINICAL-STAGE PRODUCT PIPELINE

Product	Approach	Indication	Discovery	Preclinical	Phase I	Phase II
CLINICAL PROGRAMS						
BIL03s	Domain Ab	*Solid tumors*			2H16	
BIL06v	Peptide Vaccine	*Solid tumors*			1H17	
BIL010t	Polyclonal Ab	*Basal cell carcinoma*				1H17
DISCOVERY PROGRAMS						
BIL011t	Topical dAb					
BIL04s	Next gen. systemic monoclonal					
BIL07v	Next gen. peptide vaccine					
BIL03n	Conjugate candidate					
BPM09	IHC Antibody (Diagnostics)					

Source: Biosceptre International Limited.

BIL03s (Systemic)

Biosceptre is developing a systemic antibody-based therapy, BIL03s, for multiple cancer indications. BIL03s selectively binds to nfP2X$_7$ and has been shown to bind to at least six major cancer types—prostate, kidney, ovarian, melanoma, lung, and colorectal—with confirmed safety via a formal toxicology study. The production process has been established and transferred, with clinical plans established. BIL03s represents the Company's core program and is poised to enter a Phase I trial as a domain antibody (dAb) for systemic administration to treat a variety of solid- and blood-based cancers. Between 20 and 30 patients are expected to be enrolled in the forthcoming Phase I trial at two trial centers in Australia. As a **basket trial**, it will focus on lung, prostate, and colorectal cancer. Phase I clinical trials are anticipated to demonstrate safety in suitable cancer patients. Biosceptre aims to use the compound in patients, post cancer diagnosis, to boost duration and quality of life with nominal side effects.

BIL06v (Vaccine)

Biosceptre is further developing a vaccine program that recruits an individual's immune system to specifically target cancer cells expressing nfP2X$_7$. This candidate uses a precise peptide sequence conjugated to a protein to stimulate the immune system to generate antibodies that bind to nfP2X$_7$. BIL06v has been shown to reduce tumor growth *in vivo* in mice, with data also indicating safety and efficacy in humans. Biosceptre has plans to begin a Phase I trial during 2017.

BIL010t (Topical)

There are over 2.8 million new cases of basal cell carcinoma (BCC) diagnosed in the U.S. every year. Biosceptre has gained widespread experience and knowledge from informed consent patient cohorts in Australia with BIL010t to treat BCC, and other skin cancers. These Australian studies were followed by a Phase I U.S. study designed to confirm safety. A first-in-human FDA Phase I clinical trial has demonstrated safety with no adverse events related to the product. In addition, there was an indication of efficacy, with 85% of patients showing that their tumor decreased in size or at least stopped growing over the 28-day period of the trial. Following the Phase I results, which showed favorable safety outcomes and indications of efficacy, Biosceptre is now focused on optimizing BIL010t as well as treatment protocols and is planning a clinical follow-up study.

- Importantly, while BIL010t is the most advanced candidate in Biosceptre's pipeline (having already completed Phase I), the Company believes that earlier stage candidates BIL03s and BIL06v have far higher potential for return on investment. Accordingly, Biosceptre's order of priorities as it relates to its development efforts are its dAb, followed by its therapeutic anticancer vaccine, and then its topical antibody formulation.

Discovery Programs

Biosceptre has several other programs in its pipeline that it could develop into a second wave of therapies. In particular, included in the Company's discovery program is a nanoparticle technology using BIL03s to deliver either an imaging payload to the tumor site, or alternatively a cytotoxin payload which takes advantage of the precise targeting and specificity arising from targeting nfP2X$_7$ to maximize anti-tumor action while minimizing off-target side effects.

Employees and Headquarters

The Company has headquarters in the UK in the Jonas Webb Building, a research building designed to provide a highly flexible chemistry and molecular biology laboratory as well as office space. Biosceptre's headquarters are depicted in Figure 2. The Company also has offices in Australia. Altogether, Biosceptre employs 18 individuals.

Figure 2
CORPORATE HEADQUARTERS

Source: Biosceptre International Limited.

Corporate Background

Biosceptre's science is based on research by Dr. Julian Barden at the University of Sydney in the late 1990s. Dr. Barden's work delved into the P2X family of receptors in search of therapeutic opportunities and targets. This research program identified and characterized novel epitopes on the nfP2X$_7$ receptor that are not visible on functional P2X$_7$. These neo-epitopes were found to be present on malignant B-lymphocytes and later on the surface of prostate cancer cells. Importantly, these neo-epitopes were not found on the surface of healthy cells expressing P2X$_7$.

Biosceptre was formed and acquired the intellectual property and science from the University of Sydney in 2003. The Company has initiated a translational science program to develop an immunohistochemistry diagnostic product, a therapeutic candidate addressing topical cancers, a fully human dAb for solid tumors, and a peptide protein conjugate vaccine to activate patients' immune systems, all against the nfP2X$_7$ target. Biosceptre continues to innovate in the science and development of nfP2X$_7$, including completing a Phase I clinical study of its topical candidate BIL010t, continuing ongoing fundamental research into the etiology of the nfP2X$_7$ target, and planning Phase I trials for its other therapeutic candidates, antibody BIL03s, and vaccine BIL06v.

Funding

Figure 3 summarizes funds sought by Biosceptre. For each of the Phase I trials for the Company's systemic antibody and therapeutic vaccine, the Company anticipates that it needs £5 million and £3 million, respectively. For its topical agent's Phase II, the Company will likely need an additional £3 million. Thus, Biosceptre is seeking £25 million (~US$32.8 million), which includes a contingency amount. Biosceptre believes this would be sufficient to fund its operations through an IPO phase after Phase I trials are complete.

Figure 3
POTENTIAL FUNDING

Product	Approach	Indication				
CLINICAL PROGRAMS						
BIL03s	Domain Ab	*Solid tumors (Phase I)*				5
BIL06v	Peptide Vaccine	*Solid tumors (Phase I)*				3
BIL010t	Polyclonal Ab	*Basal cell carcinoma (Phase II)*				3
DISCOVERY PROGRAMS						
Combined	Imaging and Therapeutic					2
GENERAL COSTS						
18 Months x Ongoing Burn Rate						5
IPO preparation and fundraising costs						2
Balance Sheet Cash @ IPO (coverage 18 months forward burn rate)						5
					TOTAL	£25M

Source: Biosceptre International Limited.

Intellectual Property

From the outset, Biosceptre has been rigorous in the patent process. Its earliest patent covers the target itself, nfP2X$_7$, and expires in 2022. Since that patent was granted, the Company has continued to apply for, and has been granted, over 100 patents, including 13 U.S. patent series, and holds a global portfolio with protection out through 2032. Figure 4 (continued on page 9) summarizes the Company's current IP position.

With the full portfolio, the Company believes it controls freedom to operate over the nfP2X$_7$ target itself to 2033. Some of the areas that are covered include diagnostics, antibodies distinguishing P2X$_7$ and nfP2X$_7$ sequence, use of receptor as vaccine, animal antibodies, antibodies in topicals, specific monoclonals, epitopes for antibodies, epitope peptides, production of mAbs, and high-affinity dAbs. This protection is also applicable to cell therapies (CAR-T, NK cell, etc.).

Figure 4

INTELLECTUAL PROPERTY SNAPSHOT

Issued U.S. Patents (Patent Families)			
#	Patent Number	Title	Issue Date
1	9,328,155	Peptides for inducing antibodies to a non-functional P2X.sub.7 receptor	May 3, 2016
2	9,181,320	Peptides for generating an antibody selectively binding to a non-ATP-binding P2X7 receptor but not to an ATP-binding P2X7 receptor	November 10, 2015
3	9,127,059	Anti P2X7 receptor antibodies and fragments thereof	September 8, 2015
4	8,835,609	Antigen binding sites to non-functional oligomeric P2X7 receptors and methods of use thereof	September 16, 2014
5	8,709,425	Antibodies to non-functional P2X.sub.7 receptor	April 29, 2014
6	8,658,385	Purinergic (P2X) receptors in extra-cellular body fluid	February 25, 2014
7	8,597,643	Antibodies for binding to non-functional P2X.sub.7 receptors in trimeric form	December 3, 2013
8	8,440,186	P2X7 epitopes	May 14, 2013
9	8,399,617	Non-functional P2X.sub.7 receptor	March 19, 2013
10	8,293,491	Purinergic (P2X) receptors in extra-cellular body fluid	October 23, 2012
11	8,080,635	Non-functional P2X.sub.7 receptor	December 20, 2011
12	8,067,550	Hybridomas producing antibodies against non functional P2X7 receptor	November 29, 2011
13	7,183,064	Method for identifying pre-neoplastic and/or neoplastic states in mammals	February 27, 2007

Source: the U.S. Patent and Trademark Office (USPTO).

Figure 4 (cont.)

INTELLECTUAL PROPERTY SNAPSHOT

Published U.S. Patent Applications			
#	App. Number	Title	Publication Date
1	20160130342	Novel P2X7 Epitopes	May 12, 2016
2	20150274839	Antibodies to Non-Functional P2X7 Receptor	October 1, 2015
3	20150266969	Anti P2X7 Receptor Antibodies and Fragments Thereof	September 24, 2015
4	20150218283	Antibodies to Non-Functional Oligomeric P2X7 Receptors	August 6, 2015
5	20150004179	Combination Therapy	January 1, 2015
6	20140323693	Antibodies to Non-Functional P2X7 Receptor	October 30, 2014
7	20140135475	Antibodies for Binding to Non-Functional P2X7 Receptors in Trimeric Form	May 15, 2014
8	20130266592	Companion Animal Treatments	October 10, 2013
9	20130245226	Antibodies to Non-Functional P2X7 Receptor	September 19, 2013
10	20130171666	Purinergic (P2X) Receptors in Extra-Cellular Body Fluid	July 4, 2013
11	20120329076	Antibodies to Non-Functional Oligomeric P2X7 Receptors	December 27, 2012
12	20120282278	Anti P2X7 Receptor Antibodies and Fragments Thereof	November 8, 2012
13	20120059151	Non-Functional P2X7 Receptor	March 8, 2012
14	20110177080	Novel P2X7 Epitopes	July 21, 2011
15	20110111431	Method for Identifying Pre-Neoplastic and/or Neoplastic States in Mammals	May 12, 2011
16	20100248266	Purinergic (P2X) Receptors in Extra-Cellular Body Fluid	September 30, 2010
17	20080227122	P2Y Purinergic Receptor Expression for Identifying Preneoplastic and Neoplastic States	September 18, 2008

Source: the U.S. Patent and Trademark Office (USPTO).

Milestones

Figures 5, 6, 7, and 8 (continued on page 11) provide summaries of key corporate milestones achieved as well as those forecast by the Company for each of its product candidates, with each milestone representing a potentially significant value inflexion point for the Company's business strategy.

Figure 5
POTENTIAL MILESTONES

FINANCIAL	
2H 2016	Private Round Fundraising (£25m)
CLINICAL	
2H 2016	Phase I Systemic Clinical Trials (antibody)
1H 2017	Phase I Systemic Clinical Trials (vaccine)
1H 2017	Start of 1 X Phase II Topical Clinical Trial
1H 2017	Initial Data from Clinical Trials
COMMERCIAL	
2H 2016	2 Material Transfer Agreements (MTA) with Pharma
2H 2016	1 Due Diligence
2016	3 Ongoing Pharma Discussions
2H 2016, 1H 2017	Potential for Multiple Licensing Events

Source: Biosceptre International Limited.

Key Data Milestones for BIL03s (Lead Systemic Antibody)

Biosceptre is seeking Australia's **Therapeutic Goods Administration (TGA)** approval and expects to begin a Phase I trial in 2016 for BIL03s. With regard to technology transfer, the company manufacturing BIL03s is Pacific GMP in San Diego, California. Roughly three weeks after Biosceptre had signed a contract and proceeded with its transfer to Pacific GMP, Pacific GMP announced that it had been acquired by a larger biotech company, Abzena plc, from Cambridge, UK.

Figure 6
MILESTONES: BIL03s (SYSTEMIC)

Systemic BIL03s	2H 2016	1H 2017	2H 2017
Obtain TGA Approval	✓		
Start Phase I Trial	✓		
Initial data (recruitment, tolerability, QOL)		✓	
Complete Phase I		✓	
Final Data		✓	
Phase II Trial Start			✓

Source: Biosceptre International Limited.

Key Data Milestones for BIL06v (Vaccine)

Biosceptre is seeking TGA approval for BIL06v and a Phase I trial is due to start in 2017. With no production issues, the process of producing BIL06v is expected to be straightforward and follow the anticipated timeline shown in Figure 7.

Figure 7
MILESTONES: BIL06v (VACCINE)

Vaccine BIL06v	1H 2017	2H 2017	1H 2018
Obtain TGA Approval	✓		
Start Phase I Trial	✓		
Initial data (recruitment, tolerability, QOL)	✓		
Complete Phase I	✓		
Final Data		✓	
Phase II Trial Start			✓

Source: Biosceptre International Limited.

Key Data Milestones for BIL010t (Topical)

Biosceptre has stated an interest in licensing its topical BIL010t product, unlike its other two products, which the Company seeks to move into Phase II trials. Licensing discussions are ongoing with interested parties. Figure 8 outlines the expected milestones for this product candidate.

Figure 8
MILESTONES: BIL010t (TOPICAL)

Topical BIL010t	1H 2017	2H 2017	1H 2018
Obtain TGA Approval	✓		
Start Phase I Trial	✓		
Initial data (recruitment, tolerability, QOL)	✓		
Complete Phase I		✓	
Final Data		✓	
Phase II Trial Start			✓

Source: Biosceptre International Limited.

Leadership

Executive Management and Key Individuals

The accompanying section provides brief biographies for each of the Company's executive management and key leadership figures.

Gavin Currie, Chief Executive Officer (CEO)

Mr. Currie was appointed CEO of Biosceptre in October 2012, having been a Board member since 2009. Before taking the role as CEO at Biosceptre, he was General Manager of Creata Ventures, a family-held investment fund with a strong focus in biotech. Biosceptre was a key investment within that fund. Mr. Currie previously founded a boutique transaction services company and has significant experience in mergers and acquisitions (M&A), particularly integrating businesses post transaction. He has developed a reputation for delivering value by commercializing previously unseen opportunities and has been employed internationally in Australia, New Zealand, England, the U.S., and Hong Kong, with experience in cross-border transactions and investments.

Dr. Shaun McNulty, Ph.D., Chief Scientific Officer

Dr. McNulty joined Biosceptre in January 2014 with over two decades of experience working in the pharmaceutical and biotech sectors across a range of functions—from target identification, drug discovery, and portfolio management to product and commercial development. Dr. McNulty is experienced in strategic planning, drug discovery, and product development, bringing broad industry understanding to the scientific and commercial sides of the business. Having obtained a doctorate from the University of York, Dr. McNulty undertook five years of post-doctoral study at the University of Cambridge. He then held positions at GlaxoSmithKline, Pfizer, and Syntaxin, managing a number of scientific teams, international drug discovery projects, and drug development portfolios. Dr. McNulty joined ImmBio in 2008, establishing scientific links and the commercial strategy that led to the company obtaining multiple grants to develop its vaccine products. Currently, he directs Biosceptre's portfolio of drugs through research and into clinical development stages.

Daniel Barton, LL.B, B.Sc. (Mol. Biochem.), Director, Investor Relations

Mr. Barton is a seasoned commercial executive with an academic background in the life sciences and intellectual property who has worked across strategy and delivery in technology and marketing businesses, with broad professional skills across legal, administration, product development, and marketing. He has founded, run, and sold start-ups, held P&L and board reporting roles in listed companies, and led account service teams, managed creative departments, collaborated with research groups, and commissioned external and internal product development and production teams.

Brad Miller, MBL, Senior Manager, Legal and Compliance

Mr. Miller joined Biosceptre as senior manager, legal and compliance in May 2013 after five years with a private international investment fund. With practical knowledge in both financial management and legal documentation, he gained first-hand experience across a broad range of cross-border transactions, including M&A, debt financing, and equity investments (primarily in the life sciences sector). Mr. Miller holds a Master's of Business Law from the University of Sydney and a Bachelor's in business administration from Macquarie University.

Science Operations

Dr. Julian Barden, Ph.D., Director of Research

Dr. Barden is a protein structure specialist with over 30 years of experience working on protein structure analyses, molecular modeling, protein function studies, and antibody design in several areas, including the molecular mechanism of muscle contraction, actin structure and function, calcium regulating hormones, purinergic receptor structure, and function and the development of cancer diagnostics and lead cancer immunotherapeutic molecules. Dr. Barden has authored 150 papers, 16 patent families, and has presented at over 200 national and international scientific meetings.

Dr. Angus Gidely-Baird, Ph.D., Scientific Director

Dr. Gidely-Baird is responsible for Biosceptre's commercial and scientific strategy, directing the Company's research and development program. He has substantial senior-level experience in research and commercialization of research results. Dr. Gidely-Baird was a research director and director of three public biomedical companies. As well, he is an author/co-author of 39 publications in scientific journals and is an inventor/co-inventor of seven patent families.

