

## **INDEPENDENT EXPERT'S REPORT AUGUST 2010**

**Melbourne, Australia; 27 August 2010:** Attached is the signed Deloitte Independent Expert's Report as distributed to shareholders.

#### **About Mesoblast Limited**

Mesoblast Limited (ASX:MSB; ADR:MBLTY) is a world leader in commercialising biologic products for the bro field of regenerative medicine. Mesoblast has the worldwide exclusive rights for a series of patents and technologies developed over more than 10 years relating to the identification, extraction, culture and uses of adult Mesenchymal Precursor Cells (MPCs). www.mesoblast.com

For further information, please contact:

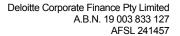
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# Deloitte.

Mesoblast Limited Independent expert's report August 2010





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# Financial services guide

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Independent Directors Mesoblast Limited Level 39 55 Collins Street Melbourne VIC 3000

10 August 2010

**Dear Directors** 

# **Independent expert's report**

### Introduction

On 12 May 2010, the independent directors of Mesoblast Limited (Mesoblast) and Angioblast Systems, Incorporated (Angioblast) announced a proposed merger, whereby Mesoblast will acquire all of the ordinary shares in Angioblast that it does not already own (the Proposed Transaction). Mesoblast and Angioblast have entered into a merger implementation agreement (MIA) which sets out the obligations of both companies in relation to the implementation of the Proposed Transaction.

Under the Proposed Transaction, Mesoblast will issue a total of 94,590,000 Mesoblast shares (the Scrip Consideration) to acquire all shares held by shareholders of Angioblast other than Mesoblast (Angioblast Shareholders). Angioblast Shareholders also have the right to elect to receive cash in respect of up to 15% of their shareholding, with reference to the price of a Mesoblast share on the date of approval by shareholders of Mesoblast (the 15% Cash Option). If the Proposed Transaction proceeds, convertible noteholders of Angioblast (Convertible Noteholders) will convert their notes into shares in Angioblast in accordance with the convertible note deed and subsequently exchange their shares in Angioblast for shares in Mesoblast shares in accordance with the Proposed Transaction.

On 2 June 2010, Mesoblast invited the Convertible Noteholders to tender their convertible notes in Angioblast directly to Mesoblast for purchase (the Convertible Note Offer). If the Convertible Noteholders take up the Convertible Note Offer and Mesoblast chooses to accept their respective tenders, the Convertible Noteholders will receive the same number of Mesoblast shares as if the convertible notes were converted into Angioblast shares and acquired by Mesoblast under the Proposed Transaction.

As the Convertible Note Offer has no impact on our assessment of the Proposed Transaction, we have assumed that the Convertible Noteholders do not pursue the Convertible Note Offer.

Mesoblast currently owns 32.6% of Angioblast (on a fully diluted basis), and the companies share a common significant shareholder (Professor Silviu Itescu) and common directors (Professor Itescu and Donal O'Dwyer). Accordingly, Mesoblast and Angioblast are related parties for the purposes of the Corporations Act 2001 (Cth) (the Corporations Act).

The independent directors of Mesoblast (the Independent Directors) have requested Deloitte Corporate Finance Pty Limited (Deloitte Corporate Finance) to prepare an independent expert's report advising whether the Proposed Transaction is fair and reasonable from the perspective of the shareholders of Mesoblast that are not associated with Angioblast (the Non-Associated Shareholders).

The Independent Directors have prepared a notice of meeting (the Mesoblast Notice of Meeting) containing the detailed terms of the Proposed Transaction. An overview of the Proposed Transaction is set out in Section 1 of our detailed report. The Proposed Transaction is subject to the approval of the Non-Associated Shareholders at an extraordinary general meeting (EGM) to be held on [x] 2010.

Upon completion of the Proposed Transaction, which is expected to be in August 2010, Angioblast will become a wholly owned subsidiary of Mesoblast.

## Purpose of the report

This independent expert's report is required pursuant to Chapter 10 of the Listing Rules of the Australian Securities Exchange (ASX Listing Rule 10) and Chapter 2E and Section 611 of the Corporations Act to assist the Non-Associated Shareholders in their decision whether to vote in favour of the Proposed Transaction.

In evaluating whether the Proposed Transaction is fair and reasonable to the Non-Associated Shareholders we have considered ASX Listing Rule 10, Chapter 2E and Section 611 of the Corporations Act, the Australian Securities and Investments Commission (ASIC) Regulatory Guides and common market practice.

This report is to be included in the Mesoblast Notice of Meeting prepared for the EGM, where the approval from the Non-Associated Shareholders will be sought for the Proposed Transaction. We are not responsible to you, or anyone else, whether for our negligence or otherwise, if the report is used by any other person for any other purpose.

### Section 611 of the Corporations Act

An issue of shares by a company to a shareholder that will increase the shareholder's relevant interest in the company from above 20% to less than 90% is prohibited under Section 606 of the Corporations Act unless the proposed transaction is approved by shareholders at a general meeting, in accordance with item 7 of Section 611 of the Corporations Act.

If the Proposed Transaction is completed, Professor Itescu's shareholding in Mesoblast will increase from 22.9% up to 36.4% (on a fully diluted basis). An independent expert's report is therefore required under Section 611 of the Corporations Act to provide the Non-Associated Shareholders an independent view as to whether the Proposed Transaction is fair and reasonable, and to provide them with sufficient information to make an informed decision as to whether to vote in favour of the Proposed Transaction.

#### ASX Listing Rule 10

ASX Listing Rule 10.1 requires a listed entity to obtain shareholder approval before it acquires a substantial asset from, or disposes of a substantial asset to, an entity that is in a position of significant influence (or a related party) when the consideration to be paid, or the value of the asset, constitutes more than 5% of the equity interest of that entity.

Professor Itescu is considered to be in a position of significant influence, given his directorship and substantial shareholding in both Mesoblast and Angioblast. Professor Itescu's 41.9% shareholding in Angioblast (on a fully-diluted basis) also represents a substantial asset, which will be acquired by Mesoblast if the Proposed Transaction is completed.

Pursuant to ASX Listing Rules 10.1 and 10.10, the listed entity undertaking the transaction must prepare a notice of meeting containing an independent expert's report stating whether the proposed transaction is fair and reasonable to the non-associated shareholders whose votes are not to be disregarded.

The Independent Directors have prepared the Mesoblast Notice of Meeting to be sent to the Non-Associated Shareholders for the purposes of seeking their approval of the Proposed Transaction. Our report is to be included in the Mesoblast Notice of Meeting and has been prepared for the exclusive purpose of assisting the Non-Associated Shareholders in their consideration of the Proposed Transaction. We are not responsible to you, or anyone else, whether for our negligence or otherwise, if the report is used by any other person for any other purpose.

## **Basis of evaluation**

## Section 611 of the Corporations Act

Given that Professor Itescu is a major shareholder in Mesoblast and Angioblast, if the Proposed Transaction is approved his shareholding in Mesoblast will increase from 22.9% to possibly up to 36.4% (on a fully diluted basis). As a consequence, if the Non-Associated Shareholders approve the Proposed Transaction, they are potentially foregoing the opportunity to receive a takeover offer. The resulting effect of the Proposed Transaction on the Non-Associated Shareholders is therefore similar to a scrip takeover bid under Chapter 6 of the Corporations Act.

Accordingly, we have analysed the Proposed Transaction as a control transaction and assessed whether the Proposed Transaction is fair and reasonable to the Non-Associated Shareholders as set out under ASIC Regulatory Guide 111.

In order to assess whether the Proposed Transaction is fair and reasonable to the Non-Associated Shareholders for the purpose of Section 611 of the Corporations Act, we have had regard to the Corporations Act, ASIC Regulatory Guide 111 and common market practice. We have assessed:

- whether the Proposed Transaction is fair by estimating the fair market value of a share in Mesoblast on a control basis before completion of the Proposed Transaction and comparing that value to the estimated fair market value of a share in the proposed merged entity (the Proposed Merged Entity) on a minority interest basis after completion of the Proposed Transaction. The Proposed Transaction is fair if the value of a share in the Proposed Merged Entity on a minority interest basis is greater than the value of a share in Mesoblast on a control basis before the completion of the Proposed Transaction
- the reasonableness of the Proposed Transaction by considering other advantages and disadvantages of the Proposed Transaction to the Non-Associated Shareholders.

## **ASX Listing Rule 10**

In our opinion, the most appropriate basis on which to evaluate whether the Proposed Transaction is fair and reasonable to the Non-Associated Shareholders for the purpose of ASX Listing Rule 10.1, is to consider the overall effect of the Proposed Transaction on the Non-Associated Shareholders, and to form a view as to whether the expected benefits to the Non-Associated Shareholders outweigh any disadvantages that may result from the Proposed Transaction.

In undertaking this analysis, we have assessed the fair market value of Angioblast on a control basis and compared that value with the value of the Scrip Consideration under the Proposed Transaction.

In this context, value is an important element, but not the only element of this assessment. Therefore, we have also considered various other factors relevant to the Proposed Transaction so far as the Non-Associated Shareholders are concerned.

In forming our opinion as to whether the Proposed Transaction is fair and reasonable we have treated the concepts of fairness and reasonableness as a single opinion, that is, the Proposed Transaction is, or is not, fair and reasonable.

# **Summary and conclusion**

We consider that the Proposed Transaction is fair and reasonable and therefore in the best interest of the Non-Associated Shareholders for the purpose of Section 611 of the Corporations Act.

In our opinion, the Proposed Transaction is fair and reasonable to the Non-Associated Shareholders for the purpose of ASX Listing Rule 10.

In arriving at these opinions, we have had regard to the following factors:

# The Proposed Transaction is fair for the purpose of Section 611 of the Corporations Act

Set out in the table below is a comparison of our assessed fair market value of a share in Mesoblast on a control basis before the Proposed Transaction with our assessed fair market value of a share in the Proposed Merged Entity on a minority interest basis.

Table 1: Comparison of a share in Mesoblast and a share in the Proposed Merged Entity

|   | Section | Low value<br>per share<br>(AUD) <sup>1</sup> | High value<br>per share<br>(AUD) |
|---|---------|--|----------------------------------|
| Estimated fair market value of a share in Mesoblast on a control basis                            | 10.4    | 2.20   | 2.55                             |
| Estimated fair market value of a share in the Proposed Merged Entity on a minority interest basis | 11.5    | 2.35   | 2.65                             |

Source: Deloitte Corporate Finance analysis

Note:

1. AUD – Australian dollar.

We have adopted a consistent valuation approach in determining the fair market value of each of Mesoblast, Angioblast and the Proposed Merged Entity. We engaged Acuity Technology Management Pty Limited (Acuity) to prepare separate projected cash flows for Mesoblast and Angioblast and these projected cash flows are discounted using a range of discount rates determined by us to derive values for Mesoblast, Angioblast and the Proposed Merged Entity.

Given that the fair market value of a share in the Proposed Merged Entity on a minority interest basis is above the range of our estimate of the fair market value of a share in Mesoblast on a control basis, the Non-Associated Shareholders are effectively receiving a control value for their shareholding in Mesoblast under the Proposed Transaction. Accordingly, the Proposed Transaction is fair.

## Valuation of a share in Mesoblast

We have estimated the fair market value of a share in Mesoblast on a control basis to be in the range of AUD 2.20 to AUD 2.55, using the discounted cash flow methodology which is summarised in the following table.

Table 2: Valuation of Mesoblast on a control basis

|   | Section | Unit               | Low value | High value |
|---|---------|--------------------|-----------|------------|
| Value of Mesoblast's mesenchymal                              | 10.1.2  | AUD million        | 190.0     | 230.0      |
| precursor cell (MPC) technology                               | 10.1.3  |                    |           |            |
| 32.6% interest in Angioblast                                  | 10.2    | AUD million        | 125.9     | 142.5      |
| Enterprise value (on a control basis)                         |         | AUD million        | 315.9     | 372.5      |
|   |         |                    |           |            |
| Net cash position   | 10.3.1  | AUD million        | 43.7      | 43.7       |
| Equity value (on a control basis)                             |         | <b>AUD</b> million | 359.6     | 416.2      |
|   |         |                    |           |            |
| Number of shares on issue                                     |         |                    |           |            |
| (on a fully diluted basis)                                    | 6.3     | million            | 161.8     | 161.8      |
|   |         |                    |           |            |
| Value of a Mesoblast share                                    |         |                    |           |            |
| (on a control basis)  |         | AUD                | 2.22      | 2.57       |
|   |         |                    |           |            |
| Deloitte Corporate Finance selected value per Mesoblast share |         |                    |           |            |
| (on a control basis)  |         | AUD                | 2.20      | 2.55       |
| (on a control basis)  |         | NOD                | 2.20      | 2.00       |

Source: Deloitte Corporate Finance analysis

To provide additional evidence, we have considered the recent share trading of Mesoblast. Whilst we acknowledge that the shares in Mesoblast are thinly traded, in the absence of any suitable cross checks, we are of the opinion it is relevant to consider the recent share trading in Mesoblast shares. In comparison to the volume weighted average price (VWAP) of Mesoblast shares for the three month period to 30 April 2010<sup>1</sup> of AUD 2.00, our assessed value of a Mesoblast share implies a control premium of 10.0% to 27.5%. Having regard to the control premiums typically paid in transactions involving ASX listed entities, we consider the Mesoblast share price broadly supports our valuation of Mesoblast.

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<sup>&</sup>lt;sup>1</sup> Mesoblast was in a trading halt from 30 April 2010 until 12 May 2010. Therefore, we have considered Mesoblast's VWAP for the period to 30 April 2010.

## Valuation of a share in the Proposed Merged Entity

We have estimated the fair market value of a share in the Proposed Merged Entity on a minority interest basis to be in the range of AUD 2.35 to AUD 2.65.

We have estimated the fair market value of a share in the Proposed Merged Entity using the sum of the parts methodology and based on the all scrip offer, as summarised in the following table.

Table 3: Valuation of the Proposed Merged Entity

| Section | Unit                     | Low value  | High Value   |
|---------|--------------------------|--|--|
|         |                          |  |  |
|         |                          |  | 820.0  |
| 11.3.2  | AUD Million              | 59.3   | 59.3   |
|         | <b>AUD Million</b>       | 779.3  | 879.3  |
| 11.4    |                          | 20%  | 20%  |
|         | AUD million              | 623.5  | 703.5  |
| 6.3     | million                  | 263.2  | 263.2  |
|         | AUD                      | 2.37   | 2.67   |
|         | AUD                      | 2.35   | 2.65   |
|         | 11.2.3<br>11.3.2<br>11.4 | 11.2.3 AUD million 11.3.2 AUD Million AUD Million  11.4  AUD million  6.3 million  AUD | 11.2.3 AUD million 720.0 11.3.2 AUD Million 59.3 AUD Million 779.3  11.4 20%  AUD million 623.5  6.3 million 263.2  AUD 2.37 |

Source: Deloitte Corporate Finance analysis

Based on the above, our assessed value of the Proposed Merged Entity on a minority basis is in the range of AUD 623.5 million and AUD 703.5 million and the value of a share in the Proposed Merged Entity is in the range of AUD 2.35 and AUD 2.65.

The value of the Proposed Merged Entity will vary depending on the extent to which the Angioblast Shareholders elect to receive cash under the 15% Cash Option and the market price of a Mesoblast share on the date of approval by the Non-Associated Shareholders. However, we consider the impact of paying 15% of the consideration in cash on the value of a share in the Proposed Merged Entity to be insignificant.

# The Proposed Transaction is reasonable for the purpose of Section 611 of the Corporations Act

In accordance with ASIC Regulatory Guide 111, a proposed transaction is reasonable if it is fair. On this basis, in our opinion the Proposed Transaction is reasonable. Other advantages and disadvantages of the Proposed Transaction are set out below.

# The Proposed Transaction is fair and reasonable for the purpose of ASX Listing Rule 10

For the purpose of ASX Listing Rule 10, we have considered the overall effect of the Proposed Transaction on the Non-Associated Shareholders.

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**Deloitte Corporate Finance:** Mesoblast Limited – Independent expert's report

In our opinion the Proposed Transaction is fair and reasonable, as the expected benefits of the Proposed Transaction to the Non-Associated Shareholders outweigh any disadvantages that may result from the Proposed Transaction. Our discussion on the advantages and the disadvantages of the Proposed Transaction are set out below.

## **Advantages of the Proposed Transaction**

The likely advantages to the Non-Associated Shareholders if the Proposed Transaction is approved include:

The fair market value of the interest in Angioblast is higher than the fair market value of the Scrip Consideration being offered

Our assessed fair market value of 67.4% interest in Angioblast is in the range of AUD 306.1 million and AUD 346.6 million, which is higher than our assessed value of the Scrip Consideration, which is in the range of AUD 222.3 million and AUD 250.7 million. Our analysis is set out in the table below.

Table 4: Comparison of the value of 67.4% of Angioblast and the value of the Scrip Consideration

|   | Section | Unit        | Low value | High value |
|---|---------|-------------|-----------|------------|
| Estimated fair market value of Angioblast on a control basis                  | 9.3     | AUD million | 454.2     | 514.2      |
| Estimated fair market value of 67.4% of Angioblast on a control basis         |         | AUD million | 306.1     | 346.6      |
| Value of a share in the Proposed Merged Entity (on a minority interest basis) |         | AUD         | 2.35      | 2.65       |
| Number of Mesoblast shares offered  |         | million     | 94.6      | 94.6       |
| Estimated fair market value of the Scrip Consideration                        |         | AUD million | 222.3     | 250.7      |

Source: Deloitte Corporate Finance analysis

We have estimated the fair market value of Angioblast on a control basis using the discounted cash flow methodology, as summarised in the following table.

Table 5: Valuation of Angioblast on a control basis

|   | Section | Unit        | Low value | High value |
|---|---------|-------------|-----------|------------|
| Value of Angioblast's MPC technology <sup>1</sup> | 9.1.3   | AUD million | 450.0     | 510.0      |
| Net cash position <sup>1</sup>                    | 9.2.3   | AUD million | 4.2       | 4.2        |
| Equity value (on a control basis)                 | 9.3     | AUD million | 454.2     | 514.2      |

Source: Deloitte Corporate Finance analysis

Note:

1. Converted to AUD based on the spot United States dollar (USD)/AUD exchange rate of 0.86.

## The Proposed Merged Entity will be more diversified than Mesoblast

Mesoblast is currently a small biotechnology company focusing on the development of the MPC technology for orthopaedic applications, with a significant holding in Angioblast. If the Proposed Transaction is approved, the Proposed Merged Entity will have:

- a more diversified portfolio of products than that of Mesoblast on a standalone basis.
   The Proposed Merged Entity will have the right to develop the MPC technology for a wider spectrum of applications, including cardiovascular diseases and orthopaedic and non-orthopaedic conditions
- a larger portfolio of products than Mesoblast has as a standalone company. The probability of the Proposed Merged Entity receiving Food and Drug Administration (FDA) approval for at least one product from a larger portfolio of products will be higher than that for Mesoblast
- access to the market potential within much larger therapeutic markets, being the cardiovascular disease market and other non-orthopaedic markets held by Angioblast
- the ability to operate as one company with a common research and development (R&D) strategy. The Proposed Merged Entity will have improved ability to consolidate and prioritise its R&D efforts and allocate funding towards key products to achieve an optimal outcome for the shareholders to a greater extent than Mesoblast and Angioblast can as separate entities
- the ability to potentially achieve a better bargaining position when conducting commercial negotiations with the major pharmaceutical companies as it will be able to execute a negotiation strategy across the entire range of products.

### The Proposed Merged Entity should have increased scale

The Proposed Merged Entity is likely to have a market capitalisation in excess of AUD 500 million. The increased market capitalisation of the Proposed Merged Entity and enlarged shareholder base may attract greater analyst coverage and may enhance the profile of the Proposed Merged Entity with institutional investors. These factors should provide increased liquidity and greater trading depth than that currently experienced by the current holders of Mesoblast shares. This may also result in a positive re-rating of shares in the Proposed Merged Entity.

As a result of the increased market capitalisation, the Proposed Merged Entity may have improved access to capital markets on possibly more attractive terms compared with those currently available to Mesoblast.

#### The Proposed Merged Entity will have improved market transparency

Currently, Angioblast is a United States (US) based private company with limited disclosure requirements compared to Mesblast, which is listed on the ASX. The limited understanding of and transparency around the operations of Angioblast may have historically limited access to capital by Angioblast. Angioblast has been reliant on Mesoblast to provide the necessary capital for its operations.