Dr. David Chin, Ph.D., Director of Bioproduction and Research Collaboration

Dr. Chin has worked in biopharmaceuticals for nearly two decades, with significant experience in recombinant protein expression in both microbial and mammalian cell systems, and mAb discovery and engineering. Upon completion of a Ph.D. at the University of New South Wales, Australia, he was awarded a research fellowship by the Australian Research Council (ARC), through which he researched various biopharmaceuticals in the fields of oncology and inflammation. With further training in business administration, Dr. Chin has been appointed to several senior and managing positions. Prior to joining Biosceptre, Dr. Chin was operations manager at National Biologics Facility (NBF) at the Australian Institute for Bioengineering and Nanotechnology, University of Queensland, in the area of recombinant protein production, cell line generation, and protein characterization. In this post, he managed over 20 scientific staff controlling a budget of over AUS$30 million, established over 30 collaborations between the biotech industry and academia, and accomplished over 300 commercial and research projects at Australian Institute of Bioengineering (AIBN). Dr. Chin was also appointed as chief operating officer at Stem Cell Limited, a spin-off from University of Queensland and Monash University.

Board of Directors

Peter Newton, Non-Executive Chairman

Mr. Newton has an extensive financial background, having spent 26 years as a stockbroker. He is a former CEO of County Natwest, is currently the chairman of Metals X Ltd., and is a director of two other Australia-based companies. Mr. Newton has enjoyed success in guiding investment and growth, and has substantial experience in corporate governance issues.

Gavin Currie, Chief Executive Officer

Biography on page 12.

Dr. Sir Gregory Winter, CBE, FRS, FMedSci, HonFRCP

Dr. Sir Gregory Winter is a member of the Medical Research Council's Laboratory of Molecular Biology (LMB) in Cambridge, and a Fellow of Trinity College Cambridge. He has served LMB as a head of division, deputy director and acting director. His scientific career has almost entirely been based in Cambridge, where his work included protein sequencing (aminoacyl tRNA synthetases) and nucleic acid sequencing (influenza virus). He later developed technologies for making humanized antibodies by grafting hypervariable regions from rodent antibodies to human antibodies and for making human antibodies in bacteria by use of antibody repertories and phage display technologies. Most of the therapeutic antibodies on the market were developed using methods devised by him. He was a founder and director of Cambridge Antibody Technology (acquired by AstraZeneca), a founder and director of Domantis (acquired by GlaxoSmithKline), and more recently a founder and director of Bicycle Therapeutics. Sir Gregory has received numerous international prizes and awards, and in 2004, was knighted for services to molecular biology.

Michael Lovett, Non-Executive Director

Mr. Lovett is chairman of MobiLife Pty Ltd, a drug compounding company; owner of Bioption Investments (HK) Ltd, a private investment fund; owner of Ambrosia Trading (Shanghai) Ltd, a manufacturing business; non-executive director of KaosKey Pty Ltd, a medical device company; and a non-executive director of Dr's Beck & Stone, a China-based veterinary hospital group. He is a qualified psychologist, founded and was the CEO of one of the UK's largest social care businesses, which, after growing organically and through acquisitions, he sold to private equity. After moving to Hong Kong, Mr. Lovett expanded his entrepreneurial interests by setting up a private investment vehicle through which he invests predominantly in the medical sciences and medical device sector. He is a Fellow of the Royal Society of Arts and of the Institute of Directors.

Dr. Ron Watts, Ph.D., Non-Executive Director

Dr. Watts has worked at senior levels in government and at the CEO and Board level across a range of technology-based enterprises. His management experience covers software and telecommunications industries, and as a consultant, he has worked with companies on strategy and fundraising in biotech, utilities, food processing, and energy. He co-founded Australia's largest energy market intermediary, Energy Action, and served as its chairman. Dr. Watts has served on a number of government and industry oversight bodies, and as Adjunct Research Fellow at UniSA. He has a B.S. (Honors) from the University of New South Wales and a Ph.D. from Cambridge University.

Andrew Walton-Green, Non-Executive Director

Mr. Walton-Green joined Biosceptre in December 2014. He is a Chartered Accountant and a member of the Chartered Institute of Taxation. Most recently, Mr. Walton-Green was a founder and CEO of the Car Finance Company, one of the fastest growing companies in Europe over the past four years. He is also a part owner of a renewable energy business in the UK, a technology distribution company, and a fast-growing wholesale pharmaceutical business. Before this, he was the CEO of Gresham Computing plc for 10 years, gaining significant exposure to the banking and financial services sector at a senior level. He spent the first 13 years of his career in practice predominately with Ernst & Young, followed by Deloitte.

Jon Collins, Non-Executive Director

Mr. Collins joined the board of Biosceptre in December 2014. He is the owner and chairman of the Coco Group, an investment and business expansion consultancy based in Australia, with global connections. Mr. Collins moved to Australia in 1987 to rebuild an existing group of businesses for which he led a successful management buy-out from the UK owners in 1993, and became the sole owner in 1997. This business developed into a leading manufacturer of specialized pumping equipment with offices in the U.S., Indonesia, UK, Middle East, and South Africa. The company was sold to an ASX-listed company in November 2010. Mr. Collins started his industrials career in 1967, in capital equipment sales and equipment rental, taking posts in the U.S. and Ireland, and rose through the ranks from junior management to a directorship. With a keen interest in rugby, he has also served as a director of the New South Wales Waratahs (Super 15) and the Australian Rugby Union.

Paul Axon, Non-Executive Director (Alternate to Jon Collins)

Mr. Axon is a qualified pharmacist and a Chartered Accountant in the UK and Australia, having vast experience in M&A, corporate finance, and general management. Previously, he was a partner in corporate finance at BDO in the UK and had owned his own M&A practice. More recently, Mr. Axon was the CEO of Sykes Pumps, until the sale of the business to National Hire in 2010. Currently, he is the CEO and equity holder of the Coco Group, which invests in and manages a vast array of businesses in Australia and the Middle East, including interests in equipment rental, mining services, retail, biotech, and resources.

Science Advisory Board

Dr. Sir Gregory Winter, CBE, FRS, FMedSci, HonFRCP

Biography on page 14.

Professor Terence Rabbitts, FRS, FMedSci

Professor Rabbitts worked in Cambridge from 1973 to 2006 in the MRC Laboratory of Molecular Biology, where he was head of the Division of Protein & Nucleic Acid Chemistry until 2002. He moved to become director of the Leeds Institute of Molecular Medicine (from 2006 to 2010). Professor Rabbitts is a Member of the European Molecular Biology Organization (EMBO), a Fellow of the Royal Society (FRS), and a Founder Fellow of the Academy of Medical Sciences (FMedSci). His scientific work includes pioneering the method of cDNA cloning, mapping human antibody genes, methods for chimeric antibody production, and single domains for blocking protein interactions inside cells. Professor Rabbitts defined the linkage of antibody and T cell receptor genes with cancer-specific chromosomal translocations, identified new families of oncogenes (such as the LMO2 and HOX11 families), and identified a first gene fusion in a solid tumor (FUS-CHOP). He developed the first gene fusion knock-in as well as methods for creating chromosomal translocations de novo. Professor Rabbitts has corporate biotech experience as chairman of the Scientific Advisory Board (SAB) of Cambridge Antibody Technology and Quadrant Healthcare until their respective IPOs, and as a member of the Domantis SAB until the company's acquisition by GlaxoSmithKline. He is currently chairman of the SAB of Kymab and is a member of the SAB of Oryzon Genomics and of DiThera.

Clinical Advocates

Dr. Bob Li, MBBS, B.Sc. (Med.), MPH, Ph.D., FRACP

Dr. Li is medical oncology Fellow and clinical investigator at Memorial Sloan Kettering Cancer Center. He has received the ASCO Young Investigator Award, American Society of Clinical Oncology and Conquer Cancer Foundation; ASCO Merit Award, American Society of Clinical Oncology and Conquer Cancer Foundation; and AACR Young Investigator Translational Cancer Research Award, American Association for Cancer Research and Conquer Cancer Foundation.

Prof. Gavin Marx, B.Sc. (Med.), MBBS (Hons.), FRACP

Professor Marx is chair of the Section of Oncology at the SAN, director of the SAN Clinical Trials Unit, clinical director of the SAN Integrated Cancer Centre, and associate professor at the University of Sydney.

Asst. Prof. Nick Pavlakis, B.Sc., MBBS, MMed (Clin. Epi.), Ph.D., FRACP

Assistant Professor Pavlakis is head of the Department of Medical Oncology, Royal North Shore Hospital, Sydney; chair of the Scientific Advisory Committee of the Australasian Lung Cancer Trials Group; and director of the Northern Sydney Cancer Trials Network.

Dr. Tom Borody, B.Sc. (Med.) (Hons.), MBBS (Hons.), M.D., Ph.D., FRACP, FACG, FACP, AGAF

Dr. Borody is founder and medical director of the Center for Digestive Disease and a reviewer for medical journals, including the *American Journal of Gastroenterology*, *Digestive Diseases & Sciences,* the *Journal for Gastroenterology and Hepatology,* and *Digestive and Liver Diseases*.

Core Story

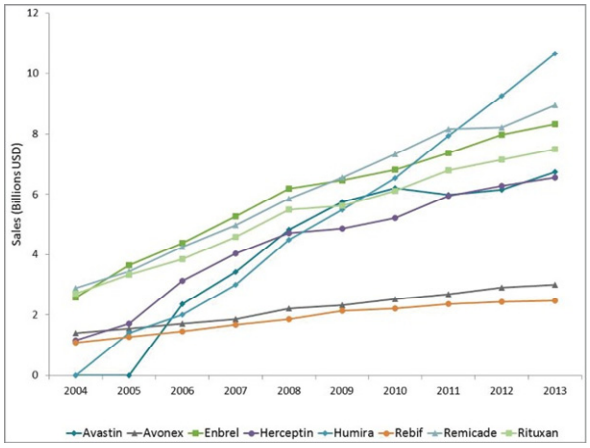
MARKET OPPORTUNITIES

Cancer is among the leading causes of morbidity and mortality worldwide, with approximately 14.1 million new cases globally and 8.2 million cancer-related deaths occurring each year as of 2012 (Source: World Health Organization [WHO]). Most importantly, the number of new cases is expected to rise by roughly 70% over the next two decades, which does not include the more than 32 million people currently fighting the disease (i.e., within five years of diagnosis). In the U.S., there will be an estimated 1.7 million new cancer cases diagnosed and 596,000 deaths in 2016, as shown in Figure 10 (page 17). Among men, the five most common cancers are lung, prostate, colon/rectum, stomach, and liver; among women, the five most common cancers are breast, colon/rectum, lung, cervix, and stomach.

To treat the growing number of cancer patients, the market for therapeutics continues to embrace new developments and commercialization efforts. The pipeline of oncology drugs in clinical development during the past decade has expanded by more than 60%, with now almost 90% of the focus on targeted agents—cancer medications that are directed specifically at a certain component in the body versus systemic (whole body) treatments. The issue with non-targeted therapies, such as chemotherapy options, is that they indiscriminately attack healthy cells in an effort to destroy tumor cells. With the potential to achieve greater efficacy with fewer adverse effects, targeted therapeutics are a highly desirable quality in cancer care. Since peaking in the 1990s, cancer death rates have declined 23%, and roughly 83% of survival gains have been linked to new treatments. Today, two out of three people diagnosed with cancer survive at least five years.

The global oncology market was valued at $107 billion in 2015 (Source: IMS Health), and by 2020, it may account for $153 billion in revenue, as forecast by Statista (a statistical research portal). Targeted therapies encompass the biggest selling class of cancer therapeutics, and sales of targeted monoclonal antibodies (mAbs) specifically have been consistently growing for the past decade (as shown in Figure 9). At these growth rates, sales of currently approved mAbs plus revenue from new products approved in the coming years may drive worldwide mAb sales to approximately $94 billion by 2017 and nearly $125 billion by 2020 (Source: the National Institutes of Health, U.S. Library of Medicine).

Figure 9
ANNUAL SALES OF LEADING MONOCLONAL ANTIBODY PRODUCTS (2004-2013)



Source: BioProcess Technology Consultants, Inc.

Figure 10

ESTIMATED NUMBER OF NEW CANCER CASES AND DEATHS BY SEX, U.S., 2016

	Estimated New Cases			Estimated Deaths		
	Both sexes	Male	Female	Both sexes	Male	Female
All Sites	1,685,210	841,390	843,820	595,690	314,290	281,400
Oral cavity & pharynx	48,330	34,780	13,550	9,570	6,910	2,660
Tongue	16,100	11,700	4,400	2,290	1,570	720
Mouth	12,910	7,600	5,310	2,520	1,630	890
Pharynx	16,420	13,350	3,070	3,080	2,400	680
Other oral cavity	2,900	2,130	770	1,680	1,310	370
Digestive system	304,930	172,530	132,400	153,030	88,700	64,330
Esophagus	16,910	13,460	3,450	15,690	12,720	2,970
Stomach	26,370	16,480	9,890	10,730	6,540	4,190
Small intestine	10,090	5,390	4,700	1,330	710	620
Colon†	95,270	47,710	47,560	49,190	26,020	23,170
Rectum	39,220	23,110	16,110			
Anus, anal canal, & anorectum	8,080	2,920	5,160	1,080	440	640
Liver & intrahepatic bile duct	39,230	28,410	10,820	27,170	18,280	8,890
Gallbladder & other biliary	11,420	5,270	6,150	3,710	1,630	2,080
Pancreas	53,070	27,670	25,400	41,780	21,450	20,330
Other digestive organs	5,270	2,110	3,160	2,350	910	1,440
Respiratory system	243,820	132,620	111,200	162,510	89,320	73,190
Larynx	13,430	10,550	2,880	3,620	2,890	730
Lung & bronchus	224,390	117,920	106,470	158,080	85,920	72,160
Other respiratory organs	6,000	4,150	1,850	810	510	300
Bones & joints	3,300	1,850	1,450	1,490	860	630
Soft tissue (including heart)	12,310	6,980	5,330	4,990	2,680	2,310
Skin (excluding basal & squamous)	83,510	51,650	31,860	13,650	9,330	4,320
Melanoma of the skin	76,380	46,870	29,510	10,130	6,750	3,380
Other nonepithelial skin	7,130	4,780	2,350	3,520	2,580	940
Breast	249,260	2,600	246,660	40,890	440	40,450
Genital system	297,530	191,640	105,890	57,730	26,840	30,890
Uterine cervix	12,990		12,990	4,120		4,120
Uterine corpus	60,050		60,050	10,470		10,470
Ovary	22,280		22,280	14,240		14,240
Vulva	5,950		5,950	1,110		1,110
Vagina & other genital, female	4,620		4,620	950		950
Prostate	180,890	180,890		26,120	26,120	
Testis	8,720	8,720		380	380	
Penis & other genital, male	2,030	2,030		340	340	
Urinary system	143,190	100,920	42,270	31,540	21,600	9,940
Urinary bladder	76,960	58,950	18,010	16,390	11,820	4,570
Kidney & renal pelvis	62,700	39,650	23,050	14,240	9,240	5,000
Ureter & other urinary organs	3,530	2,320	1,210	910	540	370
Eye & orbit	2,810	1,510	1,300	280	150	130
Brain & other nervous system	23,770	13,350	10,420	16,050	9,440	6,610
Endocrine system	66,730	16,200	50,530	2,940	1,400	1,540
Thyroid	64,300	14,950	49,350	1,980	910	1,070
Other endocrine	2,430	1,250	1,180	960	490	470
Lymphoma	81,080	44,960	36,120	21,270	12,160	9,110
Hodgkin lymphoma	8,500	4,790	3,710	1,120	640	480
Non-Hodgkin lymphoma	72,580	40,170	32,410	20,150	11,520	8,630
Myeloma	30,330	17,900	12,430	12,650	6,430	6,220
Leukemia	60,140	34,090	26,050	24,400	14,130	10,270
Acute lymphocytic leukemia	6,590	3,590	3,000	1,430	800	630
Chronic lymphocytic leukemia	18,960	10,830	8,130	4,660	2,880	1,780
Acute myeloid leukemia	19,950	11,130	8,820	10,430	5,950	4,480
Chronic myeloid leukemia	8,220	4,610	3,610	1,070	570	500
Other leukemia‡	6,420	3,930	2,490	6,810	3,930	2,880
Other & unspecified primary sites‡	34,170	17,810	16,360	42,700	23,900	18,800

*Rounded to the nearest 10; cases exclude basal cell and squamous cell skin cancer and in situ carcinoma except urinary bladder. About 61,000 cases of carcinoma in situ of the female breast and 68,480 cases of melanoma in situ will be diagnosed in 2016. †Deaths for colon and rectal cancers are combined because a large number of deaths from rectal cancer are misclassified as colon. ‡More deaths than cases may reflect lack of specificity in recording underlying cause of death on death certificates and/or an undercount in the case estimate.

Source: Estimated new cases are based on 1998-2012 incidence data reported by the North American Association of Central Cancer Registries (NAACCR). Estimated deaths are based on 1998-2012 US mortality data, National Center for Health Statistics, Centers for Disease Control and Prevention.

Source: American Cancer Society, Inc.

The American Society of Clinical Oncology ([ASCO] the world's leading organization for physicians and oncology professionals caring for people with cancer) marked the organization's 50th anniversary by calling on the cancer community to help select the five most pivotal clinical cancer research advances since the organization's founding. The ballot consisted of 32 advances drawn from Cancer Progress's Major Milestones timeline, with over 2,000 votes cast to determine the "Top Five Advances" in the field. Figure 11 summarizes these advances, highlighting targeted therapies in transforming the treatment of a rare leukemia in 2001.

Figure 11
TOP 5 ADVANCES IN MODERN ONCOLOGY

Chemotherapy Cures Hodgkin Lymphoma, 1965
Vaccine Approved To Prevent Cervical Cancer, 2006
Targeted Drug Transforms Treatment For Rare Leukemia, 2001
New Treatment Cures Men With Testicular Cancer, 1977
Powerful Anti-Nausea Drugs Alleviate Major Side Effect of Cancer Treatment, 1991

Source: American Society of Clinical Oncology.

Figure 12
FORECAST OF TOP 20 CANCER DRUGS WORLDWIDE BY REVENUE IN 2020 (MM U.S. DOLLARS)

Revlimid (Celgene)	$ 10,110
Imbruvica (AbbVie/J&J)	8,213
Avastin (Roche)	6,733
Opdivo (BMS)	6,201
Xtandi (Medivation)	5,700
Rituxan (Roche)	5,407
Ibrance (Pfizer)	4,722
Perjeta (Roche)	4,669
Herceptin (Roche)	4,573
Keytruda (Merck & Co.)	3,560
Pomalyst (Merck & Co.)	2,358
Alimta (Eli Lily)	2,335
Tasigna (Novartis)	2,305
Yervoy (BMS)	2,280
Abraxane (Celgene)	2,184
Xgeva (Amgen)	2,183
Cazyva (Roche)	2,138
MPDL3280A (Roche)	2,029
Zytiga (J&J)	1,895
Kadycla (Roche)	1,722

Source: Statista.

Figure 12 highlights what Statista predicts will become the top 10 oncology products worldwide by 2020, ranked according to revenue forecast. Based on this analysis, the leading drug over the next four years could be Revlimid, a chemotherapy-like drug for multiple myeloma, mantle cell lymphoma, and myelodysplastic syndrome (MDS) manufactured by U.S.-based company Celgene.

Approved Targeted Cancer Therapies

As discussed, targeted cancer therapies are drugs or other substances that block the growth and spread of cancer by interfering with specific molecules (molecular targets) that are involved in cancer's growth, progression, and spread. Sometimes called molecularly targeted drugs, molecularly targeted therapies, precision medicines, or similar names, targeted cancer therapies differ from standard chemotherapeutics in the following ways:

- they act on specific molecular targets that are associated with cancer, where most standard chemotherapies act on all rapidly dividing normal and cancerous cells;
- they are deliberately chosen or designed to interact with their target, where many standard chemotherapies were identified due to the fact that they kill cells; and
- they are often **cytostatic** (block tumor cell proliferation), where standard chemotherapy agents are **cytotoxic** (they kill tumor cells).

A great deal of research and development (R&D) is taking place within the area of targeted therapies for anticancer drug development, as they are a cornerstone of precision medicine—an approach that uses information about a person's genes and proteins to prevent, diagnose, and treat disease. Numerous targeted cancer therapies have been approved by the U.S. Food and Drug Administration (FDA) to treat specific types of cancer (as shown in Figure 13 [page 19]), with thousands of others being studied in clinical trials (in people) and many more are in preclinical testing.

Figure 13
APPROVED TARGETED THERAPIES FOR SPECIFIC TYPES OF CANCER

Adenocarcinoma of the stomach or gastroesophageal junction: Trastuzumab (Herceptin®), ramucirumab (Cyramza®)

Basal cell carcinoma: Vismodegib (Erivedge®), sonidegib (Odomzo®)

Brain cancer: Bevacizumab (Avastin®), everolimus (Afinitor®)

Breast cancer: Everolimus (Afinitor®), tamoxifen (Nolvadex), toremifene (Fareston®), Trastuzumab (Herceptin®), fulvestrant (Faslodex®), anastrozole (Arimidex®), exemestane (Aromasin®), lapatinib (Tykerb®),letrozole (Femara®), pertuzumab (Perjeta®), ado-trastuzumab emtansine (Kadcyla®), palbociclib (Ibrance®)

Cervical cancer: Bevacizumab (Avastin®)

Colorectal cancer: Cetuximab (Erbitux®), panitumumab (Vectibix®), bevacizumab (Avastin®), ziv-aflibercept (Zaltrap®), regorafenib (Stivarga®), ramucirumab (Cyramza®)

Dermatofibrosarcoma protuberans: Imatinib mesylate (Gleevec®)

Endocrine/neuroendocrine tumors: Lanreotide acetate (Somatuline® Depot)

Head and neck cancer: Cetuximab (Erbitux®)

Gastrointestinal stromal tumor: Imatinib mesylate (Gleevec®), sunitinib (Sutent®), regorafenib (Stivarga®)

Giant cell tumor of the bone: Denosumab (Xgeva®)

Kaposi sarcoma: Alitretinoin (Panretin®)

Kidney cancer: Bevacizumab (Avastin®), sorafenib (Nexavar®), sunitinib (Sutent®), pazopanib (Votrient®),temsirolimus (Torisel®), everolimus (Afinitor®), axitinib (Inlyta®), nivolumab (Opdivo®), cabozantinib (Cabometyx™), lenvatinib mesylate (Lenvima®)

Leukemia: Tretinoin (Vesanoid®), imatinib mesylate (Gleevec®), dasatinib (Sprycel®), nilotinib (Tasigna®),bosutinib (Bosulif®), rituximab (Rituxan®), alemtuzumab (Campath®), ofatumumab (Arzerra®),obinutuzumab (Gazyva®), ibrutinib (Imbruvica®), idelalisib (Zydelig®), blinatumomab (Blincyto®), venetoclax (Venclexta™)

Liver cancer: Sorafenib (Nexavar®)

Lung cancer: Bevacizumab (Avastin®), crizotinib (Xalkori®), erlotinib (Tarceva®), gefitinib (Iressa®), afatinib dimaleate (Gilotrif®), ceritinib (LDK378/Zykadia™), ramucirumab (Cyramza®), nivolumab (Opdivo®),pembrolizumab (Keytruda®), osimertinib (Tagrisso™), necitumumab (Portrazza™), alectinib (Alecensa®)

Lymphoma: Ibritumomab tiuxetan (Zevalin®), denileukin diftitox (Ontak®), brentuximab vedotin (Adcetris®),rituximab (Rituxan®), vorinostat (Zolinza®), romidepsin (Istodax®), bexarotene (Targretin®), bortezomib (Velcade®), pralatrexate (Folotyn®), ibrutinib (Imbruvica®), siltuximab (Sylvant®), idelalisib (Zydelig®),belinostat (Beleodaq®), obinutuzumab (Gazyva®)

Melanoma: Ipilimumab (Yervoy®), vemurafenib (Zelboraf®), trametinib (Mekinist®), dabrafenib (Tafinlar®),pembrolizumab (Keytruda®), nivolumab (Opdivo®), cobimetinib (Cotellic™)

Multiple myeloma: Bortezomib (Velcade®), carfilzomib (Kyprolis®), panobinostat (Farydak®), daratumumab (Darzalex™), ixazomib citrate (Ninlaro®), elotuzumab (Empliciti™)

Myelodysplastic/myeloproliferative disorders: Imatinib mesylate (Gleevec®), ruxolitinib phosphate (Jakafi®)

Neuroblastoma: Dinutuximab (Unituxin™)

Ovarian epithelial/fallopian tube/primary peritoneal cancers: Bevacizumab (Avastin®), olaparib (Lynparza™)

Pancreatic cancer: Erlotinib (Tarceva®), everolimus (Afinitor®), sunitinib (Sutent®)

Prostate cancer: Cabazitaxel (Jevtana®), enzalutamide (Xtandi®), abiraterone acetate (Zytiga®), radium 223 dichloride (Xofigo®)

Soft tissue sarcoma: Pazopanib (Votrient®)

Systemic mastocytosis: Imatinib mesylate (Gleevec®)

Thyroid cancer: Cabozantinib (Cometriq®), vandetanib (Caprelsa®), sorafenib (Nexavar®), lenvatinib mesylate (Lenvima®)

Source: National Cancer Institute.

Biosceptre has identified a novel receptor and oncology target, nfP2X$_7$, and is developing a product pipeline directed at this receptor to treat a range of cancers. nfP2X$_7$ has shown to be highly specific to cancer cells, with the Company having demonstrated low cross-reactivity in humans—a feature that could prove disruptive within the field of immunotherapy oncology. Further, nfP2X$_7$ occurs across a broad range of cancers, including lung, breast, colorectal, and prostate tumors but is not found on healthy tissue. Pages 23-35 details Biosceptre's development efforts, followed by descriptions of currently marketed products that may be considered competitive to Biosceptre (Competition [pages 36-40]).

Ways in Which Targets for Targeted Cancer Therapies Are Identified

Targeted therapeutic development requires the identification of good targets—those that play a vital role in cancer cell growth and survival. Accordingly, targeted therapies are at times referred to as the product of rational drug design. One method of identifying potential targets is to compare the amounts of individual proteins in cancer cells with those in normal cells. Proteins that exist in cancer cells but not normal cells (such as is the case for Biosceptre's development candidates) or that are more plentiful in cancer cells are possible targets, particularly if they are recognized as being involved with cell growth or survival. One such example of a differentially expressed target is human epidermal growth factor receptor 2 protein (HER-2), which is expressed at high levels on the surface of some cancer cells. Several targeted therapies are directed against HER-2, including trastuzumab (Herceptin®), which is approved to treat certain breast and stomach cancers that overexpress HER-2 (described under Competition [page 38]).

An alternative way to recognize potential targets is to assess whether cancer cells produce mutant (altered) proteins that drive the progression of cancer. For instance, the cell growth signaling protein BRAF is present in an altered form (known as BRAF V600E) in many melanomas. Vemurafenib (Zelboraf®) targets this mutant form of the BRAF protein and is approved to treat patients with inoperable or metastatic melanoma that contains this altered BRAF protein. Scientists further look for chromosomal abnormalities that manifest in cancer cells but not in normal cells. From time to time, these chromosomal abnormalities result in the creation of a fusion gene (a gene that incorporates parts of two different genes), which produces a fusion protein that may drive cancer development. Fusion proteins could become potential targets for targeted cancer therapies.

Development of Targeted Therapies

Upon identifying a target, the next step is to develop a therapy that affects the target in such a way as to inhibit its ability to promote cancer cell growth or survival. For example, a targeted therapy may reduce the activity of the target or prevent it from binding to a receptor that it normally activates, among other possible mechanisms. The majority of targeted therapies are either small molecules or mAbs. Small-molecule compounds are typically used for targets located inside the cell since these compounds are able to enter cells relatively easily. The mAbs are comparatively large and usually cannot enter cells, so they are used against targets outside cells or on the cell surface.

Small-molecule candidates can be identified via high-throughput screening (HTS), a process by which the effects of thousands of test compounds on a specific target protein are observed. Compounds that affect the target (also called **lead compounds**) can be chemically modified to produce many closely related versions of the lead compound, where these related compounds are then tested to determine which are most effective and have the fewest effects on non-target molecules.

With advances in antibody engineering techniques, it is now possible to mimic the humoral immune system *in vitro* by the expression of antibody repertoires on the surface of bacteriophage. This antibody engineering technology is named "phage display" and was pioneered by Sir Gregory Winter (Biosceptre board member and head of the Company's Science Advisory Board) among others. The phage display methodology offers the opportunity to isolate high-affinity antibodies and bypass conventional hybridoma technology with its inherent cross species reactivity limitations.

When seeking novel antibodies by this method, naïve human lymphocyte repertoires can be panned to detect and isolate cell lines delivering fully human antibodies against specific antigens or targets. In circumstances where an appropriate antigen can be used to immunize human patients prior to collection of blood serum, it is possible to isolate lymphocytes producing antibodies against the desired target which have naturally undergone the immune systems' antibody optimization processes giving further advantages of higher specificity and affinity. This approach is available to Biosceptre through its compassionate access patients who are receiving the vaccine BIL06v, and thus producing an autologous antibody response against nfP2X$_7$, which can be panned for next-generation therapeutic candidates.

Types of Targeted Therapies

There have been a significant number of targeted therapies approved for use in cancer treatment, including hormone therapies, signal transduction inhibitors, gene expression modulators, apoptosis inducers, immunotherapies, mAbs that deliver toxic molecules, cancer vaccines, and gene therapy, as overviewed below.

- ***Hormone therapies***. These therapies slow or stop the growth of hormone-sensitive tumors, which require certain hormones to grow. They act by preventing the body from producing the hormones or by interfering with the action of the hormones and are approved for use in both breast cancer and prostate cancer.

- ***Signal transduction inhibitors***. These therapies block the activities of molecules that participate in signal transduction—the process in which a cell responds to signals from its environment. During this process, once a cell has received a specific signal, the signal is relayed within the cell through a series of biochemical reactions that eventually yield the appropriate response(s). In certain cancers, these malignant cells are stimulated to divide continuously without being prompted to do so by external growth factors.

- ***Gene expression modulators***. These therapies modify the function of proteins that play a role in controlling gene expression.

- ***Apoptosis inducers***. These therapies cause cancer cells to undergo controlled cell death via a process called apoptosis. While apoptosis is one of the methods the body uses to rid itself of unneeded or abnormal cells, cancer cells have ways of avoiding apoptosis. Apoptosis inducers have been developed to circumvent these strategies to cause the death of cancer cells.

- ***Angiogenesis inhibitors***. These therapies block the growth of new blood vessels to tumors (via tumor angiogenesis). Tumors need a blood supply to be able to grow beyond a certain size as blood provides the oxygen and nutrients that tumors need for continual growth. Treatments that impede angiogenesis may block tumor growth, with some targeted therapies that inhibit angiogenesis interfering with the action of **vascular endothelial growth factor (VEGF)**, a substance that stimulates new blood vessel formation.

- ***Immunotherapies***. These therapies trigger the immune system to destroy cancer cells. Some immunotherapies are mAbs, which distinguish certain molecules on the surface of cancer cells. Binding of the mAb to the target molecule results in the destruction or suppression of cells that express that target molecule—Biosceptre's BIL03s and BIL010t are therapies that fall into this category. Other mAbs bind to certain immune cells to assist these cells in killing cancer cells—these therapies are typically described as checkpoint inhibitors.

- ***Using mAbs to deliver toxic molecules***. These therapies can specifically cause the death of cancer cells and are also called Antibody Drug Conjugates (ADCs). Upon an antibody binding to its target cell, the toxic molecule that is linked to the antibody—such as a radioactive substance or a poisonous chemical—is taken up by the cell, which results in the killing of that cell, noting that the toxin does not affect cells that lack the target for the antibody (which is the majority of cells in the body).

- ***Cancer vaccines and gene therapy***. These can be considered targeted therapies since they impede the growth of specific cancer cells by eliciting a response from the patient's own immune system which acts against those cells. Biosceptre's BIL06v falls into this category.

Determining Whether a Patient is a Candidate for Targeted Therapy

For certain types of cancer, most patients who have that cancer will have the appropriate target for a particular targeted therapy, and thus, are determined to be candidates for treatment with that therapy. However, for other types of cancer, a patient's tumor tissue must be tested to determine whether an appropriate target is present. Use of a targeted therapy may be limited to patients whose tumor has a particular gene mutation that codes for the target. In contrast, patients who do not have the mutation would not be candidates since the therapy would have nothing to target. At times, a patient is a candidate for a targeted therapy only if he or she meets specific criteria (e.g., their cancer either did not respond to other therapies, has spread, or is inoperable).

Biosceptre's target nfP2X$_7$ is found on a large proportion of the most frequent cancers by diagnosis, and in large proportions of individual tumors within those cancer types. Bearing this in mind, while Biosceptre does have a diagnostic candidate in its pipeline, as well as a candidate that could be used for imaging of tumors, diagnostic screening of patients may not be necessary if the response rate is consistently high.

Limitations of Targeted Cancer Therapies

Targeted therapies have some limitations, including that cancer cells can become resistant to them. Such resistance occurs in two ways: the target itself changes via mutation such that the targeted therapy no longer interacts well with it or the tumor finds another pathway to grow independent of the target. Because of this, targeted therapies may work best in combination. With its favorable safety profile, Biosceptre's proprietary target, nfP2X$_7$, may make an excellent candidate as a target for use in combination with other established therapies.

A recent study found, for example, that using two therapies that target different parts of the cell signaling pathway that is altered in melanoma by the BRAF V600E mutation slowed the development of resistance and disease progression to a greater extent than using just one targeted therapy. An alternative approach is to use a targeted therapy in combination with one or more traditional chemotherapy drugs. For instance, the targeted therapy trastuzumab (Herceptin®) has been used in combination with docetaxel, a traditional chemotherapy drug, to treat women with metastatic breast cancer that overexpresses the protein HER-2/neu. An added constraint of targeted therapy is that drugs for some identified targets are a challenge to create due to the target's structure and/or the manner in which its function is regulated in the cell.

Side Effects of Targeted Cancer Therapeutics

Researchers had believed that targeted cancer therapies would be less toxic than traditional chemotherapeutics since cancer cells are more dependent on the targets than are normal cells. Yet, current targeted cancer therapies still carry substantial side effects which make compliance a problem, the most common being diarrhea and liver side effects, such as hepatitis and elevated liver enzymes. Other potential side effects observed in patients taking targeted therapies may include the following:

- Skin problems (acneiform rash, dry skin, nail changes, and hair depigmentation),
- Problems with blood clotting and wound healing,
- High blood pressure, and
- Gastrointestinal perforation (a rare side effect of some targeted therapies).

Biosceptre is developing a systemic antibody, BIL03s, which has a confirmed safety profile via a formal toxicology study.