Given that its investment in Angioblast is a key asset of Mesoblast, the value of Mesoblast may have been adversely affected by the lack of transparency associated with the investment in Angioblast.

If the Proposed Transaction is approved, the Proposed Merged Entity will continue to be required to meet its continuous disclosure obligations with the ASX with respect to any major operating activities and clinical trial results, including those of Angioblast. Greater transparency should assist market participants better understand Angioblast's activities, which may enhance the trading price of shares in the Proposed Merged Entity.

# Disadvantages of the Proposed Transaction Professor Itescu's interest in Mesoblast will increase

Currently, the Non-Associated Shareholders hold 76.7% of Mesoblast, whilst Professor Itescu holds 22.9% and Mr O'Dwyer holds 0.4% of Mesoblast (on a fully diluted basis).

If the Proposed Transaction is approved, Professor Itescu's shareholding will increase by 11.6% to approximately 34.5% and possibly up to 36.4% (on a fully diluted basis). The increase in Professor Itescu's shareholding of between 11.6% and 13.5% could reduce the likelihood of a potential takeover offer in the future.

However, given Professor Itescu already has a significant interest in Mesoblast before the Proposed Transaction, and his stake in the Proposed Merged Entity will not increase to a control level if the Proposed Transaction is approved, we consider the likelihood of the Proposed Merged Entity receiving a potential takeover offer is not likely to be significantly reduced by the Proposed Transaction.

Further, in this respect, we note that the Proposed Merger Entity may actually be of greater interest to potential acquirers given the consolidation of the MPC technologies within the Proposed Merged Entity (as opposed to previously being held across Mesoblast and Angioblast).

The Non-Associated Shareholders' interest in Mesoblast will be diluted to between approximately 49.7% and 51.9% and shareholders of Angioblast, other than Mesoblast, Professor Itescu and Mr O'Dwyer, will hold approximately 13.1% and 12.8%.

#### Reduced exposure to Mesoblast's portfolio of orthopaedic applications

If the Proposed Transaction is approved, the Non-Associated Shareholders' exposure to Mesoblast's portfolio of orthopaedic applications will be reduced as any commercial success of Mesoblast's products will be shared with the current holders of Angioblast shares. However, this is mitigated by the Non-Associated Shareholders gaining exposure to Angioblast's products for cardiovascular diseases and other non-orthopaedic applications.

# Conclusion on the advantages and disadvantages of the Proposed Transaction

On balance, in our opinion, the advantages of the Proposed Transaction outweigh the disadvantages.

# **Opinion**

We consider the Proposed Transaction is fair and reasonable to the Non-Associated Shareholders for the purpose of Section 611 of the Corporations Act.

In our opinion, the Proposed Transaction is fair and reasonable to the Non-Associated Shareholders for the purpose of ASX Listing Rule 10.

This opinion should be read in conjunction with our detailed report which sets out our scope and findings.

Yours faithfully

DELOITTE CORPORATE FINANCE PTY LIMITED

**Stephen Reid** 

Director

Tapan Parekh

Director

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# 1. Terms of the Proposed Transaction

# 1.1 Summary

On 12 May 2010, the Independent Directors of Mesoblast announced the Proposed Transaction, whereby Mesoblast will acquire all of the ordinary shares in Angioblast that Mesoblast does not already own. Mesoblast and Angioblast have entered into an MIA, which sets out the obligations of both companies in relation to the implementation of the Proposed Transaction.

Under the Proposed Transaction, Mesoblast will issue a total of 94,590,000 Mesoblast shares (the Scrip Consideration) to acquire all shares held by shareholders of Angioblast other than Mesoblast (Angioblast Shareholders). Angioblast Shareholders also have the right to elect to receive cash in respect of up to 15% of their shareholding, with reference to the price of a Mesoblast share on the date of approval by shareholders of Mesoblast (the 15% Cash Option). If the Proposed Transaction proceeds, convertible noteholders of Angioblast (Convertible Noteholders) will convert their notes into shares in Angioblast in accordance with the convertible note deed and subsequently exchange their shares in Angioblast for shares in Mesoblast shares in accordance with the Proposed Transaction.

On 2 June 2010, Mesoblast invited the Convertible Noteholders to tender their convertible notes in Angioblast directly to Mesoblast for purchase. If the Convertible Noteholders take up the Convertible Note Offer and Mesoblast chooses to accept their respective tenders, the Convertible Noteholders will receive the same number of Mesoblast shares as if their convertible notes were converted into Angioblast shares and acquired by Mesoblast under the Proposed Transaction.

As the Convertible Note Offer has no impact on our assessment of the Proposed Transaction, we have assumed that the Convertible Noteholders do not pursue the Convertible Note Offer.

Mesoblast currently owns 32.6% of Angioblast (on a fully diluted basis), and the companies share a common significant shareholder (Professor Itescu) and common Directors (Professor Itescu and Mr O'Dwyer). Accordingly, Mesoblast and Angioblast are considered to be related parties for the purposes of the Corporations Act.

The Proposed Transaction is conditional on Mesoblast successfully concluding a minimum capital raising of AUD 20 million via an institutional share placement, prior to the EGM on [x] 2010. This condition was satisfied when Mesoblast successfully completed a capital raising of AUD 23.8 million at AUD 1.70 per Mesoblast share on 12 May 2010. Mesoblast is seeking shareholder approval to make an additional placement of 6,724,647 Mesoblast shares at AUD 1.70 per share at the EGM for general working capital purposes.

Prior to the Proposed Transaction being completed, Mesoblast is required to provide monthly loans to Angioblast of USD 0.25 million commencing from 3 May 2010 until the earlier of:

- the date when the Proposed Transaction becomes legally effective
- the date when the MIA is terminated.

Angioblast will not be required to make repayments on the principal loan amounts and accrued interest if the Proposed Transaction is terminated or the Proposed Transaction does not occur before 120 days from the date of the MIA.

In the event that the Proposed Transaction is terminated by Mesoblast under certain circumstances (refer Section 1.2), Mesoblast will be required to pay a termination fee of USD 1 million to Angioblast.

Professor Silivu Itescu currently holds a 22.9% interest in Mesoblast (on a fully diluted basis). If the Proposed Transaction is approved, his shareholding in Mesoblast could increase to up to 36.4% (on a fully diluted basis).

Upon completion of the Proposed Transaction, Angioblast will become a wholly-owned subsidiary of Mesoblast.

# 1.2 Key conditions of the Proposed Transaction

The Proposed Transaction is subject to various conditions, the most significant being:

- the Non-Associated Shareholders approving the Proposed Transaction in compliance with the Corporations Act, the ASX Listing Rules, and the Constitution of Mesoblast
- obtaining relevant regulatory approvals from ASIC, ASX and all other necessary government agency approvals
- independent directors of Angioblast and Angioblast Shareholders approving the Proposed Transaction in compliance with Delaware General Corporation Law (DGCL)
- any other regulatory approvals under DGCL
- Mesoblast successfully completing a minimum capital raising of AUD 20 million on or prior to the date of approvals by the Non-Associated Shareholders of the Proposed Transaction. This condition has been met
- no prescribed occurrences occurring in relation to Mesoblast and Angioblast, as
  defined in the MIA between the date of the MIA and the date when the Proposed
  Transaction becomes legally effective.

# 2. Scope of the report

# 2.1 Purpose of the report

An independent expert's report is required pursuant to ASX Listing Rule Chapter 10 and Chapter 2E and Section 611 of the Corporations Act to assist the Non-Associated Shareholders in their decision whether to approve or reject the Proposed Transaction.

As such, the Independent Directors of Mesoblast, being those directors not associated with Angioblast, Professor Itescu or Mr O'Dwyer, have requested Deloitte Corporate Finance to prepare an independent expert's report advising whether the Proposed Transaction is fair and reasonable to the Non-Associated Shareholders.

In evaluating whether the Proposed Transaction is fair and reasonable to the Non-Associated Shareholders we have considered ASX Listing Rule 10, and Chapter 2E and Section 611 of the Corporations Act, the ASIC Regulatory Guides and common market practice.

This report is to be included in the Notice of Meeting being issued for the purposes of Mesoblast's EGM, where the approval from the Non-Associated Shareholders will be sought for the Proposed Transaction. We are not responsible to you, or anyone else, whether for our negligence or otherwise, if the report is used by any other person for any other purpose.

## Section 611 of the Corporations Act

An issue of shares by a company to a shareholder that will increase the shareholder's relevant interest in the company from above 20% to less than 90% is prohibited under Section 606 of the Corporations Act unless the proposed transaction is approved by shareholders at a general meeting, in accordance with item 7 of Section 611 of the Corporations Act.

Given that, if the Proposed Transaction is completed, and Professor Itescu holds shares in Angioblast, his shareholding in Mesoblast will increase from 22.9% to up to 36.4% (on a fully diluted basis).

An independent expert's report is therefore required under Section 611 of the Corporations Act to provide the Non-Associated Shareholders an independent view as to whether the Proposed Transaction is fair and reasonable, and to provide them with sufficient information to make an informed decision as to whether to vote in favour of the Proposed Transaction.

#### ASX Listing Rule 10

ASX Listing Rule 10.1 requires a listed entity to obtain shareholder approval before it acquires a substantial asset from, or disposes of a substantial asset to, an entity that is in a position of significant influence (or a related party) when the consideration to be paid constitutes more than 5% of the equity interest of that entity.

Professor Itescu is considered to be in a position of significant influence, given his directorship and substantial shareholding in both Mesoblast and Angioblast. Further to this, Mr O'Dwyer is also a common director of the two companies.

Angioblast would be considered to be a substantial asset under ASX Listing Rule 10.1.

Pursuant to ASX Listing Rules 10.1 and 10.10, the listed entity undertaking the transaction must prepare a notice of meeting containing an independent expert's report that provides an opinion as to whether the Proposed Transaction is fair and reasonable.

# 2.2 Basis of evaluation

In determining whether the Proposed Transaction is fair and reasonable, we have had regard to the Corporations Act, the ASX Listing Rules, common market practice and to ASIC Regulatory Guide 111 regarding the content of expert's report. This regulatory guide prescribes standards of best practice in the preparation of independent expert's reports.

# **2.2.1** Section 611 of the Corporations Act

Under ASIC Regulatory Guide 111, if an issue of shares by a company, which is approved under item 7 of Section 611 of the Corporations Act, has the effect of increasing a significant stake in a company for a shareholder, then the proposed transaction should be analysed as if it was a takeover bid under Chapter 6 of the Corporations Act.

Given that Professor Itescu is a major shareholder in Mesoblast and Angioblast, if the Proposed Transaction is approved his shareholding in Mesoblast will increase from 22.9% to up to 36.4% (on a fully diluted basis). As a consequence, if the Non-Associated Shareholders approve the Proposed Transaction, they are potentially foregoing the opportunity to receive a takeover offer. The resulting effect of the Proposed Transaction on the Non-Associated Shareholders is therefore similar to a scrip takeover bid under Chapter 6 of the Corporations Act.

Accordingly, we have analysed the Proposed Transaction as a control transaction and assessed whether the Proposed Transaction is fair and reasonable to the Non-Associated Shareholders as set out under ASIC Regulatory Guide 111.

In determining whether the Proposed Transaction is fair and reasonable, we have assessed:

- whether the Proposed Transaction is fair by estimating the fair market value of a share in Mesoblast on a control basis before completion of the Proposed Transaction and comparing that value to the estimated fair market value of a share in the Proposed Merged Entity
- the reasonableness of the Proposed Transaction by considering other advantages and disadvantages of the Proposed Transaction to the Non-Associated Shareholders.

# 2.2.2 ASX Listing Rule 10

Neither the ASX Listing Rules, nor the Corporations Act provides a definition of fair and reasonable for the purposes of ASX Listing Rule 10. However, Listing Rule 10 can encompass a wide range of transactions. Accordingly, fair and reasonable must be capable of broad interpretation to meet the particular circumstances of each transaction. This involves judgement on the part of the expert as to the appropriate basis of evaluation to adopt given the particular circumstances of the transaction.

ASIC Regulatory Guide 111 provides guidance in relation to the content of independent expert's reports prepared for various transactions. It does not provide specific guidance on the form and content of reports prepared in respect of related party transactions. ASIC Regulatory Guide 111 provides general guidance that an expert, in deciding the appropriate form of analysis for the report, should ensure that reasonably anticipated concerns of the people affected by the proposed transaction are adequately dealt with.

We have also had regard to the requirement of ASX Listing Rule 10, which is to state whether the transaction is fair and reasonable to shareholders of the entity whose votes are not to be disregarded.

In our opinion, the most appropriate basis, on which to evaluate whether the Proposed Transaction is fair and reasonable to the Non-Associated Shareholder under ASX Listing Rule 10.1, is to consider the overall effect of the Proposed Transaction on the Non-Associated Shareholders, and to form a view as to whether the expected benefits to the Non-Associated Shareholders outweigh any disadvantages that may result from the Proposed Transaction.

In undertaking this analysis, we have assessed the fair market value of the interest in Angioblast being acquired on a control basis and compared that value with the Scrip Consideration being offered. We have also considered various other factors relevant to the Proposed Transaction so far as the Non-Associated Shareholders are concerned.

In forming our opinion as to whether the Proposed Transaction is fair and reasonable we have treated the concepts of fairness and reasonableness as a single opinion, that is the Proposed Transaction is, or is not, fair and reasonable. It should be noted that this is different to the evaluation undertaken in respect of Section 611 (as discussed above) where we consider the concepts of 'fair' and 'reasonable' individually.

### 2.2.3 Individual circumstances

We have evaluated the Proposed Transaction for the Non-Associated Shareholders as a whole and have not considered the effect of the Proposed Transaction on the particular circumstances of individual investors. Due to their particular circumstances, individual investors may place a different emphasis on various aspects of the Proposed Transaction from the one adopted in this report. Accordingly, individuals may reach different conclusions to ours on whether the Proposed Transaction is fair and reasonable. If in doubt investors should consult an independent adviser who will have regard to their individual circumstances.

# 2.3 Limitations and reliance on information

The opinion of Deloitte Corporate Finance is based on economic, market and other conditions prevailing at the date of this report. Such conditions can change significantly over relatively short periods of time. This report should be read in conjunction with the declarations outlined in Appendix 6.

This engagement has been conducted in accordance with professional standard APES 225 Valuation Services issued by the Accounting Professional and Ethical Standards Board Limited (APESB).

Our procedures and enquiries did not include verification work nor constitute an audit or a review engagement in accordance with standards issued by the Auditing and Assurance Standards Board (AUASB) or equivalent body and therefore the information used in undertaking our work may not be entirely reliable.

# 3. Biotechnology industry

# 3.1 Structure of industry

### 3.1.1 General

The primary activities of companies in the biotechnology industry which focus on the development of biologics for regenerative medicine include:

- deoxyribonucleic acid (DNA) coding
- cell and tissue culture engineering
- process biotechnologies
- sub-cellular organisms.

Biotechnology companies undertake R&D into products, and if successful, they have historically licensed their technology to large multinational pharmaceutical companies that have the large scale manufacturing, distribution, brand and marketing capabilities to exploit the technology.

The global biotechnology industry generated total revenues of USD 227.1 billion in 2008<sup>2</sup> with the medical and healthcare segment representing 69%<sup>3</sup> of the market's value. Other key segments include service providers (15.8%) and food and agriculture (10.6%). Market concentration is low, with the four largest industry players, Amgen Inc, Genentech Inc, Biogen Idec Inc and UBC Group accounting for 17%<sup>4</sup> of industry revenue.

Both Mesoblast and Angioblast are jointly developing the adult MPC technology, with Angioblast primarily focusing on cardiovascular, eye applications and other non-orthopaedic applications and Mesoblast focusing on orthopaedic applications.

We have provided brief discussions on each of these segments of the industry and the stem cells technology below.

#### 3.1.2 Cardiovascular diseases

The global pharmaceutical market for ethical drugs generated total revenues of USD 644 billion in 2009<sup>5</sup> (calculated at ex-factory prices). The American Heart Association (AHA) estimates approximately 80 million American adults (approximately 1 in 3) have one or more forms of cardiovascular diseases. Of the Americans affected by cardiovascular diseases, approximately 38 million are estimated to be over the age of 60. Cardiovascular disease was estimated to cost the US approximately USD 415 billion in 2006<sup>6</sup>, with the burden growing as the population ages. Consequently, this is a high priority segment for many leading pharmaceutical companies, with product revenue contributing 19.8%<sup>7</sup> of total pharmaceutical revenues for ethical drugs.

<sup>&</sup>lt;sup>2</sup> Datamonitor – Global Biotechnology Industry Profile, July 2009

<sup>&</sup>lt;sup>3</sup> Ibid

<sup>4</sup> Ibid

<sup>&</sup>lt;sup>5</sup> Datamonitor – Global Pharmaceuticals Industry Profile, December 2009

<sup>&</sup>lt;sup>6</sup> US Cardiovascular Disease 2007 - Issue 2

<sup>7</sup> Ibid

Cardiovascular disease includes the following diseases:

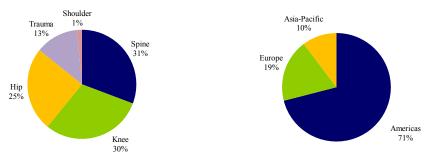
- high blood pressure
- coronary heart disease
  - myocardial infarction
  - angina pectoris
- heart failure
- stroke
- congenital cardiovascular defects.

The market segments for treating congestive heart failure and the consequences of heart attack are currently poorly serviced as treatments are relatively ineffective in their ability to prevent heart failure or rebuild heart tissue. They merely alleviate heart failure symptoms such as shortness of breath and fatigue. As none of these agents rebuild the damaged heart or stop the underlying disease, congestive heart failure inexorably progresses.

#### **Orthopaedic diseases** 3.1.3

The global orthopaedics market generated revenues of USD 19.2 billion in 2008, achieving 7.2% growth on 2007 revenues. Spinal and knee implants accounted for 61% of revenue while the Americas were the main geographic contributor.

Figure 1: Orthopaedic revenue by geographic and product segment



Source: Datamonitor

Orthopaedics is concerned with conditions involving the musculoskeletal system (the organ system which allows humans to move). Common types of orthopaedic problems are chronic cartilage degeneration and acute meniscal tears, segmental bone defects and vertebral disc degeneration.

Chronic cartilage degeneration and acute meniscal tears are both conditions where the cartilage in knee joints has degenerated or is likely to degenerate as a result of injury. They fall under the broad category of inflammatory joint diseases and a more common term for the degeneration is osteoarthritis. Osteoarthritis in the knee is the most common joint disease affecting over 10 million Americans.

Treatments for osteoarthritis in the knee cannot currently restore the cartilage and purely attempts to alleviate pain. To restore full function, joint replacement is the only option.

8

Datamonitor - Global Orthopaedics Industry Profile, December 2009

<sup>&</sup>lt;sup>9</sup> Mesoblast company website

Segmental bone defects occur when the healing process stops before bone repair is complete. Of the 5.6 million fractures occurring annually in the US, over 1 million are associated with difficult or prolonged healing. In up to 10% of these cases treatment such as bone grafting is required to successfully complete the healing process. Bone grafting is a surgical procedure which places new bone around or between defects in the bone.

Bone grafting is not without its limitations. Lack of blood supply to the new bone, chronic pain at the donor site for autografts and the possibility of immune rejection for allografts makes the process susceptible to complications.

Vertebral disc degeneration is the progressive loss of the proteoglycan material which cushions the spine. With age, the proteoglycan material that gives the cartilage its cushioning properties degenerates. This process affects 15% to 45% of the population.<sup>12</sup>

Moderate degeneration has traditionally been treated through pain management and physiotherapy with spinal fusion reserved for severe degenerative cases. Spinal fusion uses grafted bone (allograft, autograft or synthetic) to form a bridge between two vertebra. It is a major surgical procedure with complications including infection, worsening pain symptoms and risk of permanent nerve damage. Due to these risks, only in the most severe degenerative cases are considered for spinal fusion. According to the American Academy of Orthopaedic Surgeons, approximately 250,000 spinal fusions are performed each year<sup>13</sup>.

# 3.1.4 Adult stem cell technology

Stem cells are different to other type of cells in the body. All stem cells have three general properties, which are: 14

- stem cells are capable of dividing and renewing themselves for long periods
- stem cells are unspecialised
- stem cells can give rise to specialised cell types.

Stems cells are used in immature cells and are classified as either embryonic or adult, depending on the tissue they are extracted from.