BIOSCEPTRE'S TECHNOLOGY OVERVIEW

The nfP2X$_7$ Target and Pipeline Chronology

Biosceptre's novel cancer target, a non-functional variant of P2X$_7$ (nfP2X$_7$), is present in a range of cancers, including lung, breast, colorectal, and prostate tumors. However, since this target is not found on healthy tissue, it has been demonstrated to be able to minimize the potential for side effects while treating cancer with a high degree of specificity. Using its proprietary nfP2X$_7$ target, Biosceptre seeks to complete pivotal clinical trials for a portfolio of anticancer candidates—BIL03s, BIL06v, and BIL010t—and as shown in Figure 1 (page 5).

- *BIL03s*. Biosceptre's core program, BIL03s, is poised to enter a Phase I clinical trial as a mAb for systemic administration to treat a variety of solid and blood-based cancers.

- *BIL06v*. The Company's therapeutic anticancer vaccine, BIL06v, has entered preclinical development.

- *BIL010t*. The Company's most advanced development program, BIL010t, is a topical formulation, polyclonal antibody therapeutic to treat basal cell carcinoma (BCC), advanced BCC, and other skin cancers.

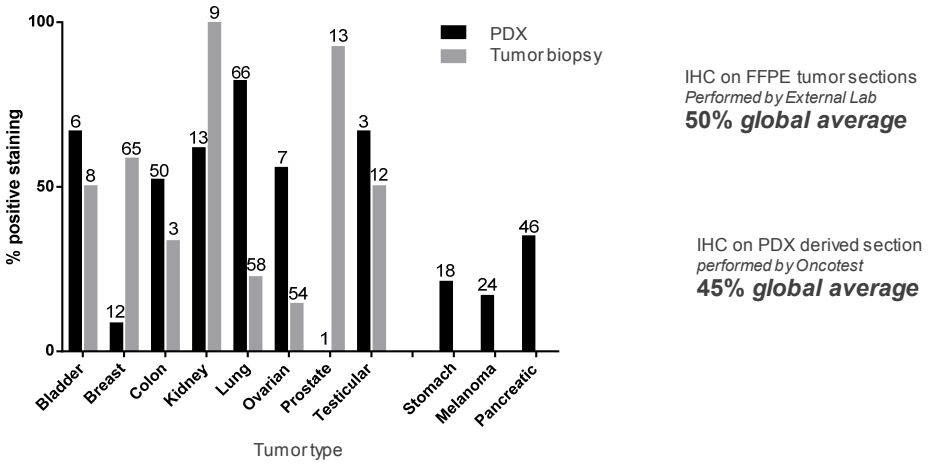
Biosceptre's order of priority for product development is as follows (depicted in Figure 1 [page 5]): (1) its dAb (BIL03s); followed by (2) its therapeutic vaccine (BIL06v); and then (3) its topical polyclonal antibody formulation (BIL010t)—noting that, while the third program is the most advanced clinically, its priority status relates to the nature of the formulation being used. BIL010t is valuable in terms of validating the nfP2X$_7$ target and the other two development programs. However, with BIL03s now in production the Company believes that the polyclonal active ingredient used in the current version of BIL010t may be replaced with the monoclonal active agent used in BIL03s with the result being a more efficient production process and better cost of goods.

Target Detected in Approximately 50% of Tumor Samples for Top Four Cancers

Biosceptre's broadly occurring target can be detected in approximately 50% of the top four cancers (lung, breast, colorectal, and prostate), as shown by Figure 14 (page 24). The numbers of new cases diagnosed references the Company's potential market. To date, Biosceptre's internal research has identified a very high prevalence of its target in the top four cancers.

Analysis of literature reports on P2X$_7$ expression and function in tumor samples and cancer cell lines show that P2X$_7$ and nfP2X$_7$ play a central role in tumor development of multiple cancer types. Inconsistencies identified in expression levels between tumors suggest that P2X$_7$ expression is heterogeneous in patient populations, demonstrating the potential need for companion diagnostics to identify patient populations that are likely to benefit from targeting nfP2X$_7$. The absence of literature reports for some cancers, however, does not prevent nfP2X$_7$ from having a significant role in these malignancies. Specific expression of nfP2X$_7$ at the surface of cancer cells but not normal cells was confirmed by three independent contract research organizations (CROs) in a panel of malignancies and normal tissues: Charles River Laboratories International, Inc., Covance Inc., and Oncotest GmbH.

Figure 14
PROPORTION OF CANCERS FOUND EXPRESSING NFP2X$_7$



Source: Biosceptre International Limited.

Lung Cancer

In a study examining P2X$_7$ mRNA expression in 26 patients with non-small cell lung cancer (NSCLC) compared to 21 patients with chronic obstructive pulmonary disease (COPD) without signs of malignancy, higher P2X$_7$ expression was observed in bronchoalveolar lavage (BAL) cells of tumors with distant metastasis (Schmid, *Lung Cancer* 2015). *In vitro* studies further showed that P2X$_7$ is expressed in the human NSCLC cell lines, including A549, PC9, and H292 cells but not in the non-malignant bronchial epithelial cells BEAS-2B (Jelassi, *Carcinogenesis* 2013; Takai, *Purinergic Signal* 2014; Takai, *J Cell Sci* 2012). In H292 cells, inhibition or downregulation of P2X$_7$ abrogated TGF-β1-induced migration and actin remodeling. P2X$_7$ demonstrated to be required for TGF-β1-induced exocytosis of ATP, which was then acting as a **paracrine** factor. While the functionality of H292 and A549 cells was not assessed, PC9 cells appear to have a constitutively active P2X$_7$ pore (Takai, *Purinergic Signal* 2014). To summarize, these studies highlight the importance of P2X$_7$ in promoting invasion in the aggressive forms of lung cancer.

Breast Cancer

In an immunohistochemistry (IHC) study analyzing P2X$_7$ expression in 40 tumor samples from diverse histological categories using Biosceptre's antibodies raised against nfP2X$_7$, nfP2X$_7$ expression was found absent in normal and hyperplastic breast epithelial samples while all samples from *in situ* or invasive lobular or ductal carcinoma were expressing a high amount of nfP2X$_7$ (Slater, *Breast Cancer Res. and Treat.* 2004). Tumor cells from invasive carcinomas displayed membrane staining compared to the tumor cells from *in situ* carcinoma, which only had intracellular staining, suggesting that nfP2X$_7$ membrane staining is a mark of the more aggressive form of the disease and that antibodies directed against nfP2X$_7$ could be used to identify the different stages of breast cancer.

P2X$_7$ mRNA and protein were also up-regulated under hypoxia in the non-invasive breast cancer cells MCF-7, which were found to have a non-functional large molecular weight pore (Tafani, *Cancer Sci* 2010; Chadet, *Carcinogenesis* 2014). Yet, two independent studies looking at P2X$_7$ expression in breast cancer tissue versus non-malignant mammary tissue showed a reduction of P2X$_7$ staining in breast cancer versus normal tissue (Li, *Purinergic Signal* 2009; Huang, *PLoS One* 2013). The antibodies used in these studies were raised against the C-terminal tail of the receptor and are therefore likely to detect P2X$_7$ variant A. Thus, notwithstanding discrepancies for the expression of P2X$_7$ variant A in breast cancer, nfP2X$_7$ appears to be specifically up-regulated at the surface of breast cancer cells. Upon ATP stimulation, P2X$_7$ was shown to drive T47D breast cancer cells invasion and migration noting, however, that the functionality of these receptors was not assessed (Xia, *Oncol Rep.* 2015).

Colorectal Cancer

Full-length $P2X_7$ protein was identified by IHC with a staining distributed throughout the cell in both normal colorectal epithelium and in colon adenocarcinoma (noting the number of biopsies was limited). $P2X_7$ was also identified in human HCT8, Caco-2, and the murine MCA38 colon cancer cell lines (Bian, *PLoS One* 2013; Coutinho-Silva, *Am J Physiol*, *Gastrointest Liver Physiol* 2005; Künzli, *Purinergic Signal* 2011). While MCA38 were shown to be functional, ethidium uptake was not directly measured in HCT8 or Caco-2 cells (Coutinho-Silva, *Am J Physiol*, *Gastrointest Liver Physiol* 2005). While these data show that $P2X_7$ is expressed in colorectal cancer, they do not demonstrate the involvement of $P2X_7$ in the disease progression. That said, Biosceptre demonstrated that treatment of two colorectal patient-derived tumor xenografts (PDXs) with its lead $nfP2X_7$ therapeutic antibody leads to reduced tumor size, suggesting that $nfP2X_7$ may be involved in colorectal cancer.

Prostate Cancer

In an IHC study examining 116 prostate cancer biopsies using Biosceptre's $nfP2X_7$ antibody, the $nfP2X_7$ protein was identified in all malignant samples regardless of stage or patient age (Slater, Histopathology 2004). The $nfP2X_7$ receptor was also detected in adjacent epithelial cells but with a different staining pattern. While malignant cells showed surface membrane staining, adjacent non-malignant cells showed $nfP2X_7$ in the nucleus and cytoplasm, suggesting that cancer cells require $nfP2X_7$ to localize at the membrane. In a second study from the same team, $nfP2X_7$ staining by IHC was compared to the levels of **prostate-specific antigen (PSA)** in 174 biopsies from prostate cancer patients (Slater, *J Mol Histol* 2005). Increased $nfP2X_7$ staining was found to correlate with increased PSA levels, suggesting that $nfP2X_7$ is a candidate for early diagnosis of prostate cancer. An independent group has further confirmed these results by detecting increased $P2X_7$ mRNA and protein expression in prostate tumor samples versus normal tissue (Ravenna, *Prostate* 2009).

Increased $P2X_7$ expression correlated with increased expression of Epidermal Growth Factor Receptor (EGFR) and Estrogen Receptor (ER)α, which are well-known drivers of cancer cell proliferation (Ravenna, *Prostate* 2009), suggesting that $P2X_7$ might coordinate with these receptors to promote cell proliferation. This observation is in line with the involvement of $P2X_7$ in cancer cell survival and proliferation (Adinolfi, *J Biol Chem* 2009; Adinolfi, *FASEB J* 2010). Functional $P2X_7$ was also shown to drive invasion and metastasis of prostate cancer cell lines stimulated by extracellular ATP (Qiu, *PLoS One* 2014; Ghalali, *Carcinogenesis* 2014).

Alternatively, an independent study looked at the genetic association of $P2X_7$ and VEGFR-2 polymorphisms and their correlation with overall survival in a population of 100 patients having metastatic prostate cancer (Solini, *Oncotarget* 2015). This study identified a genetic interaction between *VEGFR-2* (rs2071559, rs11133360) and *P2X7R* (rs3751143, rs208294) genotypes, which correlated with better overall survival (Solini, *Oncotarget* 2015). Rs3751143 (E496A) polymorphism is associated with non-functional $P2X_7$ pore formation while rs208294 (H155Y) is associated with increased large pore formation (Cabrini, *J Immunol* 2005). However, when both H155Y and E496A coexpression occurs, it has been shown that H155Y cannot recover the E496A loss of function (Gu, *J Biol Chem* 2001). An independent report has confirmed the significant association of rs3751143 (E496A) SNP and prostate cancer. However, when compared between less and more aggressive prostate cancer in 1,172 cases, E496A was associated with the less aggressive form of the disease (Ghalali, *Carcinogenesis* 2014). Overall, these studies support the involvement of $nfP2X_7$ and functional $P2X_7$ in prostate cancer.

Figure 15 (page 26) provides Biosceptre data in which siRNA is used to block expression of the $P2X_7$ gene. siRNA probes are used to block translation of a specific gene into protein by interfering with the mrNA stage. The sequence of the single strand siRNA probes are designed to be complementary to sequences in the single strand mRNA, and when the two are present in the cytosol of a cell they form a double stranded RNA complex which blocks the mRNA from binding to the ribosome and being translated into $P2X_7$ protein.

All of the cell lines shown in Figure 15 were shown to express the nonfunctional (nf) form of $P2X_7$ as they fail to open the large pore when exposed to high ATP concentrations for extended periods. These cell lines die when $P2X_7$ is knocked down, indicating that expression of the $nfP2X_7$ form of the $P2X_7$ protein is necessary for the survival of these cell lines.

Figure 15

nfP2X$_7$ MEDIATES SURVIVAL IN MULTIPLE CELL LINES

Cell Line	Tumor Origin	Large Pore Opening	P2X$_7$ siRNA induced death	
			A	B
PC3	Prostate	No	Yes	Yes
Du145		No	Yes	Yes
LNCaP		No	Yes	Yes
SK MEL 28	Melanoma	No	Yes	Yes
SK MEL 5		No	No	No
PC 9	Lung	No	Yes	Yes
H460		No	Yes	Yes
H520		No	Yes	Yes
MCF7	Mammary	No	Yes	Yes
SK N AS	Neuroblastoma	No	Yes	Yes
Kelly		No	Yes	Yes
MiaPaCa2	Pancreas	No	No	No
HCT116	Colorectal	No	Yes	Yes
HT1080	Fibrosarcoma	No	Yes	Yes

Source: Biosceptre International Limited.

Multi-Modality Approach Across Various Indications

The Company has been granted a patent over the nfP2X$_7$ itself based on the science of the target. The key benefit of owning access to the target in this way is that it provides Biosceptre freedom to operate in a multi-modal approach across various indications as well as accrues the benefits of validation across products.

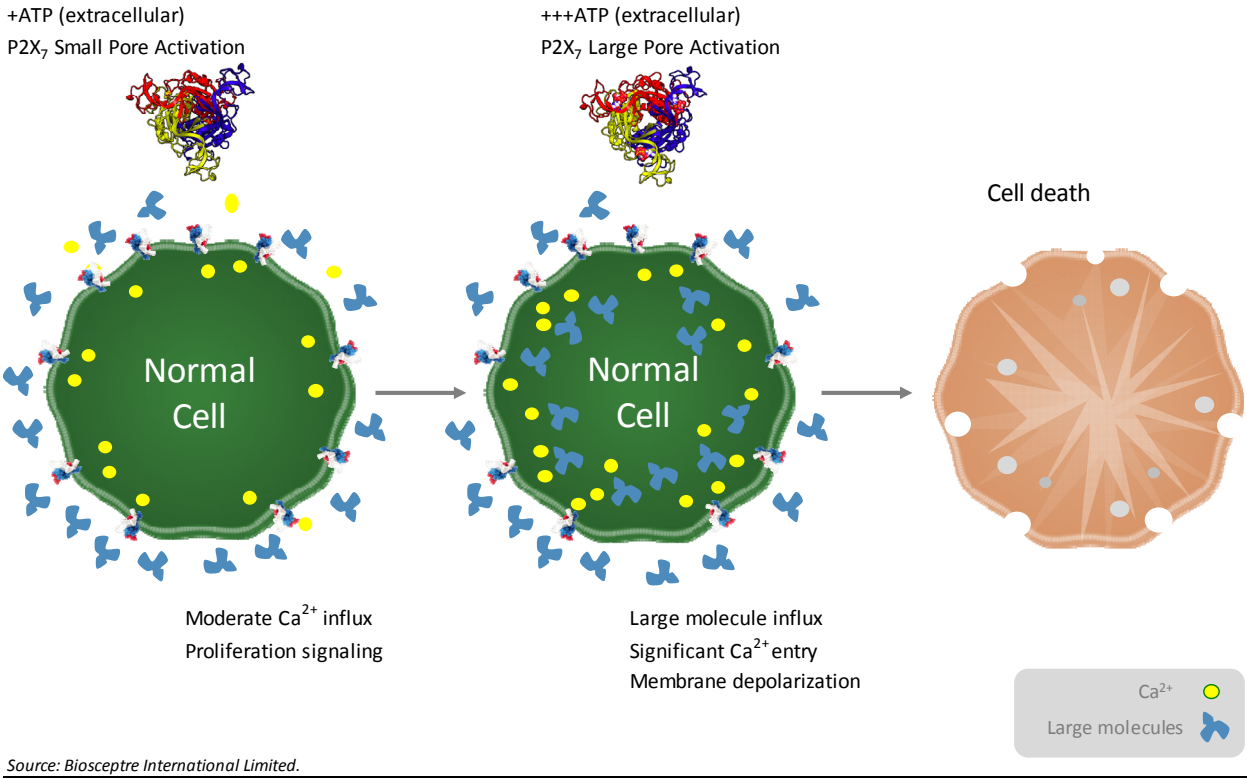
One such example of cross validation arises in the case of the vaccine therapeutic candidate BIL06v. BIL06v was utilized to hyper immunize a production sheep flock under Good Manufacturing Practice (GMP) conditions, which then generated a polyclonal antibody response against the vaccine in their blood serum. This polyclonal antibody response was then collected and purified for use as the active ingredient in the topical candidate BIL010t. The data that resulted from this approach was a significant body of safety data from the flock used for inoculation, indicating that, even with a strong systemic antibody response to P2X$_7$ there is little to no immunogeneic (or auto immune) issues arising from antibodies against the nfP2X$_7$ target. This represented one example of how having many products across the one target helps drive each product's development efforts. Furthermore, Biosceptre believes that there is likely to be a long-term potential for cost of goods (COGS) benefit since the Company would be able to produce a product that can be used for more than one indication, where the market size would be larger (should that prove to be the case). This is important given the continually changing environment of pharmaceutical costs and payers.

How the Target Forms

Normal $P2X_7$ – Two Pore States

$P2X_7$ is a ligand gated ion channel with multiple signaling roles in healthy tissues. Key functionalities are that it has two pore states. In a normal cell, subject to extracellular ATP concentrations that are relatively high, a non-selective ion channel will be activated and facilitate calcium influx, which provides a proliferation signal. When the ATP concentration in the extracellular environment remains elevated for a significant time period, the channel then enters its second state, a large pore which facilitates flow of molecules of up to 900 **Dalton** across the cell membrane, which is a signal that can lead to cell death. Consequently, the $P2X_7$ pore switches from one state to another depending on how long the ATP concentration is elevated. Figure 16 depicts this process.

Figure 16
NORMAL $P2X_7$ – TWO PORE STATES (+ATP) and (+++ATP)

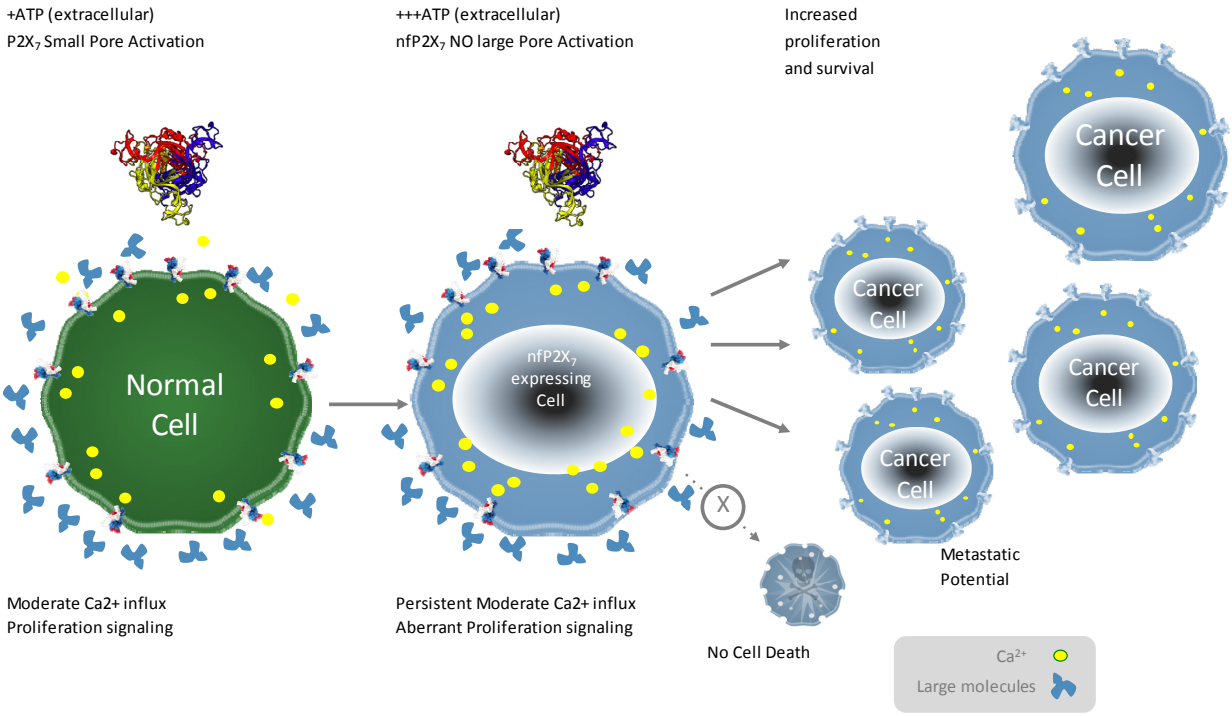


Source: Biosceptre International Limited.

nf$P2X_7$ and Cancer

While nf$P2X_7$ can show moderate calcium signaling post ATP activation, driving proliferation, there is no capacity to form the large pore that drives cell death. Thus, instead of apoptosis, there is increased proliferation and survival—this where the Company believes that the link between nf$P2X_7$ and cancer may be found, as illustrated in Figure 17 (page 28).

Figure 17
nfP2X$_7$ AND CANCER

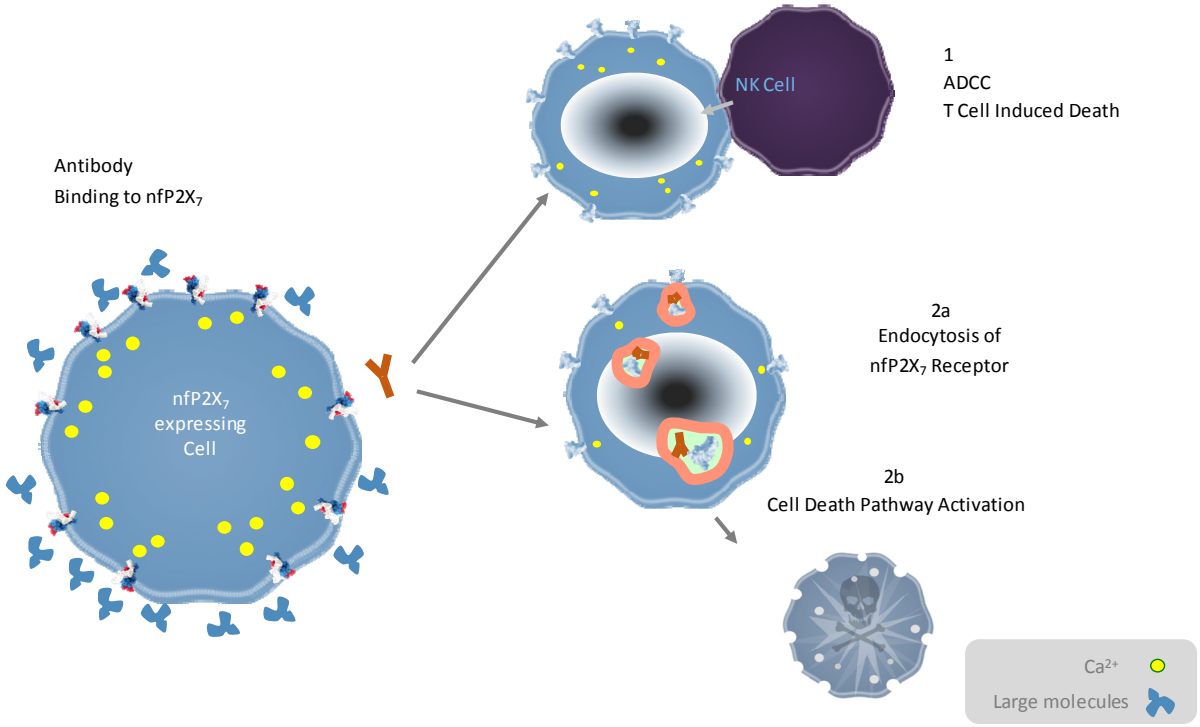


Source: Biosceptre International Limited.

Possible Mechanism of Therapeutic Action

Biosceptre has identified a target that is visible only on the nonfunctional (nf) version of the P2X$_7$ receptor and has targeted that epitope with its therapeutics (Figure 18 [page 29]). There has been evidence that T cell function may be activated when antibodies bind to that target via Fc receptor binding. Furthermore, **endocytosis** of the target occurs on binding with the antibodies. Either of these mechanisms, or a combination of these, may be the mode of action by which Biosceptre's antibodies can drive cell death. The Company continues to work toward developing more data on the precise mechanism of action.

Figure 18
POSSIBLE MECHANISMS OF THERAPEUTIC ACTION



Source: Biosceptre International Limited.

The Causes of nfP2X$_7$

It is worth noting that among the literature examining the role of P2X$_7$ in cancer, the functional state of P2X$_7$ has not been assessed. Therefore, potentially a number of the papers that are published on P2X$_7$ and cancer may be describing the nonfunctional (nf) form. Essentially the assays required to distinguish between the large pore functionality and the loss of large pore functionality are not always carried out. Some studies only check for the absence of P2X$_7$ on the cancer cell, they do not seek to determine whether the large pore function is active or not. The role of P2X$_7$ in cancer has been investigated in numerous articles, many of which imply the presence and role of nfP2X$_7$. Literature reports 11 slice variants that have a role in tumor reversion, with Variant B and J having been directly implicated in tumor progression. The second cause reported is Single Nucleotide Polymorphisms (SNP), and there are many reported around the P2X$_7$ gene. There are other potential causes, including Intracellular Binding Partners (which have been identified, including the non-muscle myosin Heavy Chain 9 [Myh9] that was shown to modulate P2X$_7$ large pore formation) and N-Glycosylation sites (located next to the ATP binding site in the extracellular domain). The Company is focusing its efforts to identify which of these approaches is most relevant for cancer.

BIOSCEPTRE'S PRODUCT DEVELOPMENT

Recent Progress with the nfP2X$_7$ Receptor

Biosceptre has successfully progressed several activities aimed at exploiting the nfP2X$_7$ receptor target for pharmacological intervention, including those detailed below.

- *Target Identification and Validation*. The nfP2X$_7$ target has been characterized and validated. Studies have confirmed the presence of the target on a range of both solid tumors and blood-based cancers and its absence on normal tissue. The nfP2X$_7$ receptor is believed to have a critical role in cancer cell survival and proliferation.

- *Antibody Development*. A high-specificity, fully human monoclonal domain antibody and polyclonal antibodies have been identified and have shown to bind selectively to nfP2X$_7$. These are being developed for clinical investigation.

- *Cell-line Development.* A high-yielding cell line has been developed for BIL03s and good manufacturing practices (GMP) production is ongoing by Pacific GMP. This work is intended to deliver clinical-grade domain antibodies for systemic use in clinical trials.

- *Safety and Toxicology Studies*. BIL03s and BIL010t have demonstrated favorable safety in animal toxicology studies. Numerous *in vivo* studies and data from compassionate use in patients have shown no safety issues for targeting nfP2X$_7$ using BIL03s, BIL010t, or BIL06v. As well, BIL010t has demonstrated favorable safety and tolerability in a formal FDA Phase I clinical trial.

- *Securing of IP*. Biosceptre has secured IP protection on the nfP2X$_7$ target until 2022 with additional protection covering therapeutic intervention until at least 2035 (with further patents currently in development).

- *Compassionate Use*. All candidates (BIL03s, BIL06v, and BIL010t) have been used as therapeutics in compassionate use in human patients with encouraging indicative efficacy signals.

In addition, detection of nfP2X$_7$ has potential as a powerful diagnostic approach, with Biosceptre investigating the development of companion diagnostics based on targeting nfP2X$_7$.

Product Pipeline Details

- *BIL03s.* Biosceptre's systemic antibody, BIL03s, selectively binds to nfP2X$_7$ and has shown the potential to modulate calcium signaling via nfP2X$_7$. Shown to bind to at least six major cancer types—prostate, kidney, ovarian, melanoma, lung, and colorectal—with confirmed safety via a formal toxicology study, the production process for BIL03s has been established and transferred, with the clinical plans established. Additional details on this candidate are provided in the accompanying section.

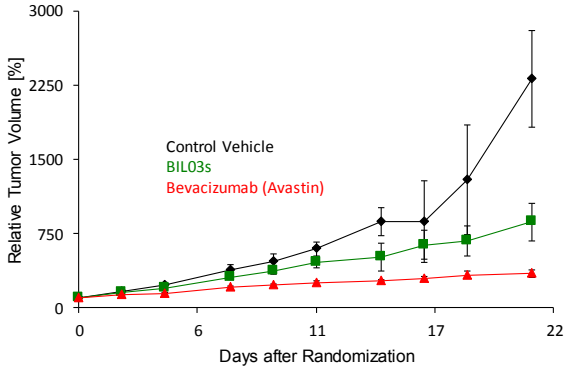
- *BIL06v.* The Company's therapeutic vaccine, BIL06v, has been shown to break immune tolerance to a "self" protein, increase antibody **titers** in mice and humans, and activate T cells in mice. As well, researchers have reported indications of efficacy in mice and informed consent patients. A candidate for clinical development has been identified and process development is ongoing to support a Phase I clinical trial. Additional details on this candidate are provided in the accompanying section.

- *BIL010t.* For its topical product, BIL010t, the Company has demonstrated indications of efficacy from informed consent and Phase I studies, as well as a favorable safety profile from preclinical studies, informed consent patients, and Phase I trials. Biosceptre is targeting basal cell carcinoma, which provides a validated disease target, where the Company has shown efficacy in humans. Additional details on this candidate are provided in the accompanying section.

BIL03s (Systemic Antibody)

In a patient-derived xenograft using a colonic tumor in immune-compromised mice, a tumor was screened and demonstrated to have a strong binding to BIL03s. The model was optimized to incorporate Avastin® as a control arm, and Biosceptre prescreened it to ensure that it could achieve a strong binding of its lead candidate at a twice weekly (10 mg) dose. As shown in Figure 19, the positive control (Avastin®) is keeping the tumor volume low and the BIL03s line represents a statistically significant result for BIL03s without an optimized model.

Figure 19
PRECLINICAL DATA SUPPORTING SYSTEMIC ANTIBODY



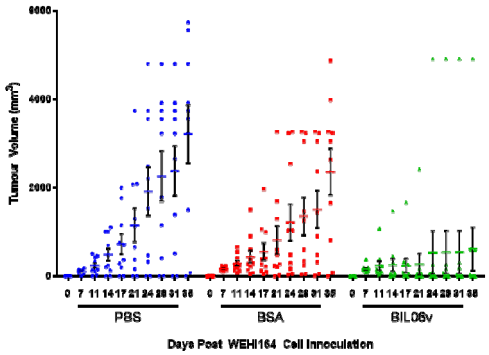
Source: Biosceptre International Limited.

BIL03s is positioned to begin Phase I in 2016, with 20 to 30 patients expected to be enrolled at two trial centers in Australia. The Company has stated that it will likely focus on lung, prostate, and colorectal cancers. The trial is expected to be a basket trial as designed by Dr. Bob Li, based at Memorial Sloan Kettering Cancer Center in the U.S. (biography on page 15). The method of delivery will likely be systemic infusions, and the study objectives are to include metrics of efficacy, safety, tolerability, and pharmacokinetics. Principal investigators Prof. Gavin Marx and Asst. Prof. Nick Pavlakis (biographies on page 15) each lead the oncology departments of the largest public and private hospitals in Sydney, Australia (The Seventh Day Adventist Hospital and the Royal North Shore Hospital).

BIL06v (Therapeutic Vaccine)

Preclinical data regarding Biosceptre's therapeutic vaccine show that it impairs tumor growth *in vivo*, as shown in mice that were immunized three times prophylactically. Prior to the inoculation, the Company immunized the mice three times with the peptide conjugate with an adjuvant and then the mice were inoculated with WEHI 164 fibrosarcoma cells subcutaneously (160,000 cells/mouse). As shown in Figure 20, there was statistical significance of the lower tumor weights resulting from this, whereby prophylactic vaccination impaired tumor growth significantly (P<0.01) compared to vehicle (PBS) controls.

Figure 20
PRECLINICAL DATA: BIL06v IMPAIRS TUMOR GROWTH *IN VIVO*



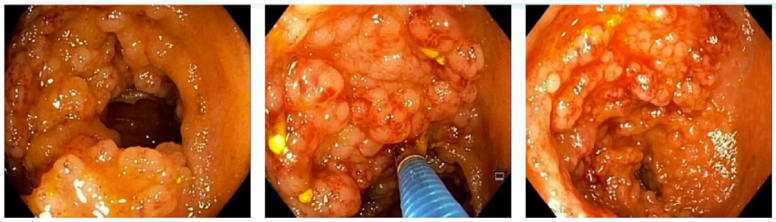
Source: Biosceptre International Limited.

Compassionate Access Data

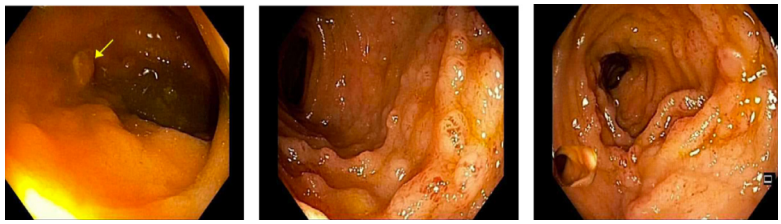
Biosceptre has compassionate access data from a case study using its therapeutic vaccine. In this case study, the vaccination was performed with peptide conjugates. This was on a patient with **follicular lymphoma** (a type of blood cancer). In the bottom left of Figure 21, there was an increasing specific antibody titer following vaccination, which persisted, so immune tolerance could be broken. The top of Figure 21 shows pre-vaccination photos of the extent of the tumor in this same region and the bottom half of the Figure shows post-vaccination images. The treating physicians accept this to be approximately a 50% visual reduction in the tumor volume. As of June 2016, the patient is healthy and continues to be treated.

Figure 21
THERAPEUTIC VACCINE (BIL06v): CLINICAL SAS CASE STUDY 1

Ileum pre-vaccination showing tumor extent



Same regions post vaccination, showing tumor volume reduced by 70%



Source: Biosceptre International Limited.

Biosceptre further treated prostate cancer patients with the therapeutic vaccine and, post vaccination, was able to drive and maintain an antibody response as well as also see an increase to the doubling period of blood PSA levels from four months to seven months; in other words, PSA levels rose more slowly while treatment was ongoing. In addition to indications of efficacy, Biosceptre has been able to obtain favorable indications of safety in humans from the aforementioned compassionate access patients.

Proposed Phase I Trial

In the proposed Phase I basket trial, the therapeutic vaccine is to be administered to 20 to 30 patients at two trial centers (the Seventh Day Adventist Hospital and the Royal North Shore Hospital in Australia) with the same lead investigators and trial designers as the systemic therapeutic. The primary study objectives are to monitor safety, antigen-specific antibody titers, and other immune functions. A secondary objective is to monitor known biomarkers of disease severity for efficacy indications. The protocol has been in development and may be ready to commence in the U.S. during 2017.