Embryonic stem cells are derived from embryos that develop from eggs that have been fertilized in an in vitro fertilization clinic and then donated for research purposes with the informed consent of the donors. There is significant debate regarding the usage of embryonic stem cells, since harvesting of embryonic stem cells results in the destruction of the embryo from which they are harvested<sup>15</sup>.

An adult stem cell is an undifferentiated cell, found among differentiated cells in a tissue or organ that can renew itself and can differentiate to yield some or all of the major specialized cell types of the tissue or organ. The primary roles of adult stem cells in a living organism are to maintain and repair the tissue in which they are found. <sup>16</sup>

<sup>&</sup>lt;sup>10</sup> Mesoblast Program Summaries, January 2010

<sup>11</sup> Mesoblast company website

Abdi S, et al. Epidural Steroids in the Management of Chronic Spinal Pain: A Systematic Review. Pain Physician 10:185, 2007

<sup>10:185, 2007

13</sup> American Academy of Orthopaedic Surgeons, 24 November 2009

<sup>&</sup>lt;sup>14</sup> The National Institute of Health resource for stem cell research

<sup>&</sup>lt;sup>15</sup> Key ethical issues in embryonic stem cell research, department of Parliamentary Library Australia 2002 op. cit.

There are two types of adult stem cells, haematopoietic precursors and MPCs. Haematopoietic precursors do not normally give rise to tissues other than blood cells and cannot easily expand in culture. This type of stem cells is not suitable for transplants as the cells are immediately recognised as foreign and rejected by the recipient's body. MPCs can be used to cultivate cells and tissues which form solid organs. They give rise to a variety of cell types, such as bone, cartilage, fat, and other connective tissue cells. The research in the technology to efficiently isolate and expand sufficient numbers of MPCs for commercial application has lagged that of haematopoietic precursors.

The delivery of stem cells to a patient for therapeutic purposes is a new approach to therapeutic intervention and currently there are no products generating substantial income. An effective cell therapy could potentially have a large market, as it would substitute many existing therapies, and provide treatment for conditions which are currently untreatable. Currently, no therapy has progressed beyond clinical trials.

## 3.1.5 Therapeutic modality development timeline

Development of a new therapeutic modality is risky and is composed of several stages, during which the sponsor gathers evidence to convince government regulators that it can consistently manufacture a safe and efficacious form of the treatment for the medical condition it is intended to address. At the end of each stage, the sponsor uses the technological and market information revealed up to that point to decide whether to abandon or continue development.

Using available empirical evidence on the statistical likelihood of a project (at any given stage) progressing to the next stage, we set out in the table below the various generic stages together with the necessary clinical trials and associated probability of progressing to the next stage (as advised by Acuity, an independent technical expert engaged by Deloitte Corporate Finance).

Figure 2: Generic stages of study required

| Stage of<br>development | Probability of<br>successfully<br>moving to next<br>phase | Cumulative<br>probability of<br>successfully<br>moving to next<br>phase | Description  |
|-------------------------|---|---|--|
| Phase I                 | 70.7%   | 70.7%   | Testing is generally conducted on a small number of healthy volunteers to obtain information on toxicity and safe dosing ranges in humans.  Data is also collected on the drug's absorption and distribution in the body, its metabolic effects, and the rate and manner in which the drug is eliminated from the body.  In order to progress, it is important to demonstrate that there are no immunological responses from the recipient, that the cell formulation does not contain substances and other cell types which can be detrimental, and that cells grow and divide in a predictable and desirable manner.  It is also unethical to administer living cells to healthy humans and the most likely approach for a Phase I study is to select patients who may receive some therapeutic benefit or individuals where |
| Phase II                | 47.7%   | 33.7%   | an adverse consequence may have limited impact on their prognosis.  The treatment is administered to a larger number of individuals selected from among patients for whom the adult stem cell therapy is intended.  Successful Phase II trials provide significant evidence on efficacy and additional data on safety and dosage level.  Final product specification and manufacturing process are generally finalised at this stage.  |
| Phase III               | 56.7%   | 19.1%   | The final pre-marketing phase involves large-scale trials on patients to obtain additional evidence of efficacy.  Larger sample sizes increase the likelihood that benefits found will be statistically significant, and that any adverse reactions that may occur infrequently in patient populations, will be observed.  Phase III trials are designed to closely approximate the manner in which the drug or therapy will be used after marketing approval.   |

| Stage of<br>development | Probability of<br>successfully<br>moving to next<br>phase | Cumulative<br>probability of<br>successfully<br>moving to next<br>phase | Description  |
|-------------------------|---|---|--|
| Regulatory<br>approval  | 80.0%   | 15.3%   | After the clinical trial phases have been completed and the company believes it has sufficient evidence for approval, it submits an application to the regulatory authority in each country where it wishes to market and sell that product. |

Source: Mesoblast Prospectus dated 16 November 2004, Acuity

Angioblast and Mesoblast have entered human clinical trials. From information supplied to the market by Mesoblast and Angioblast, Acuity have advised that both companies will, subject to FDA final approvals, be required to undertake an abbreviated clinical trial program to that normally required for novel chemical-based pharmaceuticals, termed new chemical entities (NCE). In particular, it is apparent from trials being undertaken by other companies, including Osiris Therapeutics Incorporated (Osiris), that Phase I trials will not be required for adult stem cells. It is also anticipated that, depending upon results, Phase II trials may be abbreviated.

We note that both Angioblast and Mesoblast are able to bypass the majority of Phase I requirements for treatments using both autologous (cells from a patient used to treat that patient only)<sup>17</sup> and allogeneic cells (cells and/or organs obtained from a donor which are then used to treat another person).<sup>18</sup> However, the route to market (particularly the regulatory approvals required) for stem cells is still evolving due to the technology being new and both companies are amongst the pioneers.

# 3.2 Competing technologies for orthopaedic and cardiovascular disease

There are currently clinical trials in progress or planned to commence shortly, by parties other than Angioblast and Mesoblast, using adult stem cells (although not mesenchymal stem cells) for therapeutic applications. One of these is directed at the treatment of cardiovascular and orthopaedic diseases.

US-based Osiris is a stem cell therapeutic company focused on developing and marketing products to treat medical conditions in the inflammatory, orthopaedic and cardiovascular areas. The methods used by Osiris to isolate stem cells result in very heterogeneous populations, which contain a large population of non-stem cells. This results in culture expansion of a population of cells that are much less effective for regenerative therapy than Mesoblast's or Angioblast's proprietary MPC.

<sup>&</sup>lt;sup>17</sup> Autologous cell-based treatments are assumed to be safe as they involve the use of a patient's own cells.

<sup>&</sup>lt;sup>18</sup> Angioblast demonstrated in trials for its congestive heart disease application that the use of allogeneic cells was safe, the results of which can be applied to all indications in Angioblast and Mesoblast's portfolio of products that use allogeneic cells.

Osiris currently has two development phase products (Prochymal<sup>R</sup> and Chondrogen<sup>R</sup>), both of which are in clinical trials. In addition, Osiris had previously developed a product called Osteocel<sup>R</sup>, which was sold to NuVasive Incorporated, a medical device company focused on products for the surgical treatment of spinal disorders, in May 2008.

Osteocel<sup>R</sup> is a viable bone matrix product that preserves the native stem cell population that resides in marrow rich bone and is intended for use in orthopaedic indications for bone regeneration. Prochymal<sup>R</sup> is being evaluated in Phase III clinical trials for three indications, including steroid refractory acute graft versus host disease (GvHD), newly diagnosed acute GvHD and also Crohn's disease. Prochymal<sup>R</sup> is also being developed for the repair of heart tissue following a heart attack, the protection of pancreatic islet cells in patients with type 1 diabetes and the repair of lung tissue in patients with chronic obstructive pulmonary disease. Chondrogen<sup>R</sup> is currently being evaluated in clinical trials for the treatment of osteoarthritis in the knee.

#### 3.3 Critical success factors

Key success factors within the industry include:

- ability to raise investment funding, whether it be private or public equity or government grants
- access to, and retention of, employees with the required level of experience and training
- use of new technology, including access to the latest research and findings
- existence of a market for the technology once it is developed and ready to commercialise.

The niche market within the wider healthcare industry in which both Angioblast and Mesoblast operate, relates to a significant portion of the adult population who have some form of cardiovascular or orthopaedic disease. Therefore, there is a large potential market for an effective cell therapy in these markets. For example, if such a treatment became the standard of care for heart attack survivors or congestive heart failure, there is potential to generate billions of dollars annually in revenues.

#### **Barriers** to entry 3.4

The majority of small companies in the global biotechnology industry focus on the R&D of one product line, rather than final retailing. Revenues are generally then generated through royalties when the developed technology is licensed out.

This suggests that barriers to entry to this industry should be considered to be high as companies require access to and expenditure on:

- specialist staff with the relevant research skills and knowledge
- buildings and specialist equipment
- existence of patents to protect intellectual property (IP).

There are areas of R&D that may be considered politically sensitive, such as genetic modification. As such R&D is often subject to government regulation and community debate which are discussed further in the following sections.

13

 $<sup>^{19}</sup>$  Stem Cell Therapies & Regenerative Medicine - Current Applications & Future Possibilities. Business Communication Company, Inc. MA. December 2005

# 3.5 Regulation

#### 3.5.1 Australia

The biotechnology industry relies heavily on government funding and government initiatives. It is estimated that government funding for biotechnology R&D reached AUD 299.3 million in financial year (FY) 2005.

Regulation within the biotechnology industry in Australia is driven by ethical and environmental issues and as a result there is a high level of industry regulation over R&D practices. Ethical issues are primarily focused on embryonic stem cell research, rather than adult stem cell research. When a product reaches a commercial stage, regulation is covered by the Commonwealth Therapeutic Goods Act 1989.

Specific regulations covering R&D within the industry include:

- Commonwealth Gene Technology Act 2000 (Cth)
- Prohibition of Human Cloning Act 2002 (Cth)
- Research Involving Human Embryos Act 2002 (Cth).

### 3.5.2 United States

Regulation within the biotechnology industry in the US is governed by the FDA, a federal agency operated by the US Department of Health and Human Services.

The role of the FDA within the biotechnology industry is to ensure that human and veterinary drugs, biological products, and medical devices are safe and effective. In order to achieve this, the FDA:

- establishes licences for new products and manufacturing processes
- ensures testing methods for research to establish new products is conducted within set standards
- sets guidelines for the approval process for new products prior to being sold to the market.

The FDA is seen as a leading regulatory agency globally. For this reason, and also due to the size of the US market, many companies will commence clinical trials in the US prior to commencing trials elsewhere in the world.

## **Recent developments**

Of specific relevance to Mesoblast and Angioblast is the recent enactment of the United States Patient Protection and Affordable Care Act (HB 3590). This act, and recently updated biosimilar biological provisions (23 March 2010), could potentially increase the long-term revenue streams of Mesoblast and Angioblast by potentially providing commercial exclusivity after the expiration of their US patents. HB 3590 will:

- prohibit FDA approval for a biosimilar (interchangeable) product until 12 years after the date on which the reference product is first approved
- provide the reference product innovator with a possible further 12 years of exclusivity
  after the approval of any subsequent biologic product which has a structure that has
  been modified to result in changes in safety, purity, or potency of the biologic
  product.

# 3.6 Recent transactions

Significant recent transactions in the biotechnology and pharmaceutical sectors include:

- in November 2008, Osiris and Genzyme Corporation (Genzyme), a US-based biotechnology company, announced a partnership to further develop and commercialise two products developed by Osiris, Prochymal<sup>R</sup> and Chondrogen<sup>R</sup>, which are adult stem cell treatments for several disorders. Under the agreement, Genzyme will market the treatments internationally and will make an initial payment of USD 130 million to Osiris. Osiris could earn up to a further USD 1.25 billion if certain regulatory approvals are received and sales targets met
- in May 2008 Millennium Pharmaceuticals Incorporated (Millennium), a biopharmaceutical company focused on discovering, developing and commercialising medicines for cancer, inflammatory bowel diseases and other inflammatory diseases, merged with Takeda Pharmaceutical Company Limited (Takeda), a global pharmaceutical company based in Japan, in a deal worth USD 8.1 billion. Millennium's flagship product, VELCADE<sup>R</sup>, will enhance Takeda's goal of becoming a global leader in oncology
- in March 2008 Pharmion Corporation, a global pharmaceutical company that acquires, develops and commercialises products for the treatment of haematology and oncology patients, merged with Celgene Corporation, a multinational integrated biopharmaceutical company, in a deal worth USD2.7 billion. The merger will bring together three key medical therapies; Revlimid<sup>R</sup>, Thalomid<sup>R</sup> and Vidaza<sup>R</sup>.
- in August 2007, Peptech Limited (subsequently renamed to Arana Therapeutics Limited (Arana)) acquired EvoGenix Limited (EvoGenix), an Australian product-focused biotechnology company developing novel therapeutics, for a cash and stock consideration of AUD 1.12 per share, or an approximate consideration of AUD 156 million. Arana has a strong cash base which will be able to support EvoGenix's clinical trials in the coming years
- in August 2009, Cephalon Inc (Cephalon) a US listed pharmaceutical company completed the acquisition of all the shares it did not already own in Arana. The acquisition will enhance Cephalon's inflammatory disease pipeline and provide a means for Arana's key compound to complete clinical trials, and if successful, reach international markets.

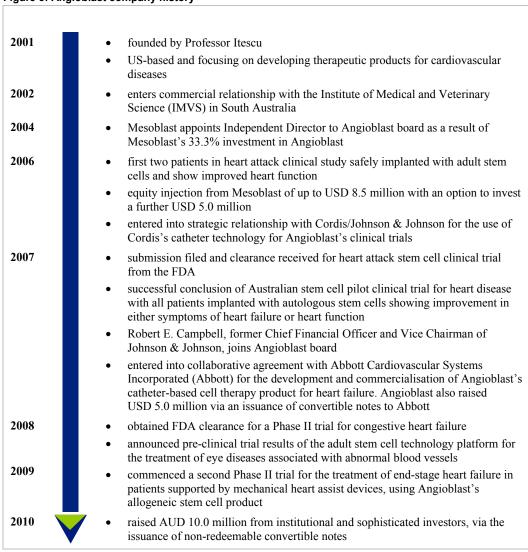
# 4. Profile of Angioblast

Angioblast is primarily focused on developing therapeutic products for non-orthopaedic indications, and is currently focused on cardiovascular and eye diseases. Incorporated and based in the US, the company aims to commercialise its patented product portfolio which focuses on regulated blood vessel growth. By regulating blood vessel growth these products and the related technologies will potentially provide an effective solution to diseases such as diabetic diseases.

# 4.1 Company history

An overview of the company history is provided in Figure 3 below.

Figure 3: Angioblast company history

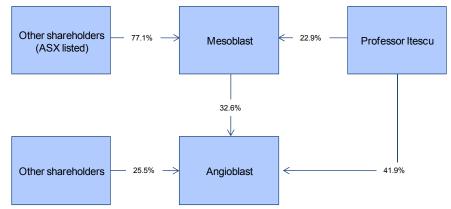


Source: Angioblast company website and Mesoblast public announcements

# 4.2 Group structure

The figure below sets out a simplified group structure for Angioblast and Mesoblast as at 30 June 2010 (and therefore excluding the shares to be issued as a consequence of the capital raising discussed in Section 1.1).

Figure 4: Angioblast and Mesoblast organisational structure as at 30 June 2010 (on a fully diluted basis)



Source: Mesoblast management

#### Mesoblast

Mesoblast holds 32.6% of the outstanding shares in Angioblast (on a fully diluted basis) and is focused on commercialising adult stem cell technology for orthopaedic applications. For further details on Mesoblast, please refer to Section 5.

#### **Professor Itescu**

Professor Itescu is the founder of Angioblast and Mesoblast. He is recognised worldwide for his research in the areas of stem cells, autoimmune diseases, organ transplantation and heart failure. He holds a 22.9% interest in Mesoblast and a 41.9% interest in Angioblast.

# 4.2.2 R&D relationship between Mesoblast and Angioblast

During the early clinical trial stages, Mesoblast and Angioblast implemented a costsharing agreement which allowed both companies to participate in the benefits of MPC development while reducing the financial burden. Shared costs predominantly related to pre-clinical trial expenditure and cell manufacturing.

# 4.3 Angioblast's technologies

Angioblast has a number of platform technologies under development; the primary and most advanced is the MPC technology for the treatment of cardiovascular diseases.

The MPC technology was initially developed by scientists at the IMVS. Angioblast subsequently entered into a commercial relationship with the IMVS for the entire IP of the MPC technology. The MPC technology is a tool that enables efficient extraction, isolation and scale-up of adult MPCs. Specifically, the MPC technology can isolate a pure population of highly potent MPCs which are characterised by certain surface markers. The use of cultured stem cells derived from this technology is highly effective for regeneration of the recipient's own tissues and growth of new bones and heart muscles. Angioblast owns the patent applications protecting the use of MPCs.

Angioblast also holds other IP relating to the culture or manufacture of cells and the application of MPCs to treat specific medical conditions.

Two other technologies are also under development, being a peptide therapeutic stromal-derived factor 1 (SDF-1), and drug eluting stents based on ribonucleic acid (RNA) silencing technology, with the lead candidate targeting plasminogen activator inhibitor (PAI-1).

Plans for further development and commercialisation are the most advanced for the MPC technology, which has:

- completed pre-clinical manufacturing of the two vital components, being:
  - o the hybridoma derived monoclonal antibodies
  - o the MPC isolation (using the monoclonal antibodies), storage, expansion and administration.

Both components can be conducted under mandatory Good Manufacturing Practice (GMP) guidelines and the cell therapies component is adequate for both autologous and allogeneic treatments

- demonstrated efficacy<sup>20</sup> in animal models of congestive heart failure and acute myocardial infarction<sup>21</sup> or heart attack
- completed a pilot human clinical trial in Australia as an autologous treatment for acute myocardial infarction. The results showed an improvement in heart muscle function and reduced symptoms of both heart failure and severe angina
- commenced Phase II human clinical trials in the US as an allogeneic treatment for heart attack patients
- commenced Phase II human clinical trials in the US as an allogeneic treatment for congestive heart failure. Pre-clinical trials have been shown to improve heart muscle function and reverse established heart failure
- received investigational new drug (IND) approval to undertake Phase Ib trial with patients undergoing bone marrow transplantation
- completed pre-clinical trials on non-human primates as an allogeneic treatment for macular degeneration and diabetic retinopathy
- successful achievement of key milestones in relation to the Phase II human clinical trials in the US as an allogeneic treatment for congestive heart failure. Follow up clinical trials for higher dosages have been approved.

### **Applications**

Angioblast has an assignment of patents lodged initially in the name of Adelaide's IMVS, which provides rights to applications of MPC in all fields other than orthopaedic applications.

Angioblast's interest in MPCs is for the treatment of heart and vascular diseases, including congestive heart failure and myocardial infarction, bone marrow transplants and treatment of eye diseases associated with abnormal blood vessels. At a later date, Angioblast may also explore applications associated with wound healing and skin ulcers, peripheral artery disease and other non-orthopaedic diseases.

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<sup>&</sup>lt;sup>20</sup> Efficacy – capacity to produce the desired result, especially a cure or an improvement in somebody's physical condition
<sup>21</sup> Acute myocardial infarction – or heart attack; occurs when the blood supply to part of the heart muscle is severely reduced or stopped

## Acceptance and commercialisation

We understand that the medical community is highly familiar with the use of progenitor cells. The proposed use of common FDA approved carriers and delivery tools by Angioblast for the delivery of MPCs to patients follows existing procedures and tools. The carriers and delivery tools are FDA approved and are in wide use throughout the medical community. This is likely to assist the acceptance of Angioblast's technology.

Following GMP compliant cell expansion, Angioblast intends to freeze the cells and make them immediately available at the time and place of need.

Angioblast management expects a significant portion of the costs associated with the delivery of its products will be met by existing program that will form the basis for reimbursement from US and international governments and private reimbursement authorities. These programs are expected to enable a fast tracking of reimbursement schedules to reduce the cost of the therapy to end patients. Management expects that this could significantly reduce the long term health care costs to the community for ongoing treatment of patients suffering heart failure.

## Recent developments and new indications

In November 2008, Angioblast announced that it had received FDA approval to commence a Phase I/II clinical trial in the US in up to 30 patients with haematological malignancies undergoing bone marrow transplantation. Ethics approval from the Institutional Review Board at the University of Texas, M. D. Anderson Cancer Centre has been obtained and the study will be funded through a grant awarded by the US National Institutes of Health.

The MPC product will be developed for this indication under the FDA Orphan Drug designation. The Orphan Drug designation aims to make drugs available for rare conditions where development by a company may not otherwise be justified on commercial grounds. Hence it is available to conditions affecting up to 200,000 patients annually in the US, and allows for accelerated approvals, seven year market exclusivity and certain tax benefits.

After a detailed examination of potential indications for MPC, Angioblast management has concluded that certain conditions associated with pathologically restricted blood flow or blood vessel damage are potential targets for MPC therapy using the Orphaned Drug designation. As discussed below, the primary condition management has focused on is diabetic macular edema.

#### Diabetic Macular Edema

Swelling of the retina occurs in diabetes mellitis due to leaking of fluid from blood vessels within the macula. The macula is the central portion of the retina, a small area rich in cones, the specialized nerve endings that detect colour and upon which daytime vision depends. As fluid build-up develops, blurring occurs in the middle or just to the side of the central visual field. Visual loss from macular edema can progress over a period of months and make it impossible to focus clearly. In diabetes, blood vessel endothelial cells are damaged by substances produced or inappropriately released as a consequence of the disease condition.

The prevalence of diabetes in the US is currently 7%, meaning that 21 million of the 300 million Americans alive today have diabetes. The prevalence of diabetic macular edema among US diabetics approaches 30% in adults who have had diabetes for 20 years or more, and varies with the stage of diabetic retinopathy. It can occur at any stage of diabetes and can predate the appearance of other findings of diabetic retinopathy.

Diabetic retinopathy becomes nearly ubiquitous with long-standing diabetes. After 20 years with the disease, 60% of type 2 diabetics and virtually 100% of type 1 diabetics will manifest some form of retinopathy. Untreated, 20% to 30% of patients with diabetic macular edema will experience a doubling of the visual angle within 3 years; with current treatment, this risk drops by 50%.

It is estimated that in excess of 500,000 Americans have macular edema with up to 75,000 new cases developing each year.

Current treatments include photocoagulation, which prevents ongoing damage but will not restore lost eyesight, anti-vascular endothelial growth factor therapy (monoclonal antibodies such as Lucentis<sup>R</sup> and Avastin<sup>R</sup>) although definitive studies have yet to be completed, and corticosteroids.

# 4.4 Patents

Angioblast has exclusively licensed and received assignment rights to a portfolio of patents for the commercialisation of MPCs.

The assigned patents and others applied for in the name of Angioblast aim to provide an exclusive and protected position for MPC composition-of-matter, methods for MPC isolation and use indications for cell therapy.

The patents cannot preclude competitors and medical practitioners from using crude bone marrow aspirates containing MPCs, but they will not be able to purify or concentrate MPCs without infringing patents. The result for anyone attempting such procedures will be cell mixtures containing exceedingly low numbers of MPCs which will, by definition, be significantly less effective than Angioblast's MPC products and potentially unsuitable for allogeneic administration.

# 4.5 Directors and management

We set out below details regarding the directors of Angioblast:

#### Carter Eckert - Non-executive chairman

Mr Eckert has extensive experience in the industry over the past 28 years and currently serves as a director of Anesiva, Incorporated. He is the former Chairman of the Board of AlgoRx, Incorporated and is a former director of Impath, Incorporated, Andrx, Incorporated, Orasure Technologies Incorporated, and Boron Lepore, Incorporated.

### **Donal O'Dwyer – Non-executive director**

Mr O'Dwyer is the Mesoblast appointed director of Angioblast. He has over 20 years of experience in the cardiovascular and medical devices industry and is also a director of Cochlear Limited, AtCor Medical Limited and Sunshine Heart Limited.

#### Michael Esposito – Non-executive director

Mr Esposito is a senior partner at Norbridge Incorporated, a Boston-based consulting firm, and has over 15 years of experience in a variety of functionally-oriented and corporate planning assignments for pharmaceutical, biotechnology, medical device and diagnostic companies.

#### **Professor Silviu Itescu – Executive director**

Refer to Section 4.2 for background information on Dr Itescu.

### Robert Campbell - Non-executive director

Mr Campbell is a retired Vice Chairman of The Board of Directors of Johnson & Johnson where he also was Chairman of the Professional Sector Worldwide. During his career he held numerous positions at Johnson & Johnson in financial and general management including Treasurer, Vice President Finance, and Executive Committee Member.

We set out below details regarding the management of Angioblast:

#### Dr Donna Skerret - Director of Medical Affairs

Dr Skerret is a stem cell expert who most recently was an Associate Director of Transfusion Medicine at Princeton University.

## Michael Schuster - Vice-President of Operations

Mr Schuster is a co-founder of Angioblast and Mesoblast and has extensive experience in biotechnology research.

## Elliot Bendrihem – Chief Financial Officer (CFO)

Mr Bendrihem has over 30 years of experience in the areas of finance, taxation, consulting and investment banking. He was the CFO of three multi-billion dollar banking institutions, including Vice President/CFO of Barclays Bank in New York.

# 4.6 Competitive position of Angioblast

The table below sets out the strengths, weaknesses, opportunities and threats (SWOT) for Angioblast.

| able 6: SWOT analysis  |   |
|--|---|
| Strengths  | Weaknesses  |
| <ul> <li>six lead candidates with demonstrated proof of efficacy</li> <li>positive results from Phase II human trial with allogeneic (donor unrelated or "off-the-shelf") MPC for congestive heart failure. Follow up clinical trials for higher dosages are approved</li> <li>established manufacturing process for allogeneic MPC to be used in Phase II clinical trials</li> <li>strategic relationship with Cordis/Johnson &amp; Johnson in place</li> <li>the "Ideal Stem Cell" - allogeneic product for all patients, and at a low cost and high-margin (pharmaceutical-style business model)</li> <li>collaborative agreement in place with Abbott for the development and commercialisation of Angioblast's catheter-based cell therapy product for heart failure</li> <li>granted orphan drug designation for the use of proprietary stem cells in bone marrow transplants</li> <li>conducting the world's first allogenic stem cell trial for treatment of end-stage heart failure in patients supported by mechanical heart assist devices. Promising results in this trial to date.</li> </ul> | <ul> <li>high upfront development risk while progressing to licensing stage</li> <li>escalating cost of development as further phases are undertaken</li> <li>relatively early stage of development</li> <li>heavy reliance on external financing.</li> </ul> |
| Threats  | Opportunities   |
| <ul> <li>there is a risk that human responses may be different and that individuals may respond differently from findings from animal studies, although early data in human trials suggest this may not be the case</li> <li>if it is not possible to use MPCs in an allogeneic</li> </ul>   | <ul> <li>near-term clinical milestones including the completion of Phase II allogeneic MPC human trials for acute myocardial infarction and congestive heart failure</li> <li>SDF-1 and PAI-1 diversify the Angioblast</li> </ul>                             |

portfolio while offering individual and synergistic therapeutic benefits when combined with MPC

pre-clinical results show potential for adult stem

cell technology to be applied in the treatment of eye diseases associated with abnormal blood

growing incidence of heart failure and diabetes (and related macular degeneration) in the general

Source: Deloitte Corporate Finance Corporate Finance analysis

mode, the economic viability of the process may be

MPCs are stored with a cryoprotective agent (DMSO)

which is considered toxic but is FDA approved

competing technologies from companies such as Osiris, Aastrom Biosciences Incorporated, StemCells

stem cell research is evolving technology and the regulatory framework is still being developed.

Incorporated and ViaCell Incorporated

# 4.7 Capital structure and shareholders

As at 30 June 2010 Angioblast had the following securities on issue:

Table 7: Fully diluted capital structure (before Proposed Transaction)

| Name  | Number held            | Percentage of issued capital (%) |
|---|------------------------|----------------------------------|
| Outstanding shares (on a fully diluted basis)                   |                        |                                  |
| Professor Itescu  | 905,050                | 41.9%                            |
| Mesoblast   | 705,323 1,4            | 32.6%                            |
| Various option holders  | 201,374 <sup>2,3</sup> | 9.3%                             |
| Convertible Noteholders   | 123,898 <sup>5</sup>   | 5.7%                             |
| Abbott Cardiovascular Systems Inc.                              | 70,091                 | 3.2%                             |
| Trustees of Columbia University in the City of New York         | 63,829                 | 3.0%                             |
| Carter Eckert   | 37,500                 | 1.7%                             |
| Michael Schuster  | 20,000                 | 0.9%                             |
| ANZ Nominees Limited  | 19,950                 | 0.9%                             |
| WS Investment Company, LLC                                      | 15,000                 | 0.7%                             |
| Total outstanding shares (on a fully diluted basis)             | 2,162,015              | 100.0%                           |
| Assumes shareholders are diluted by:                            |                        |                                  |
| Options – held by various directors and employee option holders | 190,000 <sup>2</sup>   |                                  |
| Options – held by Thorney Investments                           | 11,374 <sup>3</sup>    |                                  |
| Series B preferred stock – held by Mesoblast                    | 159,167 <sup>4</sup>   |                                  |

Source: Mesoblast

#### Notes:

- 1. Represents the shareholding of Mesoblast if all of its preferred stock is converted into common stock
- Assuming conversion of 190,000 employee options. The exercise price of these options ranges from USD 0.0001 to USD 30.32, with expiry dates ranging from 30 November 2012 to 14 January 2020. We have treated these options as exercised and included them in the calculation of the total outstanding shares on a fully diluted basis
- 3. In conjunction with the issuance of the convertible notes, three tranches of approximately 3,791 options were issued to Thorney Investments and are assumed to be converted into 11,374 shares in Angioblast at the next financing event (which includes a change of control event). Accordingly, we have included them in the calculation of the total outstanding shares on a fully diluted basis
- Series B preferred stock issued is convertible into 159,167 common shares on the successful completion of a Phase II clinical trial report
- Representing the number of Angioblast shares the convertible notes are estimated to convert into based on principal and interest accrued on the convertible notes up to 31 August 2010.

The following table summarises Angioblast's share options on issue as at 30 June 2010:

Table 8: Angioblast share option summary

| Issue date       | Number of options outstanding | Exercise price<br>(USD)           | Expiry date   |
|------------------|-------------------------------|-----------------------------------|---|
| 30 November 2002 | 2,500                         | 0.0001                            | 30 November 2012  |
| 7 July 2005      | 28,500                        | 2.96                              | 7 July 2015   |
| 26 April 2007    | 47,500                        | 28.40                             | 25 April 2017   |
| 5 March 2007     | 6,000                         | 28.40                             | 5 February 2017   |
| 7 May 2007       | 12,000                        | 30.32                             | 7 May 2017  |
| 9 June 2007      | 4,000                         | 30.32                             | 9 June 2017   |
| 11 July 2007     | 4,500                         | 30.32                             | 11 July 2017  |
| 27 October 2008  | 36,000                        | 19.53                             | 26 October 2018   |
| 6 January 2009   | 1,000                         | 19.53                             | 5 January 2019  |
| 15 January 2009  | 1,000                         | 19.53                             | 14 January 2019   |
| 27 October 2009  | 47,000                        | 21.77                             | 26 October 2019   |
| 25 August 2009   | 3,79                          | 75.61                             | the later of 25 August<br>2010 and 30 days after<br>the next financing<br>event |
| 25 August 2009   | 3,791                         | Price at financing event          | the later of February<br>2011 and 30 days after<br>a financing event            |
| 25 August 2009   | 3,791                         | Price at financing event plus 10% | the later of August<br>2012 and 30 days after<br>a financing event              |
| Total            | <b>201,374</b> <sup>1</sup>   |                                   |   |

Source: Mesoblast

Note:

1. Includes rounding error.

# 4.8 Income statement

The audited income statements of Angioblast for FY 2008 and 2009 and unaudited income statement for the six months ended 31 December 2009 are summarised in the table below.

Table 9: Income statements

|                               | FY 2008<br>Audited<br>(USD 000) | FY 2009<br>Audited<br>(USD 000) | 31 December 2009<br>6 months<br>Unaudited<br>(USD 000) |
|-------------------------------|---------------------------------|---------------------------------|--|
| Trading revenue               | _                               | _                               | _  |
| Other revenue                 | 722.3                           | 161.1                           | 713.6  |
| R&D expenditure               | (2,434.7)                       | (2,340.4)                       | (1,089.4)  |
| Consulting costs              | (1,843.8)                       | (1,226.8)                       | (872.2)  |
| Other expenses                | (1,401.8)                       | (1,957.7)                       | (1,069.0)  |
| EBITDA                        | (4,958.0)                       | (5,363.8)                       | (2,317.0)  |
| Depreciation and amortisation | (11.4)                          | (11.1)                          | (349.4)  |
| EBIT                          | (4,969.4)                       | (5,374.9)                       | (2,666.4)  |
| Net interest expense          | (91.9)                          | (53.5)                          | 11.7   |
| Profit before tax             | (5,061.3)                       | (5,428.4)                       | (2,654.7)  |

Source: Angioblast management

#### Notes:

- 1. EBITDA earnings before interest, tax, depreciation and amortisation
- 2. EBIT earnings before interest and tax

In line with the current status of the business (i.e. the R&D phase), the majority of costs relate to consultants and R&D expenditure.

The net interest over the six months to 31 December 2009 is generated from cash balances of USD 5.85 million at 30 June 2008, USD 1.3 million at 30 June 2009 and USD 6.2 million at 31 December 2009. Other expenses primarily relate to compensation, legal, license, patent, rent and travel expenses. Depreciation and amortisation significantly increased for the six months ending 31 December 2009 due to the inclusion of USD 0.3 million in convertible note fee amortisation.

# 4.9 Balance sheet

The audited balance sheet of Angioblast as at 30 June 2008 and 30 June 2009, and the unaudited balance sheet of Angioblast as at 31 December 2009 are summarised in the table below.

Table 10: Financial position

|                                       | 30 June 2008<br>Audited<br>(USD 000) | 30 June 2009<br>Audited<br>(USD 000) | 31 December 2009<br>Unaudited<br>(USD 000) |
|---------------------------------------|--------------------------------------|--------------------------------------|--|
| Cash and cash equivalents             | 5,850.5                              | 1,315.6                              | 6,199.6                                    |
| Account receivables                   | 57.7                                 | 65.9                                 | 79.8                                       |
| Prepayments                           | 42.7                                 | 38.7                                 | 41.9                                       |
| Total current assets                  | 5,950.9                              | 1,420.2                              | 6,321.3                                    |
| Deposits                              | 27.9                                 | 27.9                                 | 27.9                                       |
| Property, plant and equipment         | 25.7                                 | 16.9                                 | 21.2                                       |
| Deferred loan fees - convertible note | -                                    | -                                    | 166.7                                      |
| Total non-current assets              | 53.6                                 | 44.8                                 | 215.8                                      |
| Total assets                          | 6,004.5                              | 1,465.0                              | 6,537.1                                    |
| Current payables                      | 624.6                                | 973.1                                | 282.2                                      |
| Other                                 | 22.5                                 | 12.8                                 | 17.8                                       |
| Convertible note                      | 5,208.1                              | -                                    | 8,230.0                                    |
| Total current liabilities             | 5,855.2                              | 985.9                                | 8,530.0                                    |
| Net assets                            | 149.3                                | 479.2                                | (1,992.9)                                  |

Source: Angioblast management

We make the following comments in relation to the above balance sheets:

- the net asset position has reduced significantly as at 31 December 2009, primarily due to the losses incurred for the six months ending 31 December 2009
- deferred loan fees as at 31 December 2009 of USD 166,700 were due to the convertible note issuance to the Convertible Noteholders
- if the Proposed Transaction proceeds, Angioblast will be required to pay transaction fees to financial advisors of approximately USD 4.8 million. This potential liability is not reflected in the balance sheet as at 31 December 2009.

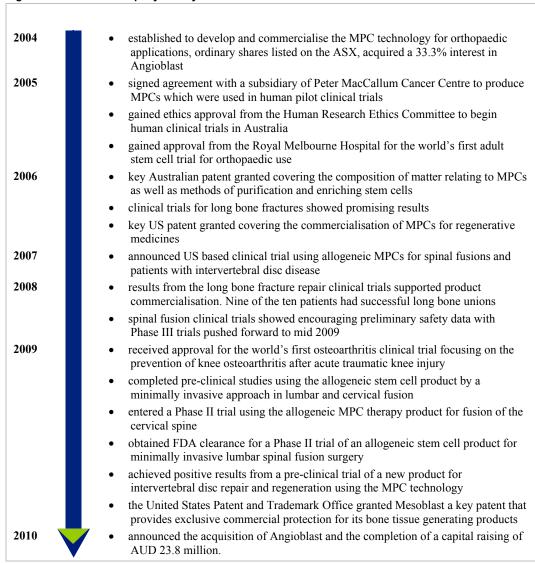
# 5. Profile of Mesoblast

Mesoblast is an ASX listed Australian biotechnology company, focused on the development and commercialisation of allogeneic stem cell products using the MPC technology for the treatment of orthopaedic conditions, including regenerating and repairing bone and cartilage. The company was established in 2004 and its ordinary shares are listed on the ASX.

# 5.1 Company history

An overview of the company history is provided in Figure 5 below.





Source: Mesoblast company announcements and website

# 5.2 Company structure

Mesoblast was founded by Professor Itescu. Please refer to Section 4.2 for details of the relationship between Angioblast and Professor Itescu.

# 5.3 Mesoblast's technologies

Mesoblast has a worldwide licence to develop and commercialise the MPC technology for orthopaedic applications (refer to Section 4.3 for a brief description). These applications aim to treat common bone diseases and injuries, including bone fractures and cartilage degeneration of knee and vertebrae.

Mesoblast and Angioblast jointly funded the early development stages of the MPC technology, and shared various initial development costs including pre-clinical studies and cell manufacturing.

Similar to other biotechnology companies, Mesoblast is required to achieve the following steps to fully commercialise its adult stem cell products:

- completion of ongoing and new Phase II clinical trials
- progression towards Phase III clinical trials
- establishing product markets in various jurisdictions
- identification and establishment of strategic partnerships to gain a first-tier distribution network and achieve long term product cashflows.

Mesoblast has recently accomplished the following milestones including:

- completed a number of large animal studies for inclusion in FDA IND submissions
- received Australian institutional ethics approval to conduct a human trial using the MPC technology for prevention of knee osteoarthritis after an acute traumatic knee injury and anterior cruciate ligament reconstruction
- completed pre-clinical studies in sheep to evaluate the effect of allogeneic MPCs on degenerated intervertebral discs. Mesoblast is in the process of filing an IND with the FDA to commence a Phase II clinical trial in the US
- following positive pre-clinical results, Mesoblast has obtained ethics approval to commence a Phase II trial of the adult stem cell product for anterior cervical interbody fusion
- initiated two Phase II clinical trials for lumbar spinal fusion. The first trial (unilateral fusion) has produced a good safety profile. The second Phase II clinical trial is targeting interbody fusion
- achieved positive Phase I clinical trial results of the autologous MPCs for repairing non-union long bone fractures.

#### **Applications**

Mesoblast is focused on commercialising three broad orthopaedic applications of the MPC technology. These applications relate to treatment for chronic cartilage degeneration and acute meniscal tears, segmental bone defects and vertebral disc degeneration.

Mesoblast intends to supply the purified MPCs to orthopaedic surgeons to administer to patients. During surgery the MPCs are delivered to the site of the bone damage, to repair the cartilage, a broken bone or disc degeneration. The MPCs speed up the normal healing process by:

- attracting the body's cells to the damaged area by secreting specific chemicals
- acting as a healing agent themselves
- increasing the number of blood vessels supplying oxygen and nutrients to the area.

### Acceptance and commercialisation

Similar to Angioblast, Mesoblast is proposing to use common FDA approved carriers and delivery tools for the delivery of MPCs to patients. As these delivery tools are widely used in the medical community, this should assist in the general acceptance of Mesoblast's technology.

Mesoblast's management also expects to access existing programs that will form the basis for reimbursement from the US and international government and private reimbursement schedules, thereby reducing the marginal cost the patient is required to pay.

## 5.4 Patents

The intellectual property of the MPC technology is owned by Angioblast. Mesoblast has the worldwide licence to utilise the technology for orthopaedic applications.