Candidate Identification Program

Biosceptre has a candidate identification program for new dAbs using a novel methodology in which the Company pans vaccinated serum from patients who have received the Company's vaccine—another example demonstrating how different Biosceptre programs validate and drive other products forward. The Company believes that it can use human response to its current vaccine candidate to derive higher affinity and more specific antibodies going forward. Furthermore, Biosceptre has a new modality that is under investigation that is an Antibody Drug Conjugate in the form of a cytotoxin bearing liposome targeted at cancer cells via an antibody coating.

Compassionate Access Data Summary

Through the Company's compassionate access program, 100% of the patients who have been appropriate for assessment have shown a titer against Biosceptre's target, meaning that the Company's vaccine is raising an endogenous antibody response to nfP2X$_7$. Regarding the systemic antibody, the Company has seen 60% of compassionate access patients show an improvement in some of their cancer outcomes. Biosceptre has observed a reduction in tumor size, blood count, and a variety of tumor markers during treatment. Figure 22 summarizes the clinical compassionate access data.

Figure 22
CLINICAL COMPASSIONATE ACCESS DATA

Therapeutic Vaccine BIL06v	+	Systemic Antibody BIL03s
100% of immunized patients appropriate for assessment show nfP2X$_7$ specific titer 30% of patients are still alive four years post diagnosis		60% of patients showed improvement in cancer outcomes (reduced tumor size, blast count, and tumor marker reduction BCR-ABL1, PSA, CEA & CA15)

Source: Biosceptre International Limited.

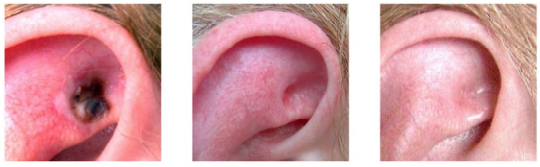
BIL010t (Topical Product)

Informed Consent Trial

Biosceptre has conducted an informed consent trial for its topical therapeutic, BIL010t. This trial was separate from its Phase I trial. In this trial, 24 non-melanoma skin cancer lesions were treated (BCC and **squamous cell carcinoma [SCC]**), and 15 lesions showed clinical clearance with a 62-day median time to clearance. This trial ran longer than the Company's Phase I study, and Biosceptre was able to see favorable results. Figures 23 and 24 show pictures of selected case studies. Figure 23 illustrates a rapid clearance within 16 days in a young and healthy patient with no recurrence; whereas Figure 24 shows an SCC with pretreatment appearance. On the right side of Figure 24, it shows the biopsy before and after, with no staining post treatment.

Figure 23
BIL010t CLINICAL DATA - EXAMPLE OF PAPULONODULAR BCC

Topical application of BIL010t cleared tumor by day 6 with with no recurrence



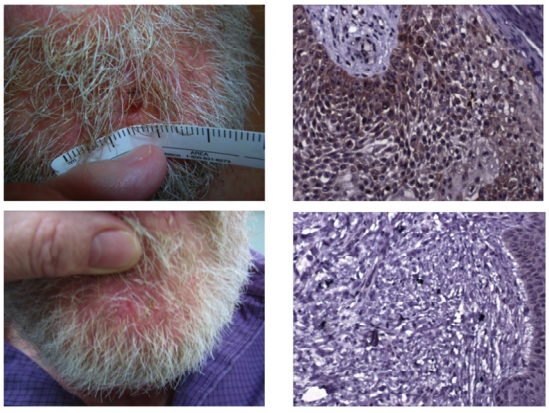
Day 1 Day 6 Day 16

Source: Biosceptre International Limited.

Figure 24
BIL010t CLINICAL DATA - EXAMPLE OF SCC WITH BIOPSY HISTOLOGY

Pre-treatment appearance

Staining of nfP2X$_7$ on cancer cells



Appearance 2 weeks post treatment with BIL010t

No staining post treatment

Source: Biosceptre International Limited.

Phase I, Complete

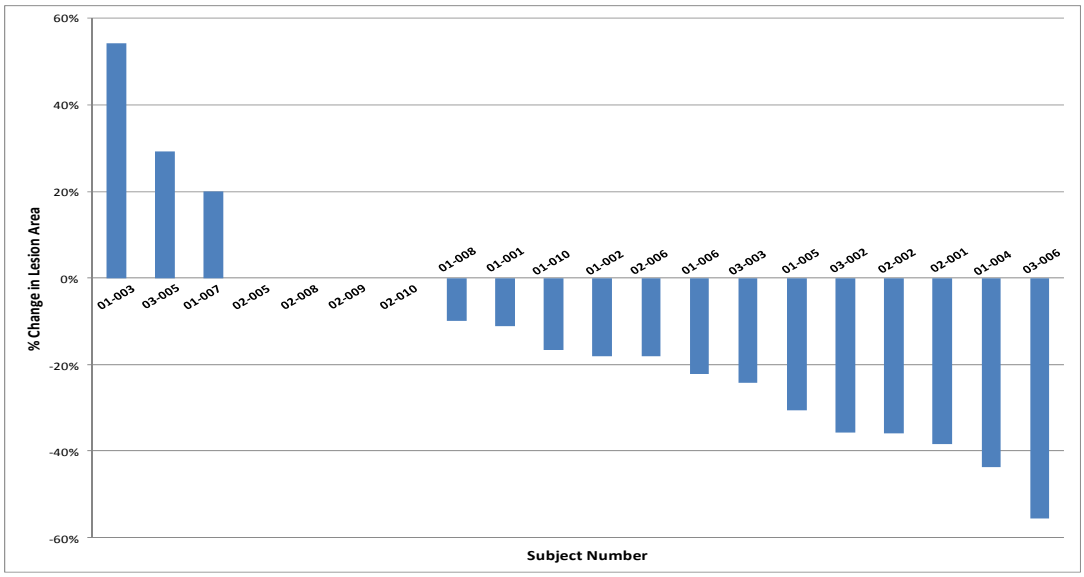
In a completed Phase I trial, there were 21 patients enrolled at three U.S.-based dermatology research centers. Patients were included after histological confirmation of superficial or nodular BCC. The treatment was self-administered using a metered topical daily dosage for 28 consecutive days. Though the trial's objectives were safety and tolerability, results of the trial demonstrated not just tolerability and safety but high compliance—something that is critically important for these indications as current medications have many serious side effects and compliance issues. Results further demonstrated a reduction of lesion size.

The only reported side effect associated with treatment was mild to moderate localized skin reactions. Levels of BIL010t were generally undetectable in patients' blood serum, and gave no evidence of immunogenicity in the majority of patients. Although efficacy was not a prescribed endpoint of the trial, researchers noted that 65% of patients (13 out of 20) who completed the study had decreases in the size of their BCC lesions. The reductions ranged from a 10% to 56% reduction in the size of the BCC during the course of treatment.

Phase I Clinical Data from the FDA Trial

Figure 25 provides data from the Company's Phase I FDA trial. The Figure contains a **waterfall plot** of percentage change in tumor area. Data points to the right (which make up approximately 65%) show regression in surface lesions over a 28-day period. There were three non-responders and four whose progression was halted. There was a statistically significant reduction in overall tumor size. The Company halted the trial at 28 days and there was no progression or follow-up data as all tumors were excised.

Figure 25
PHASE I TRIAL RESULTS FOR BIL010t: WATERFALL PLOT OF PERCENTAGE CHANGE IN TUMOR AREA



Source: Biosceptre International Limited.

Proposed Phase Ib/II Trial

Biosceptre plans to run a Phase II trial for its topical candidate in which the Company seeks to include a separate trial arm to study a revised formulation. There are expected to be three U.S.-based trial centers, with 120 in the Phase II trial.

Product Manufacturing

The Company has completed technology transfer and production is currently undergoing scale up for the lead dAb candidate BIL03s. The team leading Biosceptre's antibody development has deep experience from the Australian Institute of Bioengineering (AIBN), where they provided commercial and research services developing antibodies for therapeutic use for trials and experiments. Thus, the Company's in-house team has delivered multiple antibody projects through scale-up for treatment, which is unusual for a biotech company at the Phase I stage. A key competitive advantage for Biosceptre at its development stage includes that, when looking across each of the Company's products, each one has been used in humans, which mitigates risk across the Company's portfolio. Figure 26 summarizes the Company's product manufacturing.

Figure 26
PRODUCT MANUFACTURING COMPLETED

	Topical Polyclonal BIL010t	Systemic Antibody BIL03s	Therapeutic Vaccine BIL06v
API Manufacturer	ThermoFisher SCIENTIFIC	PACIFICGMP	AUSPEP
Purification	MicroPharm	PACIFICGMP	AUSPEP
Fill & Finish–Final Product	DPT	PACIFICGMP	AUSPEP
Stability	API 5 years (ongoing)	18 months (ongoing)	API 6 months (ongoing)
Reference Standard	✓	✓	✓
GMP Manufacturing Bio-Process	✓	✓	
Products Used in Man	✓	✓	✓

Source: Biosceptre International Limited.

Potential Competition

The oncology market has experienced a significant transformation away from cytotoxic and anti-hormonal therapies toward more targeted therapies, which are drugs or other substances that block the growth and spread of cancer by interfering with specific molecules involved in tumor growth and progression. Biosceptre's products fall into this class. Targeted therapies are capable of acting on unique targets in cancer cells. The increased selectivity afforded by these targets presents drug developers with the chance to develop medicines with greater efficacy and improved toxicity profiles. Accordingly, targeted therapies encompass the biggest selling class of cancer therapeutics, where growth, for example, from the leading mAb products, continues to take place at unprecedented levels and where the market value could reach $125 billion by 2020. Moreover, competition may continue to become more intense as a greater number of therapeutics in this class enter the market.

The accompanying section provides a summary of potentially competitive products in the market sectors Biosceptre targets, specifically including major antibodies in the market as well as one that has recently entered the market in the NSCLC arena—Opdivo. Of note is that Roche's Genentech subsidiary and Novartis sold three of the world's biggest-selling cancer drugs in 2015, while Celgene, Merck, Eli Lilly, and Johnson & Johnson also have top 10 products. Half of these drugs realized a double-digit growth in sales during 2015. Further, Figure 12 (page 18) profiles what could be the top 20 cancer drugs worldwide (by revenue), as forecast by statistics firm Statista.

BIL03s

Figure 27 summarize a sampling of the potential competition specifically for BIL03s, followed by key product details on pages 37-38.

Figure 27
COMPETITION: BIL03s

Lymphoma	Non Small Cell Lung	Colorectal	Breast	Prostate
Rituxan (rituximab)	**Opdivo** (nivolumab)	**Avastin** (bevacizumab)	**Herceptin** (vismodegib)	**Zytiga**
Targets CD20+ B cells (cancer and normal), low specificity, high cross reactivity - Limited window for treatment	15% ORR; 3.2 month survival advantage over Docetaxel; Only applicable to BRAF gene carriers with YERVOY and a BRAF inhibitor. Side reactivity in many organs	Inhibits revascularization, not cancer specific; 4 month survival advantage for colorectal patients (26 to 30 months)	Indicated for high HER2 expression only (~7% of breast cancer). Stage 4 survival advantage of 5 months (20>25)	Pre-chemo in conjunction with Prednisone 4,4 months OS advantage
2015 sales $7.10 billion	**2016 sales (est) $2.40 Billion**	**2015 sales $6.74 billion**	**2015 sales $6.59 billion**	**2015 sales $2.23 billion**

BIL03s does not knock down B cells in Special Access Patients

BIL03s seen to bind to >50% tumor samples for each indication

Source: Company reports.

Rituxan®

Rituxan (rituximab), developed by Biogen Inc. and co-promoted by Genentech (a subsidiary of Roche Group), is a mAb approved for treatment of common forms of blood cancer, including non-Hodgkin's lymphoma (NHL), follicular lymphoma, and chronic lymphocytic leukemia (CLL). It is also used to treat rheumatoid arthritis and certain types of vasculitis. Rituxan is marketed as MabThera in Europe. Rituximab makes it easier for the body to destroy cancerous B cells, and works by binding to a specialized protein on the surface of most B cells. When rituximab binds to a B cell, it causes changes in the arrangement of structures on the cell's surface, where these changes make it easier for the immune system to kill cancerous B cells. Rituximab has become an important part of lymphoma treatment and is often administered in conjunction with cyclophosphamide, doxorubicin, vincristine, and prednisone (a protocol known as "CHOP"). The combination of all five agents is referred to as "R-CHOP." A comprehensive review found that adding rituximab to CHOP led to a 3-fold higher complete remission rate over CHOP in NHL. Several studies have shown that treatment with rituximab can prolong remission of follicular and diffuse large B-cell lymphomas. Adding rituximab to chemotherapy has also been shown to improve complete response and overall survival among HIV-positive individuals with NHL. Rituximab has further been shown to confer a survival benefit when administered as maintenance therapy in people with treatment-resistant or relapsed follicular lymphoma. Reported sales of Rituxan in 2015 were US$7.10 billion.

Opdivo®

Bristol-Myers Squibb Company's Opdivo (nivolumab) is a human mAb that blocks the interaction between PD-1 and its ligands, PD-L1, and PD-L2, where the binding of the PD-1 ligands, PD-L1 and PD-L2, to the PD-1 receptor found on T cells, inhibits T-cell proliferation and cytokine production. Up-regulation of PD-1 ligands occurs in some tumors and signaling through this pathway can contribute to inhibition of active T-cell immune surveillance of tumors. Opdivo is specifically indicated to treat patients with metastatic squamous NSCLC with progression on or after platinum-based chemotherapy. Supplied as a solution for intravenous infusion, the recommended dose is 3 mg/kg administered over 60 minutes every two weeks until disease progression or unacceptable toxicity. FDA approval of Opdivo for metastatic squamous NSCLC was based on a randomized, open-label study enrolling 272 patients with metastatic squamous NSCLC who had experienced disease progression during or after one prior platinum doublet-based chemotherapy regimen. Patients received Opdivo administered intravenously at 3 mg/kg every two weeks or docetaxel administered intravenously at 75 mg/m2 every three weeks. This study included patients regardless of their PD-L1 status. The first tumor assessments were conducted nine weeks after randomization and continued every six weeks. The major efficacy outcome measure was overall survival. The trial demonstrated a statistically significant improvement in overall survival for patients randomized to Opdivo versus with docetaxel at the pre-specified interim analysis when 199 events were observed (86% of the planned number of events for final analysis). The median survival was 9.2 months versus 6.0 months for the Opdivo versus docetaxel arms, respectively. Having received approval in 2014, Opdivo was the first of a new generation of cancer immunotherapy drugs (medicines that use a patient's immune system to fight cancer). Total sales of Opdivo in 2015 were US$942 million. In 2016, consensus estimates for Opdivo are for US$2.40 billion in sales.

Avastin®

Avastin (Bevacizumab) is an angiogenesis inhibitor—a drug that slows the growth of new blood vessels. A recombinant humanized mAb, Avastin blocks angiogenesis by inhibiting vascular endothelial growth factor A (VEGF-A), which is a chemical signal that stimulates angiogenesis in a variety of diseases, especially in cancer. Avastin was the first clinically available angiogenesis inhibitor in the U.S., and is FDA approved for certain metastatic cancers. Its first approval was in 2004 for combination use with standard chemotherapy for metastatic colon cancer, and since then, the drug has been approved in certain lung cancers, renal cancers, ovarian cancers, and glioblastoma multiforme of the brain. It was at one point approved for breast cancer, but that approval was withdrawn when later studies showed no evidence of effectiveness. The drug is given through an infusion into a vein intravenously, with the first dose given over 90 minutes (the infusion time can eventually be shortened to 30 minutes if well tolerated). The amount of Avastin a patient receives depends on many factors, including height and weight, general health or other health problems, and the type of cancer or condition present. It is an expensive drug, with two 16-milliliter vials currently priced at more than $5,400. In 2015, sales of Avastin were US$6.74 billion.

Herceptin®

Herceptin (Trastuzumab) from Genentech is a mAb that interferes with the HER2/neu receptor, where it is used primarily to treat certain breast cancers. The HER receptors are proteins that are embedded in the cell membrane and communicate molecular signals from outside the cell (molecules called EGFs) to inside the cell, and turn genes on and off. The HER protein, human epidermal growth factor receptor, binds to human epidermal growth factor, and stimulates cell proliferation. In certain cancers, largely specific types of breast cancer, HER2 is overexpressed, and causes cancer cells to reproduce uncontrollably. In early stage (curable) HER2-positive breast cancer, Herceptin-containing regimens improved overall survival and disease-free survival relative to comparator arms involving treatment with placebo or chemotherapy. However, increased risk of heart failure and decline in left ventricular ejection fraction were seen in these trials. Two trials that had shorter-term treatment with trastuzumab did not differ in efficacy from longer trials but produced less cardiac toxicity. Herceptin can be used in several different ways: (1) as part of a treatment course including the chemotherapy drugs doxorubicin, cyclophosphamide, and either paclitaxel or docetaxel (this treatment course is known as "AC→TH"); (2) with the chemotherapy drugs docetaxel and carboplatin (this treatment course is known as "TCH"); or (3) alone after treatment with multiple other therapies, including an anthracycline (doxorubicin)-based therapy (a type of chemotherapy). In 2015, sales of Herceptin were US$6.59 billion.