# 5.5 Board and management

Mesoblast and Angioblast have two common directors: Professor Itescu and Mr O'Dwyer. Professor Itescu is an executive director and Mr O'Dwyer is non-executive deputy Chairman. We set out below details relating to the remaining members of the board of Mesoblast:

#### Brian Jamieson - Non-executive Chairman

Mr Jamieson has over 30 years of experience providing a range of financial services to public and private companies. He was most recently Chief Executive of Minter Ellison Melbourne and previously Chief Executive Officer (CEO) of KPMG. He is currently a non-executive director of OZ Minerals Limited, Sigma Pharmaceuticals Limited, Oxiana Limited and HBOS Australia Pty Limited.

## Michael Spooner - Non-executive director

Mr Spooner has spent the last 25 years in the financial services industry building a reputation for his competence in the rapid commercialisation of high growth companies. He was most recently Managing Director and CEO of Ventracor Limited, a life sciences company. Prior to that he has also been a Principal Partner and Director of Consulting Services with PricewaterhouseCoopers.

#### Brian McAllister - Non-executive director

Mr McAllister brings extensive knowledge in product development, quality assurance, and obtaining FDA regulatory approvals within the healthcare industry. Most recently, he was Vice President of worldwide quality assurance for the Ares-Serono Group. He is a member of the International Association of Pharmaceutical Science and Technology, American Society for Quality, and the Regulatory Affairs Professionals Society.

We set out below details regarding the remaining management of Mesoblast:

## **Dr Suzanne Lipe – Vice President of Operations**

Dr Lipe has almost 20 years of development and commercial experience in the pharmaceutical and biotech industry. She has held senior roles with ICI Pharmaceuticals (now AstraZeneca), Rhone-Poulenc Rorer (now Sanofi-aventis) and CSL Limited, as well as being Managing Director, CEO and a board member of three biotechnology start-up companies.

## Dr James T. Ryaby - Vice President of Research and Clinical Affairs

Dr Ryaby is an expert in the clinical development of orthopaedic and bone regenerative technologies. He has had extensive experience in designing and directing clinical trials. Most recently he held a similar clinical development role at the US publicly listed company, OrthoLogic Corporation.

#### Jenni Pilcher - CFO

Ms Pilcher qualified as a chartered accountant with PricewaterhouseCoopers and has worked in various corporate financial roles for Medeva Plc, Cadbury Schweppes Plc and most recently Spotless Group Limited.

# 5.6 Competitive position of Mesoblast

Given that Mesoblast and Angioblast use the same core MPC technology to develop the adult stem cell products, Mesoblast and Angioblast share a similar competitive position.

Table 11: SWOT analysis

| Table 11: SWOT analysis  |  |
|--|--|
| Strengths  | Weaknesses   |
| <ul> <li>initiated two Phase II clinical trials for lumbar spinal fusion, with the first producing good safety results</li> <li>received successful results for the Phase I non-union long bone facture repair trial, demonstrating the safety of the autologous MPC technology. There is a potential for Mesoblast to proceed to a Phase III clinical trial</li> <li>established manufacturing process for allogeneic MPCs to be used in Phase II clinical trials</li> <li>received approval for world's first osteoarthritis clinical trial focusing on the prevention of knee osteoarthritis after acute traumatic knee injury</li> <li>development of allogeneic adult stem cell products for all patients, and at a low cost and high-margin (pharmaceutical-style business model)</li> <li>Mesoblast holds a 33% interest in Angioblast and benefits from any successful clinical trial outcomes achieved by Angioblast</li> </ul> | <ul> <li>high upfront development risk while progressing to licensing stage</li> <li>escalating cost of development as further phases are undertaken</li> <li>relatively early stage of development</li> <li>heavy reliance on capital raisings</li> <li>long period of time required for the development of adult stem cell products before Mesoblast could begin to generate positive cash flows</li> </ul>          |
| Threats  | Opportunities  |
| <ul> <li>there is a risk that human responses may be different and that individuals may respond differently from findings from animal studies, although early data in human trials suggest this may not be the case</li> <li>if it is not possible to use MPCs in an allogeneic mode, the economic viability of the process may be doubtful</li> <li>MPCs are stored with a DMSO which is considered toxic but is FDA approved</li> <li>competing technologies (including drug, cell based and device technologies) from companies such as Osiris, StemCells Incorporated and ViaCell Incorporated</li> <li>stem cell research is evolving technology and the regulatory framework is still being developed</li> </ul>   | <ul> <li>following positive pre-clinical trials, Mesoblast has obtained ethics approval to commence a Phase II trial in anterior cervical interbody fusion</li> <li>growing incidence of orthopaedic related problems in the general population</li> <li>pre-clinical results provided a strong indication that the adult stem cell products may be effective in the treatment of degenerative disc disease</li> </ul> |

Source: Deloitte Corporate Finance analysis

We note that it is likely Angioblast will develop a marketable product prior to Mesoblast, as it has commenced a second Phase II trial for the treatment of end-stage heart failure in patients supported by mechanical heart assist devices.

# 5.7 Capital structure and shareholders

As at 30 June 2010, Mesoblast had 161.8 million ordinary shares on issue on a fully diluted basis, as shown in the following table.

Table 12: Top 10 Mesoblast registered shareholders as at 30 June 2010 (on fully diluted basis)

|                                 | Number of<br>shares<br>('000) | Percentage of total<br>issued shares<br>(%) |
|---------------------------------|-------------------------------|---|
| Professor Itescu                | 37,125                        | 22.9%                                       |
| Thorney Investments             | 16,529                        | 10.2%                                       |
| Aviva Investors                 | 12,399                        | 7.7%  |
| Independant Asset Management    | 11,094                        | 6.9%  |
| Telstra Super                   | 3,705                         | 2.3%  |
| Braitling Investments           | 3,480                         | 2.2%  |
| Kinetic Investment Partners     | 3,040                         | 1.9%  |
| Mr George Muchnicki             | 2,853                         | 1.8%  |
| Northcape Capital               | 2,790                         | 1.7%  |
| Mr Mark M Leibler               | 2,638                         | 1.6%  |
| Subtotal                        | 95,653                        | 59.1%                                       |
| Other shareholders <sup>1</sup> | 66,191                        | 40.9%                                       |
| Total                           | 161,844                       | 100.0%                                      |

Source: Mesoblast

Note

1. Includes 583,950 shares held by Mr O'Dwyer.

The following table summarises the share options on issue as at 30 June 2010:

Table 13: Mesoblast share option summary

| Issue date       | Number of options outstanding | Exercise price (AUD) | Expiry date      |
|------------------|-------------------------------|----------------------|------------------|
|                  |                               |                      |                  |
| 23 February 2006 | 200,000                       | 1.20                 | 30 June 2011     |
| 1 January 2007   | 15,000                        | 1.96                 | 1 January 2011   |
| 27 July 2008     | 2,130,000                     | 2.13                 | 30 June 2012     |
| 7 July 2008      | 2,308,000                     | 1.00                 | 30 June 2013     |
| 19 January 2009  | 240,000                       | 0.96                 | 18 January 2014  |
| 30 November 2009 | 1,680,000                     | 1.58                 | 30 November 2014 |
| 30 November 2009 | 300,000                       | 1.73                 | 30 November 2014 |
| 26 February 2010 | 90,000                        | 2.00                 | 26 February 2015 |
| Total            | 6,963,000                     |                      | •                |

Source: Mesoblast

# 5.8 Share price performance

A summary of Mesoblast's share price performance is provided in Table 15 below.

Table 14: Mesoblast quarterly share price information

| Date              | High (AUD) | Low (AUD) | Last Trade (AUD) | Volume (000s) |
|-------------------|------------|-----------|------------------|---------------|
| 30 June 2008      | 1.25       | 0.51      | 0.91             | 10,731        |
| 30 September 2008 | 1.35       | 0.86      | 1.10             | 5,712         |
| 29 December 2008  | 1.20       | 0.68      | 1.00             | 1,898         |
| 31 March 2009     | 1.00       | 0.73      | 0.85             | 8,389         |
| 30 June 2009      | 0.85       | 0.73      | 0.83             | 9,172         |
| 30 September 2009 | 1.30       | 0.78      | 1.03             | 8,844         |
| 31 December 2009  | 1.50       | 1.01      | 1.36             | 7,994         |
| 31 March 2010     | 2.26       | 1.37      | 2.04             | 11,184        |
| 30 April 2010     | 2.14       | 1.81      | 1.94             | 2,975         |
| 31 May 2010       | 2.17       | 1.71      | 1.90             | 3,259         |
| 30 June 2010      | 1.94       | 1.77      | 1.85             | 8,403         |
| 21 July 2010      | 1.90       | 1.72      | 1.90             | 2,068         |

Source: Capital IQ

Figure 6: Mesoblast stock activity on ASX



Source: Capital IQ and Deloitte Corporate Finance analysis

#### Notes:

- 1. AMP Limited sold approximately 4.4 million shares from 1 April to 7 April 2008
- 2. Achieved successful pre-clinical trial results for the treatment of osteoarthritis
- 3. Angioblast received FDA clearance for a Phase II trial for congestive heart failure
- 4. Key stem cell patent granted in the US
- 5. Angioblast received FDA clearance for a clinical trial for bone marrow transplant
- Angioblast commenced Phase II trials for improving heart muscle function in patients with the most severe form of heart failure sending a positive signal about the MPC technology
- 7. Mesoblast achieved successful bone marrow regeneration for cancer patients in the US
- Southern Cross Equities initiated coverage of Mesoblast. Royal Bank of Scotland upgraded its rating of Mesoblast after positive clinical trial results which suggested that Angioblast may be able to apply its technology to diabetic treatments
- Biosimilar biological production provision update in the US Patient Protection and Affordable Care Act
  potentially increases the commercial exclusivity of Mesoblast's and Angioblast's biological products.

## 5.9 Profit and loss statement

The audited profit and loss statements of Mesoblast for FY 2008 and FY 2009 and the half year ended 31 December 2009 are summarised in the table below.

Table 15: Profit and loss

|  | FY 2008<br>audited<br>(AUD 000) | FY 2009<br>audited<br>(AUD 000) | 31 December 200<br>6 months<br>audited<br>(AUD 000) |
|--|---------------------------------|---------------------------------|---|
| Trading revenue  | _                               | _                               | _   |
| Other revenue  | -                               | 186.3                           | -   |
| R&D expenditure  | (6,050.6)                       | (7,025.7)                       | (3,375.4)   |
| Management and administration  | (2,642.0)                       | (3,174.1)                       | (1,569.1)   |
| Share of losses in investments accounted for using the equity method | (2,122.8)                       | (2,856.5)                       | (1,478.1)   |
| EBITDA   | (10,815.4)                      | (12,870.0)                      | (6,422.6)   |
| Depreciation and amortisation  | (156.8)                         | (119.8)                         | (80.9)  |
| EBIT   | (10,972.2)                      | (12,989.8)                      | (6,503.5)   |
| Net interest revenue   | 909.8                           | 704.4                           | 287.4   |
| Profit before tax  | (10,062.4)                      | (12,285.4)                      | (6,216.1)   |

Source: Mesoblast

We note the following in relation to the above:

- in line with the current status of the business (i.e. R&D phase), the majority of costs relate to R&D expenditure
- other revenue relates predominantly to a commercial ready government grant received by Mesoblast in FY 2009. This grant is received when certain expenditures relating to clinical programs are incurred
- losses in investments accounted for using the equity method relate to the investment in Angioblast. The losses reflected Mesoblast's share of Angioblast's losses for the FY 2008, FY 2009 and half year ended 31 December 2009. As at 30 June 2009, Mesoblast held a 39.1% (non-diluted) interest in Angioblast and a 38.4% (non-diluted) interest as at 31 December 2009.

## 5.10 Balance sheet

The audited balance sheets of Mesoblast as at 30 June 2008, 30 June 2009 and 31 December 2009 are summarised in the table below.

Table 16: Balance sheet

|  | 30 June 2008<br>audited<br>(AUD 000) | 30 June 2009<br>audited<br>(AUD 000) | 31 December 2009<br>audited<br>(AUD 000) |
|--|--------------------------------------|--------------------------------------|--|
|  |                                      |                                      |  |
| Cash and cash equivalents                        | 14,094.2                             | 16,526.3                             | 14,653.1                                 |
| Account receivables                              | 123.9                                | 305.4                                | 315.9                                    |
| Prepayments                                      | 85.6                                 | 88.5                                 | 174.9                                    |
| Total current assets                             | 14,303.7                             | 16,920.2                             | 15,143.9                                 |
| Property, plant and equipment                    | 198.0                                | 246.1                                | 238.1                                    |
| Investment accounted for using the equity method | 12,761.3                             | 9,326.4                              | 8,745.4                                  |
| Intangible assets                                | 526.0                                | 482.3                                | 460.4                                    |
| Total non-current assets                         | 13,485.3                             | 10,054.8                             | 9,443.9                                  |
| Current payables                                 | 1,572.8                              | 1,185.1                              | 1,496.3                                  |
| Total liabilities                                | 1,572.8                              | 1,185.1                              | 1,496.3                                  |
| Net assets                                       | 26,216.2                             | 25,789.9                             | 23,091.5                                 |

Source: Mesoblast

We make the following comments in relation to the above balance sheets:

- the high cash balances held by Mesoblast reflect capital raising activities through share issuances over each of the past three years
- the investments accounted for using the equity method relates to Mesoblast's interest
  in Angioblast. As shown in Section 5.9, losses in Angioblast ranged between
  AUD 2.1 million and AUD 2.9 million from FY 2008 to FY 2009. In FY 2008 and
  FY 2009 Mesoblast increased its investment in Angioblast by AUD 6.4 million and
  AUD 0.2 million respectively
- intangible assets relate to patents and licences acquired by Mesoblast. In FY 2008, approximately AUD 0.2 million of patent costs were written off. The amount written off is included in R&D expenditure.

# 6. Profile of the Proposed Merged Entity

In this section, we have set out a profile of the Proposed Merged Entity, including

- potential outcomes in respect of the Proposed Transaction
- technologies owned by the Proposed Merged Entity
- the board of directors and control of the Proposed Merged Entity
- capital structure and shareholders of the Proposed Merged Entity
- potential market capitalisation of the Proposed Merged Entity.

We note that Mesoblast is seeking shareholder approval for an additional placement of 6,724,647 Mesoblast shares at AUD 1.70 per share at the EGM. We have assumed the share placement is approved at the EGM and adjusted the fully diluted capital in the Proposed Merged Entity and its net cash position accordingly.

## **6.1** Potential outcomes

If the Proposed Transaction is approved, Mesoblast will own a 100% interest in Angioblast, and the Non-Associated Shareholders will hold approximately 49.7% and 51.9% of the Proposed Merged Entity. The final holding in the Proposed Merged Entity by the current shareholders of Mesoblast will vary, depending on the number of shareholders of Angioblast electing the 15% Cash Option.

# 6.2 Technologies owned by the Proposed Merged Entity

The following summarises the platform technologies that will be owned by the Proposed Merged Entity:

- the MPC technology for the treatment of cardiovascular and eye diseases, type 2 diabetes and other non-orthopaedic applications
- the MPC technology for orthopaedic applications
- peptide therapeutic stromal-derived factor
- drug eluting stents based on RNA silencing technology

The Proposed Merged Entity will focus on commercialising the following applications using the MPC technology:

- cardiovascular applications including treatment for congestive heart failure and myocardial infarction, bone marrow transplants, the treatment of eye diseases associated with abnormal blood vessels and other non-orthopaedic diseases
- orthopaedic applications including treatment for chronic cartilage degeneration and acute meniscal tears, segmental bone defects and vertebral disc degeneration.

# 6.3 Capital structure and shareholders

The Proposed Merged Entity will continue to be listed on the ASX, under the current MSB code. The following table sets out the capital structure of the Proposed Merged Entity assuming the following:

• Mesoblast acquires all Angioblast shares that it does not already own by issuing a total of 94,590,000 Mesoblast shares

• Mesoblast acquires all Angioblast shares that it does not already own by issuing 83,569,721 Mesoblast shares and approximately AUD 19.2 million in cash.

Table 17: Indicative capital structure of the Proposed Merged Entity

| Scrip Consideration  | All scrip                      |  | 15% Cash O                     | ption                                    |
|--|--------------------------------|--|--------------------------------|--|
|  | Number of shares               | % of the<br>Proposed<br>Merged<br>Entity | Number of<br>shares            | % of the<br>Proposed<br>Merged<br>Entity |
| Mesoblast  |                                |  |                                |  |
| Mesoblast current shares on issue on fully diluted basis <sup>1</sup>            | 161,843,556                    | 61.5%                                    | 161,843,556                    | 64.2%                                    |
| Shares issued under the capital raising <sup>2</sup>                             | 6,724,647                      | 2.6%                                     | 6,724,647                      | 2.7%                                     |
| Total Mesoblast shares after the capital raising                                 | 168,568,203                    | 64.1%                                    | 168,568,203                    | 66.9%                                    |
| Scrip Consideration  |                                |  |                                |  |
| Scrip Consideration<br>Less: shares taken as cash under the 15%                  | 94,590,000                     |  | 94,590,000                     |  |
| Cash Option  | n/a                            |  | (11,020,279)                   |  |
| Scrip Consideration  | 94,590,000                     | 35.9%                                    | <b>83,569,721</b> <sup>3</sup> | 33.1%                                    |
| Total shares in the Proposed Merged<br>Entity                                    | 263,158,203                    | 100.0%                                   | 252,137,924                    | 100.0%                                   |
| Proposed Transaction share issuance  |                                |  |                                |  |
| Angioblast shares excluding Mesoblast's holding <sup>4</sup> Scrip Consideration | 1,456,692<br><b>94,590,000</b> |  | 1,456,692<br><b>83,569,721</b> |  |
| Implied exchange ratio   | <b>64.93</b> <sup>5</sup>      |  | <i>57.37</i> <sup>5</sup>      |  |

Source: Mesoblast and Deloitte Corporate Finance analysis

#### Notes:

- 1. Refer to Section 5.7 for detail
- 2. Refer to Section 1.1 for detail
- 3. Calculated based on the Scrip Consideration less the number of shares that Angioblast Shareholders can choose to take in cash under the 15% Cash Option (which equates to approximately 11,020,279 shares in total)
- 4. Refer to Section 4.7. This is calculated based on total Angioblast shares on issue on a fully diluted basis less Mesoblast's shareholding (705,323 shares) in Angioblast
- Calculated based on the ratio of Scrip Consideration to Angioblast shares on issue excluding those held by Mesoblast.

If the Proposed Transaction is approved, Mesoblast will remain listed on the ASX with the following capital structure:

- approximately 252.1 million to 263.2 million shares in the Proposed Merged Entity will be on issue (assuming the capital raising is approved in the EGM as discussed in Section 1.1), depending on the extent to which Angioblast Shareholders elect to receive cash under the 15% Cash Option
- approximately 83.6 million shares to 94.6 million shares will be held by shareholders of Angioblast, which is equivalent to a 33.1% to 35.9% interest in the Proposed Merged Entity

- Professor Itescu will receive approximately 50.0 million to 58.8 million shares in the Proposed Merged Entity for his 905,050 shares in Angioblast
- Professor Itescu will hold 87.1 million to 95.9 million shares in the Proposed Merged Entity or approximately 34.5% to 36.4% (on a fully diluted basis). Prior to the Proposed Transaction, Professor Itescu holds approximately 37.1 million shares or 22.9% in Mesoblast (on a fully diluted basis)
- Mr O'Dwyer will hold 2.0 million shares in the Proposed Merged Entity or approximately 0.8% (on a fully diluted basis). Prior to the Proposed Transaction, Mr O'Dwyer holds approximately 0.6 million shares or less than 1% in Mesoblast (on a fully diluted basis).

# 6.4 Potential market capitalisation

The following table shows the potential market capitalisation of the Proposed Merged Entity, assuming the Proposed Transaction is approved, using a range of share prices for the Proposed Merged Entity (based on the Mesoblast share price before and since the announcement of the Proposed Transaction). This table assumes that a total of 263.2 million Mesoblast shares will be on issue.

Table 18: Potential market capitalisation of the Proposed Merged Entity

| Proposed<br>Merged Entity       |       | Propos | sed Merged En | tity share price | e (AUD) |       |
|---------------------------------|-------|--------|---------------|------------------|---------|-------|
| (AUD million)                   | 1.50  | 1.75   | 2.00          | 2.25             | 2.50    | 2.75  |
| Potential market capitalisation | 394.7 | 460.5  | 526.3         | 592.1            | 657.9   | 723.7 |

Source: Deloitte Corporate Finance analysis

On the date of the announcement of the Proposed Transaction, shares in Mesoblast were trading at AUD 1.90. As at 21 July 2010, the Mesoblast share price was AUD 1.89.