Zytiga®

Zytiga (abiraterone acetate) by Janssen Biotech, Inc. is an oral, once-daily medication used in combination with prednisone to treat men with advanced prostate cancer. This type of advanced prostate cancer is resistant to medical (e.g., hormonal) or surgical treatments that lower testosterone, and has spread to other parts of the body (metastatic castration-resistant prostate cancer). This newly approved prostate cancer pill may extend life by up to four months in men with spreading cancer who have already been treated with chemotherapy. Prostate cancer is the most common cancer diagnosed in men besides skin cancer, according to the American Cancer Society, with one out of every six men likely to be diagnosed with prostate cancer during his lifetime. Zytiga inhibits a protein that helps form male hormones. A new study that included 1,195 men with metastatic prostate cancer whose disease had progressed after chemotherapy and who received steroid therapy along with the new pill survived for 14.8 months, on average, versus 10.9 months for those who received a placebo along with steroids. This translated into a 34% reduction in risk of dying, according to study results. Men who took the new pill also saw greater responses in PSA levels than men who received placebo. Elevated levels of PSA may be a marker for prostate cancer. The men who took Zytiga further showed improvements in disease-related symptoms and prostate cancer progression on imaging tests compared with men who received the placebo. Sales of Zytiga in 2015 were US$2.23 billion.

Erbitux®

Also of mention within this category is Erbitux, which is an IgG1 mAb designed to target and block the epidermal growth factor receptor (EGFR). Erbitux treats metastatic colorectal cancer and head and neck cancer. It has been marketed for 14 years by Bristol-Myers Squibb, and in 2015, the firm agreed to transfer the drug's North American rights to Eli Lilly & Co., which manufactures Erbitux. In 2014, Erbitux generated sales of US$723 million for Bristol-Myers Squibb, noting that U.S. exclusivity is set to expire in 2016 and the method of use patent is set to expire in late 2018.

BIL010t

Aldara™ and Erivedge®

With regard to the Company's topical therapeutic, BIL010t, competitive analysis can be made with two of the main products in the market—Aldara (imiquimod) and Erivedge (vismodegib). Aldara discovered by 3M Company (MMM-NYSE) received approval in 1997 to treat genital warts, and as well, can treat rough, raised areas of heavily sun-exposed skin (actinic keratoses), and skin cancer (basal cell carcinoma [BCC]). As of 2015, imiquimod is generic and is available worldwide under many brands, including Aldara. Worldwide sales in 2014 of Aldara were $350 million. Erivedge by Genentech is approved to treat skin cancer (BCC) via a small molecule, though carries a large number of side effects that can limit compliance. For that reason, with regard to BCC, this treatment is only used in severe cases. Global sales for Erivedge in 2015 were approximately US$174 million.

Additionally, within this group is 5-FU (5 Fluorouracil), also named Adrucil®, among other names, which is used to treat cancer. As a suicide inhibitor, 5-FU works through irreversible inhibition of thymidylate synthase. Fluorouracil has been given systemically for anal, breast, colorectal, esophageal, stomach, pancreatic, and skin cancers (especially head and neck cancers). It has also been given topically (on the skin) for actinic keratosis, skin cancers, and Bowen's disease and as eye drops for treatment of ocular surface squamous neoplasia. Side effects from this drug may be severe and limit compliance.

Biosceptre believes that its topical treatment, BIL010t, has the potential to displace the aforementioned currently marketed products. Its safety was demonstrated in Phase I, where informed consent patients showed a significant efficacy response with no reported side effects. That said, even with available medications, the most common first treatment for BCC is still surgery. Biosceptre believes that its product can be priced in such a way that it could displace surgery as well, potentially creating a much larger market.

Figure 28
COMPETITION: BIL010t

Basal Cell Carcinoma & Squamous Cell Carcinoma

Aldara (Imiquimod)	**Erivedge** (Vismodegib)
Genital wart , actinic keratosis, and BCC (secondary to surgery)	Poor compliance due to side effects (nausea, vomiting, diarrhea, constipation), muscle spasms, fatigue, hair loss, and dysgeusia
2014 sales*	**2015 sales**
$350 million	**~$174 million**

BIL010t
Safety proven in Phase I, Informed Consent Patients showed significant efficacy response with no side effects

**As of 2015, imiquimod is generic and is available worldwide under many brands.*
Source: Company reports.

Odomzo®

Odomzo® (sonidegib), marketed by East Hanover, New Jersey-based Novartis Pharmaceuticals Corporation, is also available to treat patients with locally advanced basal cell carcinoma (aBCC) that has recurred following surgery or radiation therapy, or who are not candidates for surgery or radiation therapy. As a pill taken once a day, the drug works by inhibiting a molecular pathway (called the Hedgehog pathway), which is active in basal cell cancers. Through the suppression of this pathway, Odomzo may stop or reduce the growth of cancerous lesions. Odomzo is the second drug approved by the FDA to treat basal cell carcinoma in the last three years, where in 2012, Erivedge (vismodegib) was the first drug approved to treat locally advanced and metastatic basal cell carcinoma (as described above). Odomzo carries a Boxed Warning that alerts healthcare professionals that the drug may cause death or severe birth defects in a developing fetus when administered to a pregnant woman.

The drug's efficacy was established in a multi-center, double-blind clinical trial, in which 66 patients with locally aBCC were randomly assigned to receive Odomzo 200 mg daily and 128 patients were assigned to receive Odomzo 800 mg daily. The study's primary endpoint was objective response rate [the percentage of patients who experienced partial shrinkage or complete disappearance of their tumor(s)]. Results showed that 58% of patients treated with Odomzo 200 mg had their tumors shrink or disappear. This effect lasted at least 1.9 to 18.6 months, with roughly half of the responding patients' tumor shrinkage lasting six months or longer. Response rates were similar in patients who received Odomzo 800 mg daily, though side effects were more common at this dose.

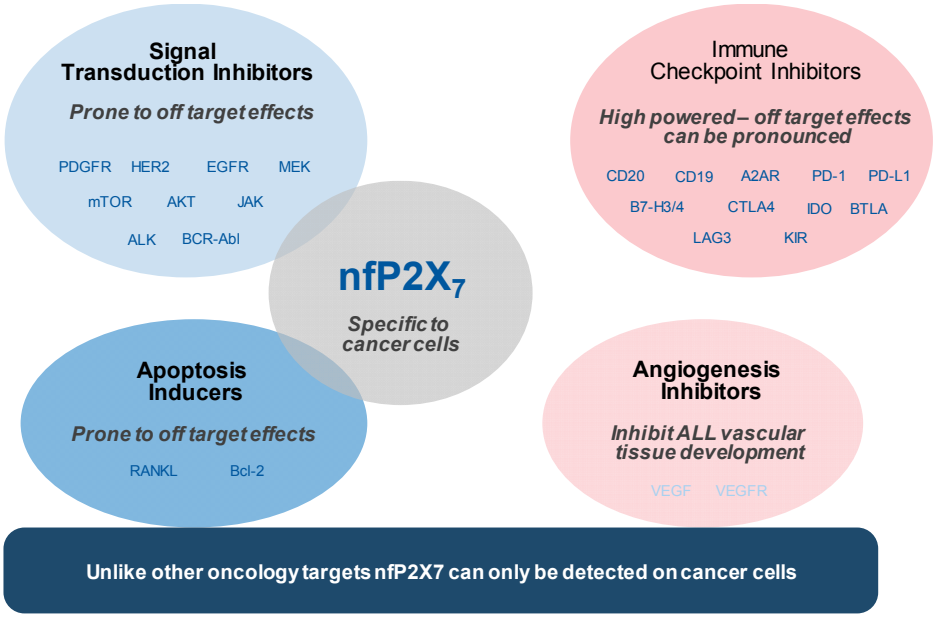
BIL06v

Biosceptre has yet to conduct a comparative analysis on its vaccine as it is still working on how to best compare its product to currently marketed products. According to ClinicalTrials.gov, there are currently 57 open clinical trials either recruiting or likely soon to be recruiting for oncology vaccines. The main benefit that Biosceptre has observed to date is that BIL06v appears to offer the potential of safe activation of the human immune system and holds potential as a companion or combination therapy with other existing cancer therapies.

nfP2X$_7$

Biosceptre has become aware of other companies covering P2X$_7$ in the past and has challenged these third-party positions, resulting in a cessation of patent activity by those parties. Figure 29 illustrates the other types of oncology targets either in development and/or available on the market. Unlike many other oncology targets, to Biosceptre's knowledge, nfP2X$_7$ can only be detected on cancer cells, and unlike most targets, nfP2X$_7$ has been successfully protected via patent.

Figure 29
NFP2X$_7$ AND OTHER ONCOLOGY TARGETS



Source: Biosceptre International Limited.

Historical Financial Results

Figures 30, 31, and 32 summarize Biosceptre's key historical financial statements: its Income Statement, Balance Sheet, and Cash Flow Statement (prepared under UK GAAP). Certain financial figures have been rounded as applicable, unless otherwise stated. Such figures should be considered as approximate figures. These financial statements have been furnished to Crystal Research Associates by Biosceptre.

Figure 30
Biosceptre Group of Companies
INCOME STATEMENT

	30-Jun-14	30-Jun-15
	GBP £	GBP £
Administrative Expenses	(7,900,358)	(3,039,136)
Other Operating Income	-	880,695
Operating Loss	(7,900,358)	(2,158,441)
Interest & Similar Income	34,109	6,128
Loss before taxation	(7,866,249)	(2,152,313)
Income tax (expense)/income	1,024,268	1,380,364
Loss for the year	**(6,841,981)**	**(771,949)**

Source: Biosceptre International Limited.

Figure 31
Biosceptre Group of Companies
BALANCE SHEET

	30-Jun-14	30-Jun-15
	GBP £	GBP £
ASSETS		
Fixed Assets	972,402	922,669
Intangible Assets	738,038	541,070
Tangible Assets	1,710,440	1,463,739
Total Fixed Assets		
Current Assets	1,030,174	1,466,581
Debtors	1,119,793	1,899,824
Cash at bank	2,149,967	3,366,405
Total Current Assets		
Less Liabilities	(2,139,542)	(779,507)
Creditors	**1,720,865**	**4,050,637**
NET ASSETS		
EQUITY	36,568	40,533
Issued Share Capital	2,925,946	7,425,729
Share Premium Account	(318,688)	(1,162,520)
Foreign Exchange Reserve	20,536,575	20,536,575
Merger Reserve	(21,459,536)	(22,789,680)
Profit and Loss Account	**1,720,865**	**4,050,637**
SHAREHOLDER FUNDS		

Source: Biosceptre International Limited.

Figure 32
Biosceptre Group of Companies
STATEMENT OF CASH FLOWS

	30-Jun-14	30-Jun-15
	GBP £	GBP £
Cash flows from Operating activities		
Receipts	-	115,060
Payments to suppliers and employees	(7,050,873)	(3,419,495)
R&D tax concession offset	1,344,155	860,187
Net cash used in operating activities	(5,706,718)	(2,444,248)
Cash flows from investing activities		
Payments for property, plant & equipment	(640,535)	(36,977)
Payment for intangible assets	(194,828)	(144,145)
Interest received	34,109	6,128
Net cash used in investing activities	(801,254)	(174,994)
Cash flows from financing activities		
Shareholder advances received (repaid)	1,104,476	(1,104,476)
Proceeds from issues of equity securities	3,692,807	4,503,748
Net cash provided by financing activities	4,797,283	3,399,272
Net increase (decrease) in cash	(1,710,690)	780,031
Cash at beginning of the financial year	2,830,483	1,119,793
Cash at the end of the financial year	1,119,793	1,899,824

Source: Biosceptre International Limited.

Risks and Disclosures

This Executive Informational Overview® (EIO) has been prepared by Biosceptre International Limited ("Biosceptre" or "the Company") with the assistance of Crystal Research Associates, LLC ("CRA") based upon information provided by the Company. CRA has not independently verified such information. Some of the information in this EIO relates to future events or future business and financial performance. Such statements constitute forward-looking information within the meaning of the Private Securities Litigation Act of 1995. Such statements can only be predictions and the actual events or results may differ from those discussed due to the risks described in Biosceptre's public statements.

The content of this report with respect to Biosceptre has been compiled primarily from information available to the public released by the Company. Biosceptre is solely responsible for the accuracy of this information. Information as to other companies has been prepared from publicly available information and has not been independently verified by Biosceptre or CRA. Certain summaries of activities and outcomes have been condensed to aid the reader in gaining a general understanding. CRA assumes no responsibility to update the information contained in this report. In addition, CRA's compensation is a cash amount of thirty-five thousand U.S. dollars and three hundred thousand options for its services in creating this report and for updates. Investors should carefully consider risks and information about Biosceptre's business and should not interpret the order in which considerations are presented in this or other filings as an indication of their relative importance. Additional risks and uncertainties not presently known to Biosceptre or that it currently believes to be immaterial may also adversely affect its business. If any of such risks and uncertainties develops into an actual event, Biosceptre's business, financial condition, and results of operations could be materially adversely affected, and the trading price of the Company's shares could decline.

There are many factors, both specific to Biosceptre and of a general nature, that may influence or affect the future operating and financial performance of the Company, the industry in which it operates, and the outcome of a potential investment in Biosceptre. Many of these factors remain beyond the control of Biosceptre. There can be no guarantee that Biosceptre will achieve its stated objectives or that forward-looking statements will be realized.

This section describes key, but not all, risks associated with a potential investment in Biosceptre. This section does not take into account the investment objectives, financial situation, taxation position, or particular needs of a potential investor and is not exhaustive. Potential investors should carefully consider the risk factors discussed in this section and as well further seek independent professional advice. Thus, this report is published solely for information purposes and is not to be construed as an offer to sell or the solicitation of an offer to buy any security in any state. Past performance does not guarantee future performance. Additional information about Biosceptre and its public filings, as well as copies of this report, can be obtained by calling + 44 1223 496 090.

General Risk Factors

Factors such as inflation, interest rates, levels of tax, taxation law and accounting practices, government legislation or intervention, natural disasters, social upheaval, industrial disruption, and war may have an impact on prices, operating costs and market conditions generally. Accordingly, Biosceptre's future revenue and operations can be affected by these factors, which are beyond the control of Biosceptre.

General Economic Conditions

Factors such as, but not limited to, domestic and international political changes, interest rates, exchange rates, inflation levels, commodity prices, industrial disruption, environmental impacts, international competition, taxation changes, and changes in employment levels and labor costs may all have an adverse impact on Biosceptre UK's revenues, operating costs, profit margins, and share price.

Regulatory and Legislative Changes

Changes in laws, regulations, and government policy may affect Biosceptre and the attractiveness of a potential investment in Biosceptre. The biotech sector in which Biosceptre operates is subject to extensive legislation, regulation, and supervision by a number of regulatory bodies in multiple jurisdictions. The regulatory regimes governing the business activities of Biosceptre are complex and subject to change. The impact of future regulatory and legislative change to the business of Biosceptre cannot be predicted. In addition, if the amount and complexity of new regulation increases, so too may the cost of compliance and the risk of non-compliance. Revenue and expenditure of Biosceptre may be affected by changes in international, federal, state, or local government laws, regulations or policies, or in taxation legislation. Government legislation and policies are subject to periodic review and revision. Such changes are beyond the control of Biosceptre and may affect industry profitability. Tax legislation and practice is subject to change, and it is possible that in the future, tax rules may be amended in ways that may be detrimental to Biosceptre. This may include changes to the "patent box" tax regime, research and development tax incentives, and the Enterprise Investment Scheme.

Competition in the Biotech Sector

Over the last decade, the oncology market has seen a significant transformation away from cytotoxic therapies and anti-hormonal therapies toward the more lucrative targeted therapies class. This class includes several of the top-selling anticancer brands and has fueled much of the recent rapid growth of the oncology market as a whole. Such targeted therapies are capable of acting on unique targets in cancer cells. The increased selectivity offered by these targets presents drug developers with the opportunity to develop drugs with greater efficacy and improved toxicity profiles. As a growing number of companies strive to enter this space, competition will inevitably become more intense as more therapeutics in this class reach the market.

Development Risk

Development risk is the risk that a company will invest in research and development that does not create valuable intangible assets. This is the primary risk facing the biotech industry. The probability of success in achieving regulatory approval for a biologic new molecular entity in preclinical development has been estimated at 11% based on the latest data provided by members of the Pharmaceutical Benchmarking Forum. As a candidate drug passes through each phase of development, the risk decreases as more data and evidence is accumulated on the safety and efficacy of the drug. However, unless the Company is able to achieve orphan drug status with early marketing approval after Phase II, it is not usually until the large-scale Phase III trials are completed that sufficient evidence is available to support a regulatory filing for approval to market a drug. Even then, there is still a significant risk that the regulatory authorities will reject the application or restrict the usage for which the drug is approved (see Regulatory Risk on page 45). There are many potential new targets for cancer drug therapy but most are speculative and very few will make it to a marketable drug. In order to be successful, Biosceptre will need to develop a drug that offers a benefit over existing cancer therapies (improved efficacy) and can be used safely. Even if there is no expression of nf$P2X_7$ on normal cells, non-specific binding of antibodies may create non-target effects that cannot be underestimated. Another technical risk is loss of the target on cancer cells (i.e., antibody candidate drugs failing to kill all cancerous cells). The translation of Biosceptre's technology to human therapeutics and diagnostics is a major challenge, where many of the hurdles cannot be forecasted.

Funding Risk

Funding risk is the risk that a company experiences when it cannot raise the capital required to run its business (e.g., develop new products). In order to undertake the necessary development activities, including clinical trials, Biosceptre will need to find new sources of funding. Biotech has been affected by a lack of investment funds in recent years following the economic crisis. Failure to raise the funds necessary for development, or having funding withdrawn for failure to meet milestones, is a significant risk. In the event that Biosceptre cannot raise the funds necessary, it may be pushed into a forced sale and/or license of the technology, which may not result in a significant premium for the technology, given the relative bargaining power of the parties. Biosceptre's exposure will increase as it further invests in research and development; however, the ability to raise funding should improve if the results in clinical trials are positive.