# 6.5 Pro forma financial performance

After the Proposed Transaction, we expect the Proposed Merged Entity's financial performance to reflect the combined R&D costs associated with the development of the MPC technology. We therefore do not expect the pro forma financial performance of the Proposed Merged Entity to be fundamentally different to that of Mesoblast and Angioblast on a standalone basis.

# 7. Valuation methodology

# 7.1 Valuation methodologies

To estimate the fair market value of the various assets held by Mesoblast, Angioblast and the Proposed Merged Entity, we have considered common market practice and the valuation methodologies recommended by ASIC Regulatory Guide 111. These are discussed below.

#### 7.1.1 Market based methods

Market based methods estimate a company's fair market value by considering the market price of transactions in its shares or the market value of comparable companies. Market based methods include:

- capitalisation of maintainable earnings
- analysis of a company's recent share trading history
- industry specific methods.

The capitalisation of maintainable earnings method estimates fair market value based on the company's future maintainable earnings and an appropriate earnings multiple. An appropriate earnings multiple is derived from market transactions involving comparable companies. The capitalisation of maintainable earnings method is appropriate where the company's earnings are relatively stable.

The most recent share trading history provides evidence of the fair market value of the shares in a company where they are publicly traded in an informed and liquid market.

Industry specific methods estimate market value using rules of thumb for a particular industry. Generally rules of thumb provide less persuasive evidence of the market value of a company than other valuation methods because they may not account for company specific factors.

#### 7.1.2 Discounted cash flow methods

Discounted cash flow methods estimate market value by discounting a company's future cash flows to a net present value. These methods are appropriate where a projection of future cash flows can be made with a reasonable degree of confidence. Discounted cash flow methods are commonly used to value early stage companies or projects with a finite life.

#### 7.1.3 Asset based methods

Asset based methods estimate the market value of a company's shares based on the realisable value of its identifiable net assets. Asset based methods include:

- orderly realisation of assets method
- liquidation of assets method
- net assets on a going concern basis.

The orderly realisation of assets method estimates fair market value by determining the amount that would be distributed to shareholders, after payment of all liabilities including realisation costs and taxation charges that arise, assuming the company is wound up in an orderly manner.

The liquidation method is similar to the orderly realisation of assets method except the liquidation method assumes the assets are sold in a shorter time frame. Since wind up or liquidation of the company may not be contemplated, these methods in their strictest form may not necessarily be appropriate. The net assets on a going concern basis method estimates the market values of the net assets of a company but does not take account of realisation costs.

These asset based methods ignore the possibility that the company's value could exceed the realisable value of its assets as they ignore the value of intangible assets such as customer lists, management, supply arrangements and goodwill. Asset based methods are appropriate when companies are not profitable, a significant proportion of a company's assets are liquid, or for asset holding companies.

# 7.2 Selection of valuation methodologies

## 7.2.1 Valuation of Angioblast

As discussed above, the majority of the value of Angioblast lies in the value of the MPC technology for cardiovascular, eye and diabetes diseases and other non-orthopaedic diseases that Angioblast is currently developing.

We are of the opinion that the most appropriate methodology to value Angioblast is the discounted cash flow methodology as:

- Angioblast has a number of discrete projects which are at early and different stages in the full market delivery life cycle
- historically, early stage projects are exposed to significant risk associated with the likelihood of success at each stage of the project's progression, which can only be adequately reflected by probability weighting the cash flows associated with the project
- significant ongoing capital expenditure will be required by Angioblast during R&D stages
- Acuity has independently prepared probability weighted long term cash flow projections in relation to Angioblast.

We have added Angioblast's net cash position to the discounted cash flow value of Angioblast's MPC technology as described above.

As a cross-check of our primary valuation methodology, we have considered the value of Angioblast implied by the trading price of a Mesoblast share prior to the announcement of the Proposed Transaction given its shareholding in Angioblast is a significant asset of Mesoblast. The most recent share trading history provides evidence of the fair market value of the shares in a company where they are publicly traded in an informed and liquid market.

## 7.2.2 Valuation of Mesoblast before the Proposed Transaction

The value of Mesoblast lies in the value of the MPC technology for orthopaedic applications that it is current developing. In addition to this, Mesoblast also has a significant interest in Angioblast.

We are of the opinion that the most appropriate methodology to value Mesoblast is also the discounted cash flow methodology due to the same factors described in Section 7.2.1.

We have added the value of Mesoblast's 32.6% interest in Angioblast (based on the value derived through the application of the approach described in Section 7.2.1 above) and Mesoblast's net cash position to our value derived under the discounted cash flow method.

As a cross-check of our valuation of Mesoblast, we have considered the value of Mesoblast implied by the trading price of a Mesoblast share prior to the announcement of the Proposed Transaction.

## 7.2.3 Valuation of the Proposed Merged Entity

In order to value a share in the Proposed Merged Entity, we have adopted the sum of the parts valuation method which considered the following:

- the value of the Proposed Merged Entity's MPC technology for cardiovascular, eye and diabetes diseases and other non-orthopaedic diseases (being that owned through Angioblast)
- the value of the Proposed Merged Entity's MPC technology for orthopaedic applications (being that owned through Mesoblast)
- the combined net cash position post the Proposed Transaction.

We note that the relative value of synergies as a result of Mesoblast's acquisition of Angioblast, from a cash flow perspective, is expected to be minimal.

To provide additional support for our valuation of the Proposed Merged Entity, we have considered the value of the Proposed Merged Entity implied by the trading price of a Mesoblast share after the announcement of the Proposed Transaction.

# 7.3 Appointment and role of the technical expert

In preparing this report, Deloitte Corporate Finance worked in association with Acuity, a technical expert in the biotechnology industry. Acuity reviewed the technology, patents and licence agreements held by Angioblast and Mesoblast, and prepared separate probability weighted cash flow projections for each of the companies. The projected cash flows prepared by Acuity formed the basis for our valuation of Mesoblast and Angioblast. The scope of Acuity's work was controlled by Deloitte Corporate Finance.

## 8. Future cash flows

## 8.1 The Models

As discussed above, Deloitte Corporate Finance engaged Acuity to prepare projections of pre-tax cash flows in USD for Mesoblast and Angioblast based on the applications the companies are engaged in developing.

Specifically, for Mesoblast these applications are directed at the treatment of osteoarthritis of the knee, acute knee injuries, intervertebral disc regeneration, cervical spinal interbody fusion, lumbar spinal interbody fusion and non-union fracture repair.

For Angioblast, the applications are directed at the treatment of congestive heart disease, macular degeneration, autologous and allogeneic bone marrow transplantation, acute myocardial infarction, diabetic macular edema and type 2 diabetes.

The cash flow projections were prepared based on the following:

- analysis of the potential markets for the IP developed by Mesoblast and Angioblast
- analysis of the possible routes to market for the IP developed by Mesoblast and Angioblast
- assessment of the technical and commercial risks for the IP developed by Mesoblast and Angioblast and the associated probability of, and the timeframe required for the products to reach their respective markets
- an assessment of the potential market size, market penetration and time to market for the IP developed by Mesoblast and Angioblast
- details of the likely costs Mesoblast and Angioblast will incur in order to achieve the routes to market
- details of the potential revenues Mesoblast and Angioblast could generate
- a general summary of the likely revenues and expenditures of Mesoblast and Angioblast over the forecast period
- the potential revenues and costs for Mesoblast and Angioblast if they license the products immediately after obtaining FDA approvals for the products.

Acuity provided us with probability adjusted projections of revenue and expenditure over the duration of the patent of the products. The probability adjusted projected cash flows (the Models) formed the basis of our discounted cash flow valuation analysis.

Acuity's work was based on information provided by Mesoblast and Angioblast, online database searches, publicly accessible subscription services, discussions with Mesoblast and Angioblast staff and management and Acuity's own experience.

The analysis we have undertaken on the Models has included:

- limited analytical procedures regarding the mathematical accuracy of the Models
- holding discussions with Acuity concerning the preparation of the projections and its views regarding the assumptions on which they are based.

Deloitte Corporate Finance has made some adjustments to the cash flow projections in the Models where it was considered appropriate. These adjustments included, but were not limited to, the probability of reaching a certain phase, market penetration, timing on full product production and inflation assumptions.

Our work did not constitute an audit or review of the projections in accordance with the AUASB (or equivalent) standards and accordingly we do not express any opinion as to the reliability of the projections or the reasonableness of the underlying assumptions. However, nothing has come to our attention as a result of our limited work that suggests that the assumptions on which the projections are based have not been prepared on a reasonable basis unless specified otherwise.

Since projections relate to the future, they may be affected by unforeseen events and they depend, in part, on the effectiveness of managements' actions in implementing the plans on which the projections are based. Accordingly, actual results are likely to be different from those projected because events and circumstances frequently do not occur as expected, and those differences may be material.

Key assumptions adopted in the Models are described in the following sections.

# 8.2 Key assumptions

The key assumptions adopted in the preparation of the projections for Mesoblast and Angioblast are as follows:

- Mesoblast and Angioblast complete necessary clinical trials at their own expense and
  obtain the relevant marketing approvals. They then license the patents to third parties
  for manufacturing and distribution. In return, Mesoblast and Angioblast will receive a
  royalty of 15% on sales revenue received by third parties (this is contingent upon
  Mesoblast and Angioblast being able to raise sufficient capital from investors to
  complete all clinical trials and obtain FDA approvals)
- the expected timeframe required to complete each trial phase for each product
- treatment pricing, market size and peak market penetration for each treatment assumptions as set out in the following table:

Table 19: Treatment assumptions (in 2010 dollars)

| Treatment                               | Treatment cost<br>per patient<br>(USD) <sup>1</sup> | Initial market size <sup>2</sup><br>('000s per annum) | Peak market penetration |
|---|---|---|-------------------------|
| Mesoblast                               |   |   |                         |
| Osteoarthritis of the knee <sup>3</sup> | 8,000   | 8,635   | 25%                     |
| Acute knee injuries                     | 15,000  | 70  | 20%                     |
| Invertebral disc regeneration           | 7,500   | 660   | 20%                     |
| Cervical spine interbody fusion         | 9,500   | 120   | 25%                     |
| Lumbar spine interbody fusion           | 7,340   | 280   | 20%                     |
| Non-union fracture repair               | 10,000  | 60  | 25%                     |
| Angioblast                              |   |   |                         |
| Congestive heart failure <sup>3</sup>   | 15,000  | 2,517   | 20%                     |
| Acute myocardial infarction             | 15,000  | 440   | 30%                     |
| Diabetic macular edema                  | 7,500   | 335   | 25%                     |
| Macular degeneration                    | 7,500   | 244   | 25%                     |
| Autologous bone marrow                  | 15,000  | 12  | 50%                     |
| transplantation                         |   |   |                         |
| Allogeneic bone marrow                  | 25,000  | 6   | 95%                     |
| transplantation                         |   |   |                         |
| Type 2 diabetes <sup>3</sup>            | 10,000  | 2,014   | 20%                     |

Source: Acuity

#### Note:

- Treatment cost is the amount receivable by the licensee to Mesoblast and Angioblast for supply of the MPC
  products, including any necessary packaging, delivery and administration systems, based on current treatment costs
- 2. As at 1 January 2010
- 3. For these indications, the market size has been determined based on the prevalence of the diseases as at 1 January 2010 adjusted for the annual growth rate in incidence, the mortality rate and the rate of cure of the disease. For all other applications, the market size is based on the initial size of the market as at 1 January 2010, adjusted for the annual growth rate in incidence.
- Mesoblast and Angioblast have indicated they will initially target the US market and therefore market share assumptions refer to the US only
- the MPC product or products supplied will be generic to the condition being treated and suitable for administration to any individual irrespective of the donor source
- the MPC product or products supplied will only require a single treatment, therefore the Models do not consider patients receiving repeat treatments of the same product (where repeat treatments of the product may be required sporadically over a patient's life span)

- long-term inflation of 2.5%, consistent with the long term historical average of inflation in the US
- the application of a 35% taxation rate on Mesoblast and Angioblast's future earnings, based on the US corporate tax rate and zero state tax.

The projected cash flows end in 2024 for all products except for products directed at the treatment of diabetic macular edema, macular degeneration and type 2 diabetes. For products treating diabetic macular edema and macular degeneration, the forecast cash flows end in 2027, and for products treating type 2 diabetes the forecast cash flows end in 2029.

We have not included a terminal value for Mesoblast and Angioblast beyond the end of the forecast cash flows. This is consistent with the duration of the current patents, and based on the assumption that after this period, due to substitute products, the products and the technology will be obsolete. However, this could be viewed as a conservative assumption.

In addition, we have not incorporated the potential benefits associated with the HB 3590. HB 3590 will provides the originator exclusive market protection by limiting the approval of a biosimilar product by the FDA.

#### Probability adjustments to future cash flows

The cash flow projections include a probability adjustment for the likelihood of achieving the cash flow. The probability adjustment is based on the cumulative probability of completing a set phase of R&D.

Generally, the evaluation of MPCs for additional indications will commence with a Phase I/II trial combining Phase I and Phase II trials for the same treatment into a single protocol in patients diagnosed with the disease or condition for which the study drug is intended (Phase 1b/IIa).

It is expected that studies will then progress directly to a Phase III or pivotal study which generates the data required by regulatory agencies to decide whether or not to approve the treatment.

A generic overview of this consideration as well as the timing and probability of the cash flows is shown in the table below:

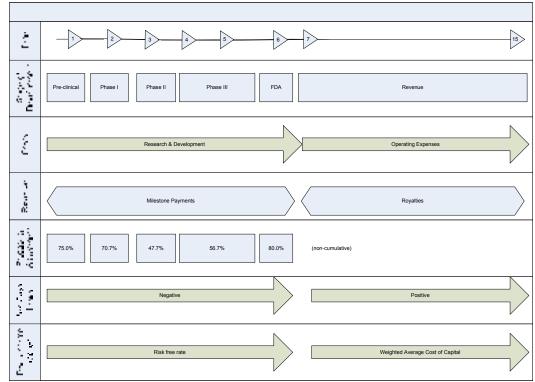


Figure 7: Generic overview of probability adjusted cash flows

Source: Acuity

Note:

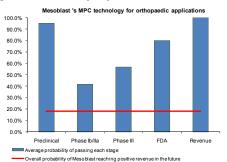
 The projected cash flows for Mesoblast and Angioblast do not include any milestone payments (refer to the revenue stage in figure above) as Mesoblast and Angioblast have not yet entered into licensing arrangements with any major pharmaceutical companies in relation to their MPC technology. Projected cash flows are premised on Mesoblast and Angioblast taking their MPC technology to the FDA stage.

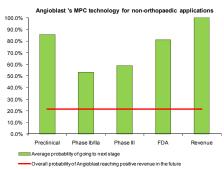
For Mesoblast and Angioblast, the probability adjustments applied to projected cash flows for each trial phase of each product varies depending on the extent of the product's development to date, as follows:

- for products which are yet to pass the pre-clinical phase, the probability associated with passing the pre-clinical phase is assumed to be between 50% and 95% where no IND approval has been granted
- for products which are yet to pass the pre-clinical phase, the probability associated with passing the pre-clinical phase is assumed to be between 100% where IND approval has been granted
- for products in the combined Phase Ib/IIa, the probability associated with passing ranges from 35% to 65%
- for products in Phase III, the probability associated with passing ranges from 57% and 80%
- once Phase III has been passed, the probability of obtaining FDA approval is approximately 80% to 90%.

The following figures illustrate the average probability of the products passing each stage of the pre-clinical, clinical trials and obtaining FDA approval, versus the overall probability of products reaching the revenue phase as assumed in the cash flows.

Figure 8: Probability adjustments assumed in the projected cash flows





Source: Deloitte Corporate Finance analysis

# 9. Valuation of Angioblast

In Section 7.2.1 above, we set out our approach to the valuation of Angioblast.

Set out in this section is the application of our valuation approach as discussed in Section 7.2.1. Section 9.1 sets out our valuation of Angioblast's MPC technology whilst Section 9.2 considers Angioblast's other assets and liabilities. Section 9.3 summarises our estimate of the value of Angioblast whilst a cross check of our estimate of value is set out in Section 9.4.

# 9.1 Valuation of Angioblast's MPC technology

The discounted cash flow method estimates market value by discounting a company's future cash flows to their net present value. To value Angioblast's MPC technology using the discounted cash flow method requires the determination of the following:

- future cash flows of Angioblast
- an appropriate discount rate to be applied to the cash flows.

Our consideration of each of these factors is presented in the following sections.

#### 9.1.1 Future cash flows

The future cash flows for Angioblast's MPC technology are discussed in Section 8.2.

### 9.1.2 Discount rates

The discount rate used to equate the future cash flows to a present value reflects the risk adjusted rate of return demanded by a hypothetical investor. We have selected a nominal after tax discount rate in the range of 15.5% to 16.5% to discount the future cash flows of Angioblast to their present value, with the exception of planned expenditures during the R&D phase, which we have discounted at the risk free rate.

In selecting this discount rate, we have considered the following factors:

### General factors

- the required rates of returns of listed companies in the biotechnology industry (having regard to their stage of development, their size and number of projects)
- the indicative rates of return required by suppliers of venture capital for investments with similar technical and commercial risks
- the risks inherent in the forecast cash flows of Angioblast

#### Factors arguing for a lower discount rate

- a portion of the technical risks associated with achieving the cash flows has already been taken into account by probability adjusting the cash flows
- the end markets targeted are very large and if a project overcomes the technical and commercial hurdles then it could be extremely valuable

## Factors arguing for a higher discount rate

• the size and stage of development of Angioblast compared to other listed companies in the industry

- the specific business and financing risks of Angioblast
- notwithstanding the probability adjustments made to the projected cash flows to take
  account of the technical risks, there still remains uncertainty with respect to market
  acceptance of Angioblast's MPC technology and products. This risk is presented not
  only in the royalty rate Angioblast may receive but also the volume and prices
  Angioblast's commercialisation partner(s) may achieve.

A detailed consideration of these matters is provided in Appendix 2.

#### 9.1.3 Discounted cash flow valuation

In determining the fair market value of Angioblast's MPC technology, we have used the discounted cash flow method and considered a number of sensitivity scenarios with respect to the following:

- discount rate ranging from 15.0% to 17.0%
- delays in the overall completion of phases by one and two years
- the royalty rate received
- peak market penetration.

The discounted cash flow valuation under each scenario is set out below.

Table 20: Valuation of the MPC technology of Angioblast (AUD million)<sup>1</sup>

|   | Value of the MPC technology of Angioblast |                         |                         |                         | it                      |
|---|---|-------------------------|-------------------------|-------------------------|-------------------------|
| Discount rate   | 15.0%                                     | 15.5%                   | 16.0%                   | 16.5%                   | 17.0%                   |
| Delay in overall completion of phases <sup>2</sup>  |   |                         |                         |                         |                         |
| Model assumption  | 592.0                                     | 562.9                   | 535.3                   | 509.1                   | 484.0                   |
| Model assumption +1 year  | 502.6                                     | 475.4                   | 449.6                   | 425.1                   | 401.8                   |
| Model assumption +2 years   | 421.2                                     | 396.1                   | 372.2                   | 349.7                   | 328.3                   |
| Royalty rate received<br>Model assumption -1%<br>Model assumption<br>Model assumption +1% | 536.4<br>592.0<br>647.6                   | 509.6<br>562.9<br>616.3 | 484.2<br>535.3<br>586.5 | 460.0<br>509.1<br>558.1 | 436.9<br>484.0<br>531.2 |
| Peak market penetration   |   |                         |                         |                         |                         |
| Model assumption -5%  | 502.9                                     | 477.2                   | 452.6                   | 429.3                   | 407.2                   |
| Model assumption  | 592.0                                     | 562.9                   | 535.3                   | 509.1                   | 484.0                   |
| Model assumption +5%  | 667.1                                     | 635.3                   | 605.1                   | 576.3                   | 548.9                   |

Source: Deloitte Corporate Finance analysis

Note:

- We have converted the value of the projected cash flows derived under the discounted cash flow method from USD to AUD based on the spot USD/AUD exchange rate of 0.86
- 2. The impact of a delay in completing the R&D phases has three effects on the value of Angioblast. Firstly, a delay in completing the clinical trial phases is assumed to result in additional costs being incurred. Secondly, the Models assume that Angioblast experiences the same delay in earning positive future cash flows, resulting in a reduced timeframe in which Angioblast can derive benefits associated with its patents. Finally, the delay in deriving positive cash flows has a timing effect.

There remains considerable uncertainty with respect to all of the factors set out above. Having regard to the analysis undertaken by ourselves and Acuity, and our experience in valuing similar projects, we consider the fair market value of Angioblast's MPC technology to be in the range of AUD 450 million to AUD 510 million.

## 9.2 Other assets and liabilities

## 9.2.1 Surplus assets

We have not identified any surplus assets held by Angioblast.

## 9.2.2 Tax losses

We have assumed any taxation losses held by Angioblast can be carried forward and offset against future profits. Tax losses have therefore been factored into our cash flow projections.

## 9.2.3 Net cash position

Angioblast's net cash position as at 31 May 2010 is USD 3.4 million.

Angioblast has 201,374 unlisted share options on issue. In order to determine the value of a share in Angioblast on a fully diluted basis, we have assumed the options are exercised and the proceeds from the exercise of these options, which amounts to USD 5.1 million, has been included in Angioblast's current net cash position.

In addition, as a result of the Proposed Transaction, Angioblast will be obliged to pay transaction fees to financial advisors of approximately USD 4.8 million, which we have deducted from Angioblast's current net cash position.

As a result, we have estimated the net cash position for Angioblast to be USD 3.6 million or AUD 4.3 million based on the spot USD/AUD exchange rate of 0.86.

Table 21: Net cash position of the Angioblast

|  | AUD million |
|--|-------------|
| Net cash position of Angioblast <sup>1</sup>   |             |
| Cash as at 31 May 2010   | 4.0         |
| Assumed proceeds from the exercise of Angioblast's unlisted share options <sup>2</sup> | 5.8         |
| Less: transaction fees paid to financial advisers                                      | (5.6)       |
| Total net cash position of Angioblast  | 4.2         |

Source: Deloitte Corporate Finance analysis

Note:

- 1. Based on the spot USD/AUD exchange rate of 0.86
- 2. Assumes conversion of the 190,000 employee options and the three tranches of options issued in conjunction with the convertible notes pursuant to the Proposed Transaction.

# 9.3 Valuation of Angioblast

The fair market value of Angioblast and the value of a share of Angioblast on a control basis is summarised below.

Table 22: Valuation of Angioblast on a control basis

|   | Section    | Unit               | Low value | High value |
|---|------------|--------------------|-----------|------------|
| Value of Angioblast's MPC technology <sup>1</sup> | 9.1.3      | AUD million        | 450.0     | 510.0      |
| Net cash position <sup>1</sup>                    | 9.2.3      | AUD million        | 4.2       | 4.2        |
| Equity value (on a control basis)                 |            | <b>AUD</b> million | 454.2     | 514.2      |
| Number of shares on issue                         |            |                    |           |            |
| (on a fully diluted basis)                        | 4.7        | '000s              | 2,162     | 2,162      |
| Value of a share in Angioblast (on a contr        | rol basis) | AUD                | 210.1     | 237.8      |

Source: Deloitte Corporate Finance analysis

Note:

1. Converted to AUD based on the spot USD/AUD exchange rate of 0.86.

## 9.4 Cross check

We have not identified a directly suitable approach available to cross check our assessed value of Angioblast, as Angioblast is an unlisted company and the most recent capital raising undertaken by the company was an issuance of a USD 9 million convertible note with a relatively complex structure.

However, in the absence of any available directly suitable approach, as Mesoblast owns approximately 32.6% of shares in Angioblast on a fully diluted basis and given the significant value attributed to Angioblast, we have considered the market prices of the recent share trading in Mesoblast on the ASX as a cross check for our valuation of Angioblast. This is discussed in Section 10.5. Notwithstanding that shares in Mesoblast are thinly traded, we consider the shares prices of Mesoblast broadly support our valuation of Angioblast.

# 10. Valuation of Mesoblast before the Proposed Transaction

In Section 7.2.2 above, we set out our proposed approach to the valuation of Mesoblast. Set out in this section is the application of our valuation approach as discussed in Section 7.2.2. Section 10.1 sets out our valuation of Mesoblast's MPC technology whilst Section 10.2 considers the value of Mesoblast's 32.6% shareholding in Angioblast. Section 10.3 considers the value of other assets and liabilities. Section 10.4 summarises our estimate of the value of Mesoblast and a cross check of our estimate of value is set out in Section 10.5.

# 10.1 Valuation of Mesoblast's MPC technology

We have used the discounted cash flow method to estimate the fair market value of Mesoblast's MPC technology for the orthopaedic applications, based on the following:

- future cash flows of Mesoblast's MPC technology for orthopaedic applications, as discussed in Section 8.2
- an appropriate discount rate to be applied to the cash flows.

## 10.1.1 Future cash flows

The future cash flows for Mesoblast's MPC technology are discussed in Section 8.2.

#### 10.1.2 Discount rate

We have selected a nominal after tax discount rate in the range of 15.5% to 16.5% to discount the future cash flows of Mesoblast's MPC technology for orthopaedic applications to their present value, with the exception of planned expenditures during the R&D period, which we have discounted at the risk free rate.

Angioblast and Mesoblast share similar risks as both companies are currently developing the same MPC technology, but for different applications, and both are at a similar stage of clinical trials for various products. Accordingly, we consider it appropriate to use the same discount rate for Angioblast and Mesoblast.

A detailed consideration of the factors contributing to our selection of this discount range is provided in Appendix 2.

## 10.1.3 Discounted cash flow valuation

In determining the fair market value of Mesoblast's MPC technology, we have used the discounted cash flow method and considered a number of sensitivity scenarios with respect to the following:

- discount rate ranging from 15.0% to 17.0%
- delays in the overall completion of phases by one and two years
- the royalty rate received
- peak market penetration.

The discounted cash flow valuation of Mesoblast under each scenario is set out below.

Table 23: Valuation of the MPC technology of Mesoblast (AUD million)<sup>1</sup>

|  | Value of the MPC technology of Mesoblast |       |       |       |       |  |
|--|--|-------|-------|-------|-------|--|
| Discount rate                                      | 15.0%                                    | 15.5% | 16.0% | 16.5% | 17.0% |  |
| Delay in overall completion of phases <sup>2</sup> |  |       |       |       |       |  |
| Model assumption                                   | 273.7                                    | 257.3 | 241.7 | 226.8 | 212.6 |  |
| Model assumption +1 year                           | 204.7                                    | 189.9 | 175.8 | 162.4 | 149.7 |  |
| Model assumption +2 years                          | 152.4                                    | 139.0 | 126.3 | 114.2 | 102.8 |  |
| Royalty rate received                              |  |       |       |       |       |  |
| Model assumption -1%                               | 242.3                                    | 227.2 | 212.7 | 199.0 | 185.9 |  |
| Model assumption                                   | 273.7                                    | 257.3 | 241.7 | 226.8 | 212.6 |  |
| Model assumption +1%                               | 305.1                                    | 287.5 | 270.7 | 254.6 | 239.3 |  |
| Peak market penetration                            |  |       |       |       |       |  |
| Model assumption -5%                               | 215.7                                    | 201.5 | 188.0 | 175.1 | 162.8 |  |
| Model assumption                                   | 273.7                                    | 257.3 | 241.7 | 226.8 | 212.6 |  |
| Model assumption +5%                               | 327.3                                    | 308.9 | 291.4 | 274.6 | 258.7 |  |

Source: Deloitte Corporate Finance analysis

#### Notes:

- We have converted the value of the projected cash flows derived under the discounted cash flow method from USD to AUD based on the spot USD/AUD exchange rate of 0.86.
- 2. The impact of a delay in completing the R&D phases has three effects on the value of Mesoblast. Firstly, a delay in completing the clinical trial phases is assumed to result in additional costs being incurred. Secondly, the Models assume that Mesoblast experiences the same delay in earning positive future cash flows, resulting in a reduced timeframe in which Mesoblast can derive benefits associated with its patents. Finally, the delay in deriving positive cash flows has a timing effect.

There remains considerable uncertainty with respect to all of the factors set out above. Having regard to the analysis undertaken by ourselves and Acuity and our experience in valuing similar projects, we consider the fair market value of Mesoblast's MPC technology to be in the range of AUD 190 million to AUD 230 million.

# 10.2 Investment in Angioblast

Mesoblast owns 705,323 shares or a 32.6% interest in Angioblast on a fully diluted basis. Based on our discounted cash flow valuation of Angioblast in Section 9.3, we have assessed the fair market value of Angioblast to be AUD 454.2 million to AUD 514.2 million on a control basis.

## Discount for minority interest

A valuation of a company based on the discounted cash flow methodology results in an estimate of the fair market value of the company on a control basis. The difference between the market value of a controlling interest and a minority interest is referred to as the premium for control. Australian studies indicate the premiums required to obtain control of companies range between 20% and 40% of the portfolio holding values. A minority interest discount is the inverse of a premium for control (*minority interest discount* =  $1-[1/(1+control\ premium)]$ ) and generally ranges between 15% and 30%.

The owner of a controlling interest has the ability to do many things that the owner of a minority interest does not. These include:

- control the cash flows of the company, such as dividends, capital expenditure and compensation for directors
- determine the strategy and policy of the company
- make acquisitions, or divest operations
- control the composition of the board of directors.

Given that Mesoblast currently holds a 32.6% interest in Angioblast, we consider an adjustment to reflect a minority interest is appropriate. In particular, we have considered the specific circumstances of Mesoblast's association with Angioblast, including:

- Mesoblast has a significant interest in Angioblast which gives Mesoblast the rights to appoint one director on the board of Angioblast, and therefore Mesoblast is able to exert significant influence over Angioblast's operations
- notwithstanding the significant interest in Angioblast held by Mesoblast, there is one shareholder (Professor Itescu) who holds a larger interest
- along with the direct benefits delivered to Mesoblast, the above factors are also likely
  to result in Mesoblast's interest being highly marketable and of interest to a number
  of parties
- Angioblast has no external debt
- we expect that the synergies that could be achieved by potential purchasers of Angioblast to be relatively low.

The level of discount that should be applied to the value of a controlling interest in order to derive a minority interest is somewhat subjective. Given the size of its interest in Angioblast, we consider a comparatively low discount is appropriate and therefore have adopted a discount for minority interest of 15% for Mesoblast's interest in Angioblast.

The value of Mesoblast's shareholding in Angioblast on a significant influence basis is shown below.

Table 24: Valuation of Mesoblast's shareholding in Angioblast on a significant influence basis

|  | Section | Unit        | Low value | High value |
|--|---------|-------------|-----------|------------|
| Equity value of Angioblast (on a control basis)                                      | 9.3     | AUD million | 454.2     | 514.2      |
| Discount for minority interest   | 10.2    | %           | 15.0%     | 15.0%      |
| Equity value of Angioblast (on a minority interest basis)                            |         | AUD million | 386.1     | 437.1      |
| Mesoblast's 32.6% interest in Angiobla   | st      | %           | 32.60%    | 32.60%     |
| Value of Mesoblast's interest in<br>Angioblast (on a significant influence<br>basis) |         | AUD million | 125.9     | 142.5      |

Source: Deloitte Corporate Finance analysis

# 10.3 Other assets and liabilities

## 10.3.1 Net cash position

Mesoblast's net cash position was AUD 33.0 million as at 31 May 2010.

Mesoblast currently has 7.0 million unlisted share options on issue. The exercise prices of these share options range from AUD 0.65 to AUD 2.13. In order to determine the value of a share in Mesoblast on a fully diluted basis, we have assumed all of these options are exercised and the proceeds from the exercise of these options, which amounts to AUD 10.7 million is included in the net cash position.

The estimated net cash position for Mesoblast is therefore AUD 43.7 million.

Table 25: Net cash position of the Mesoblast

| AUD million |
|-------------|
|             |
| 33.0        |
|             |
| 10.7        |
| 43.7        |
|             |

Source: Deloitte Corporate Finance analysis

The shares issued as a result of the assumed exercise of the employee share options are included in our calculation of the number of shares on issue.

#### 10.3.2 Tax losses

We have assumed any taxation losses held by Mesoblast can be carried forward and offset against future profits. This is factored into our cash flow projections.

## 10.4 Valuation of Mesoblast

The fair market value of Mesoblast and the value of a share in Mesoblast on a control basis is summarised below.

Table 26: Valuation of Mesoblast on a control basis

| Section | Unit                     | Low value  | High value  |
|---------|--------------------------|--|---|
| 10.1.3  | AUD million              | 190.0  | 230.0   |
| 10.2    | AUD million              | 125.9  | 142.5   |
|         | AUD million              | 315.9  | 372.5   |
| 10.3.1  | AUD million              | 43.7   | 43.7  |
|         | <b>AUD</b> million       | 359.6  | 416.2   |
| 6.3     | million                  | 161.8  | 161.8   |
|         | AUD                      | 2.22   | 2.57  |
|         | AUD                      | 2.20   | 2.55  |
|         | 10.1.3<br>10.2<br>10.3.1 | 10.1.3 AUD million 10.2 AUD million AUD million  10.3.1 AUD million AUD million  6.3 million | 10.1.3 AUD million 190.0 10.2 AUD million 125.9 AUD million 315.9  10.3.1 AUD million 43.7 AUD million 359.6  6.3 million 161.8  AUD 2.22 |

Source: Deloitte Corporate Finance analysis

Based on the above, our assessed value of Mesoblast before the Proposed Transaction on a control basis is in the range of AUD 359.6 million and AUD 416.2 million and the value of a share in Mesoblast before the Proposed Transaction on a control basis is in the range of AUD 2.20 and AUD 2.55.

# 10.5 Cross check using recent share trading

We have considered the recent share trading of Mesoblast to cross check our assessed value of a share in Mesoblast.

Where the market is well informed and liquid, the market can be expected to provide an objective assessment of the fair market value of a listed entity. Market prices incorporate the influence of all publicly known information relevant to the value of an entity's securities. As the shares in Mesoblast are thinly traded, we consider that the share price provides relatively weak evidence of the fair market value of Mesoblast's shares. But, nonetheless, in the absence of any suitable cross checks, we consider it relevant to consider the recent share trading as a cross check.

Share prices from market trading do not typically reflect the market value for control of a company as they are for portfolio holdings. Australian studies indicate the premiums required to obtain control of companies range between 20% and 40% of the portfolio holding value. Share trading in Mesoblast reflects the market's assessment of the minority interest value of Mesoblast.

Our assessed value of a Mesoblast share is in the range of AUD 2.20 and AUD 2.55 on a control basis. We have set out the recent share trading activity in Mesoblast before 30 April 2010, when Mesoblast's shares went into a trading halt. The Proposed Transaction was announced on 12 May 2010.

Table 27: Recent share trading in Mesoblast prior to the announcement of the Proposed Transaction

|   | Low value<br>(AUD) | High value<br>(AUD) | VWAP |
|---|--------------------|---------------------|------|
| Deloitte Corporate Finance selected value per<br>Mesoblast share (on a control basis) | 2.20               | 2.55                |      |
| VWAP to 30 April 2010   |                    |                     |      |
| 1 month period prior to 30 April 2010   | 1.81               | 2.14                | 2.07 |
| 3 month period prior to 30 April 2010   | 1.62               | 2.20                | 2.00 |
| 6 month period prior to 30 April 2010   | 1.04               | 2.26                | 1.81 |

Source: Capital IQ, Deloitte Corporate Finance analysis

Over the last six months the Mesoblast share price has fluctuated widely, from a high of AUD 2.26 on 18 January 2010 to a low of AUD 1.04 on 2 November 2009. The share price as at 30 April 2010 and the one month VWAP at 30 April 2010 were AUD 1.94 and AUD 2.07, respectively.

The following figure compares the daily VWAP of Mesoblast shares for the year prior to Mesoblast entering a trading halt on 30 April 2010 and the VWAP of Mesoblast's shares for the three months prior to 30 April 2010 to our selected valuation range.

3.00
2.50
2.00
2.00
0.50

May-09 Jun-09 Jul-09 Aug-09 Sep-09 Oct-09 Nov-09 Dec-09 Jan-10 Feb-10 Mar-10 Apr-10
—Daily VWAP — Deloitte selected range — 3-month VWAP before 30 April 2010

Figure 9: Comparison of share trading of Mesoblast

Source: Capital IQ, Deloitte Corporate Finance analysis

The share price of the company prior to January 2010 may not be an appropriate guide of the current fair market value due to the significant developments within the business in January 2010 (namely, the positive clinical trial results).

In comparison to the VWAP for the three month period to 30 April 2010, our assessed value of a Mesoblast share implies a control premium of 10.0% to 27.5%. Having regard to control premiums typically paid in transactions involving ASX listed entities, we consider the share prices broadly support our valuation conclusion.

# 11. Valuation of the Proposed Merged Entity

# 11.1 Introduction

We have estimated the fair market value of a share in the Proposed Merged Entity on a minority interest basis as the Non-Associated Shareholders will continue to have minority interests in the Proposed Merged Entity. Set out in this section is our valuation approach as described in Section 7.2.3.

We have assessed the value of a share in the Proposed Merged Entity based on the following:

- the value of Angioblast's MPC technology for the applications of cardiovascular diseases (refer to Section 9.3), using the discounted cash flow method
- the value of Mesoblast's MPC technology for the orthopaedic applications (refer to Section 10.4), using the discounted cash flow method
- other assets and liabilities, including the value of any surplus assets, tax losses and the current net cash position
- an appropriate discount to reflect a minority interest in the Proposed Merged Entity.

Our consideration of each of these factors is presented in Sections 11.2 to 11.5.

We have also considered recent share market trading activity in Mesoblast after the announcement of the Proposed Transaction to provide additional evidence of the fair market value of a share in the Proposed Merged Entity.

We note that, under the Proposed Transaction, Mesoblast will acquire the remaining 67.4% of Angioblast that it does not already own by issuing up to 94.6 million Mesoblast shares to Angioblast shareholders. Holders of Angioblast shares also have the option to receive cash for up to 15% of their Angioblast shareholding, and the cash component of the cash and scrip offer will be determined based on the price of Mesoblast shares on the date of approval by the Non-Associated Shareholders.

The value of the Proposed Merged Entity will vary depending on the extent to which Angioblast Shareholders elect to receive cash under the 15% Cash Option and the market price of a Mesoblast share on the date of approval by the Non-Associated Shareholders. In the event that the share price of a Mesoblast share on the date of approval by the Non-Associated Shareholders is lower than our assessed value of a share in the Proposed Merged Entity, the value of the Proposed Merged entity will be higher and vice versa. We have set out the sensitivity of our valuation of the Proposed Merged Entity to the share price of Mesoblast on the date of approval of the Proposed Transaction in Section 11.5.

For the purposes of our valuation of the Proposed Merged Entity and our valuation of a share in the Proposed Merged Entity, we have assumed that the Angioblast shareholders will elect the all scrip offer.

# 11.2 Valuation of the Proposed Merged Entity's MPC technology

#### 11.2.1 Future cash flows

The future cash flows of the Proposed Merged Entity are effectively the sum of the projected cash flows of the MPC technology for the cardiovascular and other non-orthopaedic, and orthopaedic applications currently being developed by Angioblast and Mesoblast, respectively.

The future cash flows of the MPC technology of Angioblast and Mesoblast are discussed in Section 8.2.

#### 11.2.2 Discount rate

We have selected a nominal after tax discount rate in the range of 14.5% to 15.5% to discount the future cash flows of the Proposed Merged Entity's MPC technology for the orthopaedic and cardiovascular applications to their present value, with the exception of planned expenditures during the R&D period, which we have discounted at the risk free rate.

In selecting an appropriate discount rate for the Proposed Merged Entity, we have considered the following general factors:

- required rates of returns on listed companies in the biotechnology industry (having regard to their stage of development, their size and number of projects)
- indicative rates of return required by suppliers of venture capital for investment in assets with similar technical and commercial risks
- the risks inherent in the forecast cash flows of Angioblast and Mesoblast.

Our selection of a lower discount rate for the Proposed Merged Entity in comparison with the discount rates selected for Mesoblast and Angioblast primarily reflects the following factors:

- the Proposed Merged Entity will have the potential to access capital at a lower cost of equity reflecting its increased scale
- the Proposed Merged Entity will have the opportunity to allocate capital to applications with more promising clinical trial results, away from applications with a lower chance of successfully receiving FDA approval, to a greater extent than would be the case for Mesoblast and Angioblast on standalone bases
- the Proposed Merged Entity will have greater opportunity to realise value given the increased number of applications in its portfolio compared with Mesoblast and Angioblast
- the Proposed Merged Entity will benefit from diversification across its portfolio of orthopaedic, cardiovascular and other non-orthopaedic applications and will therefore have reduced its exposure to a focussed group of applications compared with Mesoblast and Angioblast.