Regulatory Risk

Regulatory risk is the risk that a company does not meet regulatory standards governing its business or its products and is therefore unable to gain approval to market its products, has existing products withdrawn from the market, or becomes liable to fines and/or loses its license to operate. The pharmaceutical industry is highly regulated. Regulatory approvals are needed to conduct clinical trials in humans (IND or CTA applications) and to market and sell a drug for a specific indication (NDA or BLA applications). The FDA and other national regulatory bodies may (and in practice do) reject IND and NDA/BLA applications on safety grounds and in the case of NDA/BLA applications on scientific and economic grounds. In addition to the risk of not securing regulatory approval for a drug (which amplifies the development risks described above), in some cases, the regulator will request additional trials if there is doubt as to safety or efficacy of the drug. This type of delay could significantly increase the investment required by Biosceptre to launch a drug with no guarantee of a positive regulatory outcome. The delay also reduces the period of patent protection post launch, which can devalue the drug. Once a drug is approved by regulatory authorities, there are further risks relating to the price at which the drug can be sold, safety warnings that must be displayed on the drug label, and whether regulatory authorities withdraw a previously issued license.

A simple example of a safety warning risk would be if there was a warning not to use a drug in conjunction with aspirin. This could significantly limit the usage of a drug and as a result its commercial value. Pricing risks are covered under “product price risk” below; however, it should be noted that negotiating prices with governmental authorities can, in some instances, delay commercialization by 12 months or more. If evidence of adverse safety issues or lack of clinical benefit emerges after the launch of a drug, this can result in the regulatory authorities taking action to have the drug withdrawn from the market. There are instances where the pharmaceutical company voluntarily withdraws the product and instances where the regulatory authority withdraws the approval.

Biologic drugs are the result of complex manufacturing processes, which are highly regulated. Good Manufacturing Practices (GMP) are extensive regulations governing manufacturing processes, stability testing, record keeping, and quality standards as defined by the FDA and the European Medicines Agency with similar regulations in effect in other jurisdictions. Evidence of GMP compliance must be provided to the regulatory authorities as part of the approvals processes. Post approval, regulators will continue to audit compliance with the regulations and may shut down manufacturing facilities that they believe do not comply with regulations. There are also strict regulations that apply to the marketing of prescription pharmaceuticals and there have been a number of large fines and settlements involving major pharmaceutical companies in recent years relating to alleged improper conduct of sales and marketing personnel.

Product Liability Risk

Product liability risk refers to the risk of claims caused by defective products. The testing, manufacturing, marketing, and use of drugs, as well as candidate drugs in development, involve substantial risk of product liability claims. These claims may be made directly by consumers, healthcare providers, pharmaceutical companies, or others. The financial exposure associated with product liability claims can be very high. There may be significant negative publicity associated with any product liability claims, regardless of their merit, which may decrease the future demand for a company’s products and impair its goodwill.

Product liability is generally managed through the following actions:

(1) protocols governing the conduct of preclinical trials prior to testing in humans;

(2) protocols governing the conduct of clinical trials in humans;

(3) external regulatory review and interventions with respect to the above;

(4) conducting extensive clinical trials prior to commercializing a drug;

(5) conducting follow-on, post-launch studies to gather additional data, including the effects of long-term usage; and

(6) strict quality assurance and other control procedures that support adherence to GMP.

The level of risk to which Biosceptre is exposed will depend on the extent to which it is able to obtain product liability insurance and the coverage obtained. In recent years, coverage and availability of cost-effective product liability insurance has decreased. Biosceptre may therefore be unable to maintain full coverage for product liabilities that could arise including the legal costs associated with defending lawsuits.

Outsourcing Risk

It is likely that Biosceptre will extensively outsource development activities, typically performing only the start-up activities in-house and providing strategic control and oversight of the contractors. Reliance will be placed on independent third-party contract research organizations (CROs) to perform most of the clinical studies, including document preparation, site identification, screening and preparation, pre-study visits, training, program management, and bioanalytical analysis. Reliance will also be placed on independent third-party contract manufacturing organizations (CMOs) for production of antibodies and developing commercial-scale manufacturing capabilities. This outsourcing carries a number of general risks, including those listed below:

(1) Biosceptre may be unable to control the resources its contractors devote to its development programs;

(2) disputes may arise with respect to the ownership of rights to technology or other intellectual property developed with the contractors;

(3) disagreements may arise with the contractors that could cause delays in, or termination of, the research, development, or commercialization of product candidates or result in expensive litigation or arbitration; and

(4) contracts with contractors may fail to provide significant protection or may fail to be effectively enforced if one of these contractors fails to perform.

Clinical Trials Outsourcing

Many important aspects of the services performed for Biosceptre by the CROs will be out of its direct control. If there is any dispute or disruption in the relationship with the CROs, clinical trials may be delayed. In addition, Biosceptre will place reliance on the quality and validity of the clinical work performed by third-party CROs in regulatory submissions. If any of the CROs' processes, methodologies, or results are determined to be invalid or inadequate, Biosceptre's own clinical data and results and related regulatory approvals could be adversely impacted.

Manufacturing Outsourcing

Third-party manufacturers are independent entities who are subject to their own unique operational and financial risks, which are out of the Company's control. If these third-party manufacturers fail to perform as required, this could impair Biosceptre's ability to deliver products on a timely basis or cause delays in clinical trials and applications for regulatory approval. In addition, third-party manufacturers may only be able to produce some of Biosceptre's products at one or a limited number of facilities and, therefore, have limited manufacturing capacity for certain products. Production capacity constraints or unplanned plant shutdowns may lead to loss of revenues or delays in development. The contractual terms agreed with the CMOs will determine how this risk is allocated but it can be expected that Biosceptre will have some exposure to supply chain risks. Further, substantial fixed asset investments may be required by the CMO to produce materials on behalf of Biosceptre and Biosceptre may be required to bear this investment risk under the contractual terms with the CMO.

Sales, Marketing, and Distribution Outsourcing

Biosceptre may also rely on third-party distributors and other commercial partners to commercialize new products. If these third-party sales, marketing, and distribution partners fail to perform as required, this could impair Biosceptre's ability to deliver products on a timely basis or cause delays in sales.

Product Price Risk

Product price risk is the risk that values of future income streams are sensitive to external market prices or market rates. Accordingly, it is the risk that a company will not be able to sell a product for the price it originally thought it would be able to charge. In many international markets, governments control the prices of prescription pharmaceuticals, including through the implementation of reference pricing, price cuts, rebates, revenue-related taxes, and profit control, and they expect prices of prescription pharmaceuticals to decline over the life of the product or as volumes increase. In practice, products tend to be subject to significant discounts from list price and rebate obligations. Government pricing policies may adversely affect Biosceptre's ability to sell its products on a profitable basis.

In the U.S., the EU, and other significant markets, government authorities and third-party payers are increasingly attempting to limit or regulate the price of medical products and services, particularly for new and innovative products and therapies, which has resulted in lower average selling prices. However, cancer drugs have tended to have very high prices and high profit margins (excluding costs of research and development). It would be unusual for approved oncology drugs to be sold on a non-profitable basis overall. The most significant risk around price regulation is whether the margins are sufficient to enable the developer to recover its investments in research and development.

Market Risk

A company incurs market risk when it is adversely affected by cyclical or structural changes in its industry. Demand for a company's products could be affected for a number of reasons including the following:

(1) new entrants to the market which shift demand (substitute products could enter the market that are cheaper and may be just as effective);

(2) alternative products and changes in fashion; and

(3) new evidence as to the effectiveness of the product.

Sensitivity to Macro-Economic Factors

Demand for drugs treating serious diseases, such as cancer, is not generally impacted significantly by macro-economic cycles. However, the prices that those drugs command in the market (and therefore revenues) are sensitive to macroeconomic change. Recently, many countries in the EU have increased the amount of discounts required on pharmaceutical products, and these efforts are likely to continue as many European countries attempt to deal with the legacy of the severe fiscal and debt crises by exercising greater control and discipline over healthcare expenditures, including drug costs.

For example, in June 2010, Spain imposed an incremental discount on all branded drugs, and in August 2010, Germany increased the rebate on prescription pharmaceuticals. Further, cost containment pressures in the EU could lead to delays in the treatment of patients and also delay pricing approval, which could negatively impact the commercialization of new products. U.S. market dynamics have also been affected by the recent economic downturn.

Pharmaceutical companies have seen shifts in the payer mix in the U.S. as patients previously covered by private insurance moved to public reimbursement programs that require rebates or discounts on the price of the drugs (i.e., there have been shifts toward lower margin sales channels). The increased emphasis on managed healthcare in the U.S. and on country and regional pricing and reimbursement controls in the EU is likely to continue to keep downward pressure on product pricing, which will impact sales and profitability. There is a risk therefore that macro-economic factors will influence the price at which Biosceptre can command for any drugs developed using its technology.

Structural Changes Impacting the Market

There are a number of structural changes impacting the pharmaceutical market, including the following:

(1) shift in emphasis toward high growth "pharmerging" markets, which tend to be high volume but lower price and may have weaker intellectual property law and enforcement;

(2) development of biosimilar market and regulatory pathways;

(3) healthcare reforms resulting in greater payer influence, outcome-based reward for drug companies;

(4) increased use of generics;

(5) personalized healthcare;

(6) new business models (i.e., virtual research and development);

(7) shift in research base toward Asia and improvements in remote monitoring; and

(8) increased externalization, including collaboration between pharmaceutical companies, biotech firms, academia, and public research institutions.

These structural changes could have wide-ranging implications, including the following:

(1) drug companies will be paid for outcomes not products;

(2) curative and preventative treatments will gain a higher profile;

(3) more flexible pricing strategies will be needed;

(4) drug companies will need to gain access to outcomes data and demonstrate "real" value for money;

(5) drug companies will need to work more closely with regulators in an environment of increasing scrutiny;

(6) drug companies will need to collaborate with payers and providers to perform continuous trials;

(7) drug companies will need a stronger base in Asia;

(8) increased use of generics and biosimilars; and

(9) increased patent and intellectual property challenges.

The key risks associated with these changes for Biosceptre are considered to be the following:

(1) products fail to achieve regulatory approval;

(2) research and development and other operating costs are higher than projected (e.g., due to regulatory delay or additional trials or patent defense costs); and

(3) drug prices and/or sales volumes are lower than projected.

Legal Risk

Patents are a critical component of Biosceptre's business. Future success will depend to a significant degree on being able to accomplish the following:

(1) obtain patents and potentially obtaining licenses to others' patent rights;

(2) preserve confidential information and know-how;

(3) successfully defend infringement and efforts to invalidate Biosceptre's patents; and

(4) operate without infringing the property of others.

As part of Biosceptre's business strategy, it actively seeks patent protection in the major jurisdictions in which it would expect to commercialize products, and will file additional patent applications, when appropriate, to cover improvements in compounds, products, and technology. Biosceptre cannot be certain that issued patents will be enforceable or provide adequate protection or that pending patent applications will result in issued patents. Competitors may have filed patent applications or received patents and may obtain additional patents and proprietary rights that block or compete with Biosceptre's products. In addition, if competitors file patent applications covering Biosceptre's technology, Biosceptre may have to participate in litigation to determine the right to a patent. Litigation is unpredictable and expensive, such that, even if Biosceptre is ultimately successful, its financial results may be adversely affected by such events.

Patent challenges from generic companies are common for blockbuster drugs. Disputes can also arise with inventors and investors in relation to the ownership of patents. While risks are significant and must be managed carefully by Biosceptre, the nature of the technology and the fact that Biosceptre Australia has been able to patent broad groups of products (i.e., antibody families) in major territories (e.g., the U.S., Japan, and the EU) should mean Biosceptre may enjoy a higher degree of protection than companies with only product-specific patents. Clinical trials data protection and market exclusivity rights all provide an important form of protection for first-to-market biologic drugs.

Speculative Investment

The aforementioned risks should not be taken as an exhaustive compilation of the risks faced by Biosceptre or by potential investors in Biosceptre. These factors, and others not specifically referred to herein, may in the future materially affect the financial performance of Biosceptre and the enterprise value of the Company. Potential investors should consider that an investment in Biosceptre is speculative and should consult their professional advisers before deciding whether to express an interest.

Glossary

Adenosine Triphosphate (ATP)—A nucleoside triphosphate used in cells as a coenzyme often called the "molecular unit of currency" of intracellular energy transfer. ATP transports chemical energy within cells for metabolism.

Antibody (Ab)—Also known as an immunoglobulin (Ig), an antibody is a large, Y-shaped protein produced mainly by plasma cells that is used by the immune system to identify and neutralize pathogens such as bacteria and viruses.

Apoptosis—From Ancient Greek for "falling off," apoptosis is a process of programmed cell death that occurs in multicellular organisms.

Basket Trial—A new and evolving form of clinical trial design that is predicated on the hypothesis that the presence of a molecular marker predicts a response to a targeted therapy independent of tumor histology.

Cytostatic—Inhibiting or suppressing cellular growth and multiplication. Many cancer drugs aim to kill cancer cells. The word cytotoxic means toxic to cells, or cell killing. Chemotherapy is cytotoxic, not cytostatic, therapy.

Cytotoxic—Toxic to living cells.

Dalton—A unit used in expressing the molecular weight of proteins, equivalent to atomic mass unit.

Endocytosis—Endocytosis is the process of capturing a substance or particle from outside the cell by engulfing it with the cell membrane, and bringing it into the cell. Exocytosis describes the process of vesicles fusing with the plasma membrane and releasing their contents to the outside of the cell.

Epitope—Also known as antigenic determinant, it is the part of an antigen that is recognized by the immune system, specifically by antibodies, B cells, or T cells.

Follicular Lymphoma—A type of non-Hodgkin lymphoma that develops when the body makes abnormal B-lymphocytes—the lymphoma cells. (B-lymphocytes are white blood cells that fight infection.) The lymphoma cells build up in lymph nodes. The most common symptom is a painless swelling in the neck, armpit, or groin.

Lead Compounds—A peptide, small molecule, or other agent with pharmacological or biochemical properties that suggest it may have therapeutic potential and value as a starting point for drug development.

Monoclonal Antibody (mAb)—Monospecific antibodies that are made by identical immune cells that are all clones of a unique parent cell, in contrast to polyclonal antibodies, which are made from several different immune cells.

Non-melanoma Skin Cancers—All the types of cancer that occur in the skin that are not melanoma. Several types of skin cancer fall within the broader category of non-melanoma skin cancer, with the most common types being basal cell carcinoma (BCC) and squamous cell carcinoma (SCC).

Paracrine—Of, relating to, or denoting a hormone that has effect only in the vicinity of the gland secreting it.

Peptide—Biologically occurring short chains of amino acid monomers linked by peptide (amide) bonds.

Precision Medicine—A medical model that proposes the customization of healthcare, with medical decisions, practices, and/or products being tailored to the individual patient.

Prostate-Specific Antigen (PSA)—An antigenic enzyme released by the prostate and found in abnormally high concentrations in the blood of men with prostate cancer.

Specificity—In medical diagnosis, test sensitivity is the ability of a test to correctly identify those with the disease (true positive rate), whereas test specificity is the ability of the test to correctly identify those without the disease (true negative rate).

Squamous Cell Carcinoma (SCC)—Also called squamous-cell cancer (SCC or SqCC), SCC is a cancer of a kind of epithelial cell, the squamous cell. These cells are the main part of the epidermis of the skin, and this cancer is one of the major forms of skin cancer.

Therapeutic Goods Administration (TGA)—The regulatory body for therapeutic goods in Australia.

Titers—A way of expressing concentration. Titer testing employs serial dilution to obtain approximate quantitative information from an analytical procedure that inherently only evaluates as positive or negative. The titer corresponds to the highest dilution factor that still yields a positive reading.

Trimer—In chemistry, a reaction product composed of three identical molecules.

Vascular Endothelial Growth Factor (VEGF)—Originally known as vascular permeability factor (VPF), VEGF is a signal protein produced by cells that stimulates vasculogenesis and angiogenesis.

Waterfall Plot—Often used in oncology clinical trials for a graphical representation of the quantitative response of each subject to treatment.

crystal research associates

Facts Without Fiction

EXECUTIVE INFORMATIONAL OVERVIEW®

About Our Firm: For the past decade, Crystal Research Associates, LLC (www.crystalra.com) has successfully articulated the exceptional stories of small- and mid-cap companies to the Wall Street investor community. Our methods are well-established and diverse, from compiling and disseminating objective, factual information for both institutional and retail investor audiences to capitalizing on our expansive line of targeted distribution channels, which include industry-leading financial data and information providers. Our distribution efforts are accompanied by the use of prominent social media channels and by strategic and targeted appearances on national news programs and print media.

Crystal Research Associates is led by Wall Street veterans, Jeffrey Kraws and Karen Goldfarb. Together, Kraws and Goldfarb have built a unique business model, capitalizing on decades of experience as an award-winning sell-side analyst team to produce institutional-quality industry and market research in a manner that is easily understood by investors and consumers. Our firm's approach has been proven successful over the years as our products are published and available on Bloomberg, Thomson Reuters/First Call, S&P Capital IQ, FactSet, Yahoo! Finance, and scores of other popular forums.

880 Third Avenue, 6th Floor, New York, NY 10022 Office: (212) 851-6685