Reflecting some of the above benefits, empirical studies such as the Ibbotson size premium analysis demonstrate that the required rate of return for larger companies are lower than those of smaller companies. According to Ibbotson, the difference in the required rate of return between a company with a market capitalisation of USD 214 million and USD 431 million has historically been 3%.

A detailed consideration of the factors contributing to our selection of this discount rate is provided in Appendix 2.

#### 11.2.3 Discounted cash flow valuation

In determining the fair market value of the Proposed Merged Entity's MPC technology, we have used the discounted cash flow method and considered a number of sensitivity scenarios with respect to the following:

- discount rate ranging from 14.0% to 16.0%
- delays in the overall completion of phases by one and two years
- the royalty rate received
- peak market penetration.

Set out below is our analysis below.

Table 28: Valuation of the MPC technology of the Proposed Merged Entity (AUD million)<sup>1</sup>

|  | Value of | the MPC techr | nology of the P | roposed Merge | ed Entity |
|--|----------|---------------|-----------------|---------------|-----------|
| Discount rate                                      | 14.0%    | 14.5%         | 15.0%           | 15.5%         | 16.0%     |
| Delay in overall completion of phases <sup>2</sup> |          |               |                 |               |           |
| Model assumption                                   | 963.5    | 913.4         | 865.7           | 820.3         | 777.0     |
| Model assumption +1 year                           | 798.0    | 751.5         | 707.3           | 665.3         | 625.4     |
| Model assumption +2 years                          | 657.1    | 614.2         | 573.5           | 535.0         | 498.5     |
| Royalty rate received                              |          |               |                 |               | ı         |
| Model assumption -1%                               | 868.9    | 822.6         | 778.7           | 736.8         | 696.9     |
| Model assumption                                   | 963.5    | 913.4         | 865.7           | 820.3         | 777.0     |
| Model assumption +1%                               | 1,058.1  | 1,004.1       | 952.7           | 903.7         | 857.1     |
| Peak market penetration                            |          |               |                 |               |           |
| Model assumption -5%                               | 804.8    | 760.6         | 718.6           | 678.7         | 640.6     |
| Model assumption                                   | 963.5    | 913.4         | 865.7           | 820.3         | 777.0     |
| Model assumption +5%                               | 1,102.5  | 1,047.1       | 994.4           | 944.3         | 896.5     |

Source: Deloitte Corporate Finance analysis

#### Notes:

- We have converted the value of the projected cash flows derived under the discounted cash flow method from USD to AUD based on the spot USD/AUD exchange rate of 0.86
- 2. The impact of a delay in completing the R&D phases has three effects on the value of the Proposed Merged Entity. Firstly, a delay in completing the clinical trial phases is assumed to result in additional costs being incurred. Secondly, the Models assume that the Proposed Merged Entity experiences the same delay in earning positive future cash flows, resulting in a reduced timeframe in which the Proposed Merged Entity can derive benefits associated with its patents. Finally, the delay in deriving positive cash flows has a timing effect.

There remains considerable uncertainty with respect to all of the factors set out above. Having regard to the analysis undertaken by ourselves and Acuity and our experience in valuing similar projects, we consider the fair market value of the Proposed Merged Entity's MPC technology to be in the range of AUD 720 million to AUD 820 million.

## 11.3 Other assets and liabilities

#### 11.3.1 Surplus assets

We have not identified any surplus assets held by the Proposed Merged Entity.

#### 11.3.2 Net cash position

As discussed in Section 11.1, for the purposes of estimating the net cash position of the Proposed Merged Entity, we have assumed all Angioblast Shareholders accept the scrip offer.

In addition, we have included the expected proceeds from the shares issued under the proposed capital raising discussed in Section 1.1, which amounts to approximately AUD 11.4 million. We have included the shares to be issued under the proposed capital raising in our calculation of the fully diluted shares in the Proposed Merged Entity (Section 6.3).

The following table sets out the estimated net cash position of the Proposed Merged Entity.

Table 29: Net cash position of the Proposed Merged Entity (under the all scrip offer)

|  | Section | AUD million |
|--|---------|-------------|
| Net cash position of Angioblast <sup>1</sup>                               | 9.2.3   | 4.2         |
| Net cash position of Mesoblast   | 10.3.1  | 43.7        |
| Assumed proceeds from the shares issued under the proposed capital raising | 1.1     | 11.4        |
| Total net cash position of the Proposed Merged Entity                      |         | 59.3        |

Source: Deloitte Corporate Finance analysis

Note:

1. Based on the spot USD/AUD exchange rate of 0.86.

# 11.4 Discount for minority interest

As discussed in Section 10.2, a valuation of a company based on the discounted cash flow method, results in an estimate of the fair market value of the company on a control basis.

If the Proposed Transaction is completed, the Non-Associated Shareholders will individually hold shares in the Proposed Merged Entity and remain as minority shareholders. Our valuation of a share in the Proposed Merged Entity, based on the sum of the parts method where the principal assets are valued using the discounted cash flow methodology, has therefore been adjusted to reflect a minority interest basis.

The following factors have been taken into consideration in determining an appropriate minority interest discount for the Proposed Merged Entity:

- we assessed the control premiums implied by recent transactions in the Australian biotechnology sector, however there have been only three transactions identified over the past three years. The control premium ranged from nil to 67%
- the average and median control premiums implied by market transactions in the broader Australian market is in the range of 20% to 40%, implying a minority interest discount in the range of 17% to 29%
- the Proposed Merged Entity will have no debt.

Based on these considerations, we have assessed an appropriate discount for minority interest of 20% to be appropriate for the Non-Associated Shareholders' interests in the Proposed Merged Entity.

## 11.4.1 Total shares on issue for the Proposed Merged Entity

Based on the all scrip offer under the Proposed Transaction, the total shares on issue for the Proposed Merged Entity will be 263.2 million shares on a fully diluted basis. For further discussion on the issued shares in the Proposed Merged Entity, refer to Section 6.3.

# 11.5 Valuation of the Proposed Merged Entity

The fair market value of the Proposed Merged Entity and the value of a share of the Proposed Merged Entity on a minority interest basis, derived from the discounted cash flow method is summarised below.

Table 30: Valuation of the Proposed Merged Entity

|  | Section          | Unit                                      | Low value                     | High Value                    |
|--|------------------|---|-------------------------------|-------------------------------|
| Value of the MPC technology Net cash position Equity value (on a control basis)  | 11.2.3<br>11.3.2 | AUD million<br>AUD million<br>AUD million | 720.0<br>59.3<br><b>779.3</b> | 820.0<br>59.3<br><b>879.3</b> |
| Discount for minority interest  Equity Value (on a minority interest basis)  | 11.4             | AUD million                               | 20%<br><b>623.5</b>           | 20%<br><b>703.5</b>           |
| Total number of shares on issue  | 6.3              | million                                   | 263.2                         | 263.2                         |
| Value of a share in the Proposed Merged Entity (on a minority interest basis)  |                  | AUD                                       | 2.37                          | 2.67                          |
| Deloitte Corporate Finance selected value<br>per a share in the Proposed Merged Entity<br>(on a minority interest basis) |                  | AUD                                       | 2.35                          | 2.65                          |

Source: Deloitte Corporate Finance analysis

Based on the above, our assessed value of the Proposed Merged Entity on a minority basis is between AUD 623.5 million and AUD 703.5 million and the value of a share in the Proposed Merged Entity is in the range of AUD 2.35 and AUD 2.65.

As mentioned in Section 11.1, the valuation of the Proposed Merged Entity will vary depending on the extent to which the Angioblast Shareholders elect to receive cash under the 15% Cash Option and the market price of a Mesoblast share on the date of approval by the Non-Associated Shareholders.

The following table sets out the value of the Proposed Merged Entity assuming 15% of the consideration offered to Angioblast Shareholders, other than Mesoblast, is paid in cash at a range of market price of a Mesoblast share.

Table 31: Potential value of the Proposed Merged Entity at different Mesoblast share prices

| Mesoblast<br>share price | Cash to be paid <sup>1</sup><br>(AUD million) | Low equity<br>value<br>(AUD million) | High equity<br>value<br>(AUD million) | Low equity<br>value per<br>share<br>(AUD) | High equity<br>value per<br>share<br>(AUD) |
|--------------------------|---|--------------------------------------|---------------------------------------|---|--|
| 1.65                     | 18.2  | 608.9                                | 688.9                                 | 2.42                                      | 2.73                                       |
| 1.85                     | 20.4  | 607.2                                | 687.2                                 | 2.41                                      | 2.73                                       |
| 2.05                     | 22.6  | 605.4                                | 685.4                                 | 2.40                                      | 2.72                                       |
| 2.25                     | 24.8  | 603.6                                | 683.6                                 | 2.39                                      | 2.71                                       |
| 2.45                     | 27.0  | 601.9                                | 681.9                                 | 2.39                                      | 2.70                                       |
| 2.65                     | 29.2  | 600.1                                | 680.1                                 | 2.38                                      | 2.70                                       |
| 2.85                     | 31.4  | 598.3                                | 678.3                                 | 2.37                                      | 2.69                                       |
| 3.05                     | 33.6  | 596.6                                | 676.6                                 | 2.37                                      | 2.68                                       |

Source: Deloitte Corporate Finance analysis

#### Note:

The Scrip Consideration is 94.6 million Mesoblast shares. If 15% of the value of the shares in Angioblast, excluding Mesoblast's shareholding, is paid in cash, then cash to be paid is calculated based on approximately 11 million shares multiplied by the share price of Mesoblast on the date of approval by the Non-Associated Shareholders.

As can be seen from the above, the impact of the 15% Cash Option is insignificant.

# 11.6 Cross check for the Proposed Merged Entity

We have considered the share trading of Mesoblast after the announcement of the Proposed Transaction on 12 May 2010 to cross check our assessed value of a share in the Proposed Merged Entity.

The market can be expected to provide an objective assessment of the fair market value of a listed entity, where the market is well informed and liquid. Market prices incorporate the influence of all publicly known information relevant to the value of an entity's securities. Given that Mesoblast shares are thinly traded, we consider the share trading of Mesoblast shares represents weak support for our value of a share in the Proposed Merged entity.

Our assessed value of a share in the Proposed Merged Entity is in the range of AUD 2.35 to AUD 2.65 on a control basis. We have set out the recent share trading activity in Mesoblast after 12 May 2010, when the Proposed Transaction was announced.

Table 32: Analysis of recent share trading prior in Mesoblast after the announcement of the Proposed Transaction

|  | Low value<br>(AUD) | High value<br>(AUD) | VWAP |
|--|--------------------|---------------------|------|
| Deloitte Corporate Finance selected value per<br>Proposed Merged Entity share (on minority |                    |                     |      |
| interest basis)  | 2.35               | 2.65                |      |
| Share price after the announcement of the Pr   | oposed Transaction |                     |      |
| 1 day post the announcement  | 1.96               | 2.00                | 1.98 |
| 10 days post the announcement  | 1.71               | 2.17                | 1.97 |
| 30 days post the announcement  | 1.71               | 2.17                | 1.87 |

Source: Capital IQ, Deloitte Corporate Finance analysis

The table above shows the Mesoblast share price after the announcement of the Proposed Transaction is lower than our assessed value of a share in the Proposed Merged Entity. This could be driven by:

- Mesoblast successfully completed a capital raising of AUD 37 million at AUD 1.70 per Mesoblast share on 12 May 2010, which represents a discount of approximately 17.9% to the daily VWAP of AUD 2.07 on 30 April 2010. In general, we have observed that a capital raising undertaken at a discount to a company's trading price is likely to have the effect of reducing the trading price of the company immediately following the capital raising
- in the 10 day period after Mesoblast announced the Proposed Transaction, the Standard and Poor's ASX 200 Index declined by approximately 8.1%, while Mesoblast's share price, which had a 10-day VWAP of AUD 1.97 as at 26 May 2010, did not decline to the same extent. Given Mesoblast's share price did not decline to the same extent as the Standard and Poor's ASX 200 Index, this may suggest the market has already incorporated some of the effect of the Proposed Transaction
- Mesoblast's 30 day VWAP has decreased to AUD 1.87. Given the time that has
  elapsed since the announcement of the Proposed Transaction, Mesoblast's share price
  may have been affected by other market factors and uncertainty as to the likelihood of
  the Proposed Transaction proceeding
- there is limited understanding of and transparency around Angioblast's MPC technology by market participants, which may have resulted in the market undervaluing Angioblast. While the Proposed Transaction has been announced, the market's level of understanding of Angioblast's MPC technology has not changed in comparison to before the announcement. Therefore, Mesoblast's share price may not have fully incorporated the effect of the Proposed Transaction and therefore the underlying value of Angioblast's MPC technology.

# 12. Evaluation and conclusion

# 12.1 Assessment for the purpose of Section 611 of the Corporations Act

Under Section 606 of the Corporations Act, an issue of shares by a company to a shareholder that will increase the shareholder's relevant interest in the company from above 20% to less than 90% is prohibited, unless the proposed transaction is approved by the shareholders at a general meeting in accordance to Section 611 of the Corporations Act. If the Proposed Transaction is approved, Professor Itescu's shareholding in the Proposed Merged Entity will increase from 22.9% to up to 36.4% (on a fully diluted basis).

In assessing whether the Proposed Transaction is fair and reasonable for the purpose of Section 611 of the Corporations Act, we have assessed:

- whether the Proposed Transaction is fair by estimating the fair market value of a share in Mesoblast on a control basis before completion of the Proposed Transaction and comparing that value to the estimated fair market value of a share in the Proposed Merged Entity
- the reasonableness of the Proposed Transaction by considering other advantages and disadvantages of the Proposed Transaction to the Non-Associated Shareholders.

#### 12.1.1 Fairness

Set out in the table below is a comparison of our assessed fair market value of a share in Mesoblast on a control basis, before the Proposed Transaction, and with fair market value of a share in the Proposed Merged Entity on a minority interest basis.

Table 33: Comparison of a share in Mesoblast and a share in the Proposed Merged Entity

|   | Section | Low value<br>per share<br>(AUD) | High value<br>per share<br>(AUD) |
|---|---------|---------------------------------|----------------------------------|
| Estimated fair market value of a share in Mesoblast on a control basis                            | 10.4    | 2.20                            | 2.55                             |
| Estimated fair market value of a share in the Proposed Merged Entity on a minority interest basis | 11.5    | 2.35                            | 2.65                             |

Source: Deloitte Corporate Finance analysis

Given that the fair market value of a share in the Proposed Merged Entity on a minority interest basis is above the range of our estimate of the fair market value of a share in Mesoblast on a control basis, the Non-Associated Shareholders are effectively receiving a control value for their shareholding in Mesoblast under the Proposed Transaction. Accordingly, in our opinion, the Proposed Transaction is fair.

If the Angioblast Shareholders elect to receive cash under the 15% Cash Option, the following table sets out the value of a share in the Proposed Merged Entity, assuming 15% of Angioblast's shares are acquired using cash, at a range of market prices of a Mesoblast share.

Table 34: Comparison of the value of a Mesoblast share with potential value of a share in the Proposed Merged Entity

|  | Low equity value<br>per share<br>(AUD) | High equity value<br>per share<br>(AUD) |
|--|--|---|
| Fair market value of a share in Mesoblast on a control basis                                   | 2.20                                   | 2.55                                    |
| Value of a share in the Proposed Merged Entity at different market prices of a Mesoblast share |  |   |
| 1.65   | 2.42                                   | 2.73                                    |
| 1.85   | 2.41                                   | 2.73                                    |
| 2.05   | 2.40                                   | 2.72                                    |
| 2.25   | 2.39                                   | 2.71                                    |
| 2.45   | 2.39                                   | 2.70                                    |
| 2.65   | 2.38                                   | 2.70                                    |
| 2.85   | 2.37                                   | 2.69                                    |
| 3.05   | 2.37                                   | 2.68                                    |

Source: Deloitte Corporate Finance analysis

Based on the above analysis, the Proposed Merged Entity remains fair if Angioblast Shareholders elect to receive cash under the 15% Cash Option and if Mesoblast's share price varies in the range of AUD 1.65 and AUD 3.05.

#### 12.1.2 Reasonableness

In accordance with ASIC Regulatory Guide 111, a proposed transaction is reasonable if it is fair. On this basis, in our opinion the Proposed Transaction is reasonable.

Notwithstanding this, we have also considered the advantages and disadvantages of the Proposed Transaction, which are set out in Section 12.3.

# 12.2 Assessment for the purpose of ASX Listing Rule 10

Pursuant to ASX Listing Rule 10.1 the Proposed Transaction is considered a related party transaction, given that Mesoblast will effectively acquire a substantial asset from Professor Itescu, who is also is a director and a significant shareholder of Mesoblast.

As such, we have evaluated whether the Proposed Transaction is fair and reasonable (being a compound phrase) to the Non-Associated Shareholder under ASX Listing Rule 10.1 by considering the overall effect of the Proposed Transaction. This requires consideration of the advantages and disadvantages of the Proposed Transaction so far as the Non-Associated Shareholders are concerned. Our analysis of the advantages and disadvantages is set out in Section 12.3 below.

Having regard to this analysis, in our opinion, the Proposed Transaction is fair and reasonable as the expected benefits of the Proposed Transaction, so far as the Non-Associated Shareholders are concerned, outweigh the disadvantages associated with the Proposed Transaction.

# 12.3 Advantages and disadvantages of the Proposed Transaction

In this section, we have discussed the advantages and disadvantages of the Proposed Transaction, which we have considered in forming our opinion regarding the reasonableness of the Proposed Transaction for the purpose of Section 611 of the Corporations Act.

We have also had regard to the advantages and disadvantages in determining whether the Proposed Transaction is fair and reasonable (being a compound phrase) for the purposes of ASX Listing Rule 10.1.

#### **Advantages of the Proposed Transaction**

The likely advantages to the Non-Associated Shareholders if the Proposed Transaction is approved include:

# The fair market value of the interest in Angioblast being acquired is higher than that being paid for it

Under the Proposed Transaction, Mesoblast will issue a total of 94,590,000 shares to acquire all of the shares in Angioblast that Mesoblast does not already own. Based on the assessed value of a share in the Proposed Merged Entity (refer to Section 11.5) the total value of the Scrip Consideration is in the range AUD 222.3 million to AUD 250.7 million.

Based on our analysis in Section 9.3, our assessed fair market value of the 67.4% interest in Angioblast is in the range of AUD 306.1 million and AUD 346.6 million.

Our analysis is set out in the table below.

Table 35: Comparison of the value of 67.4% of Angioblast and the value of the Scrip Consideration

|  | Section | Unit           | Low value    | High value   |
|--|---------|----------------|--------------|--------------|
| Estimated fair market value of Angioblast on a control basis   | 9.3     | AUD million    | 454.2        | 514.2        |
| Estimated fair market value of 67.4% of Angioblast on a control basis  |         | AUD million    | 306.1        | 346.6        |
| Value of a share in the Proposed Merged<br>Entity (on a minority interest basis)<br>Number of Mesoblast shares offered | 11.5    | AUD<br>million | 2.35<br>94.6 | 2.65<br>94.6 |
| Estimated fair market value of the Scrip Consideration   |         | AUD million    | 222.3        | 250.7        |

Source: Deloitte Corporate Finance analysis

Based on the above, our assessed value of 67.4% interest in Angioblast is higher than our assessed value of the Scrip Consideration.

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We note that the future price of a share in the Proposed Merged Entity will vary, based on market movements, future developments in health, medical and biotechnology industries and changes in the Proposed Merged Entity's specific circumstances. We have set out in the table below the value of the Scrip Consideration for a range of possible market prices for a share in the Proposed Merged Entity.

Table 36: Sensitivity of the value of the Scrip Consideration per Angioblast share (AUD)

| Value of a share in the<br>Proposed Merged Entity<br>on minority interest basis | Value of the<br>Scrip Consideration |
|---|-------------------------------------|
| 1.75  | 165.5                               |
| 2.00  | 189.2                               |
| 2.25  | 212.8                               |
| 2.50  | 236.5                               |
| 2.75  | 260.1                               |
| 3.00  | 283.8                               |

Source: Deloitte Corporate Finance analysis

#### The Proposed Merged Entity will be more diversified than Mesoblast

Mesoblast is currently a small biotechnology company focusing on the development of the MPC technology for orthopaedic applications, with a significant holding in Angioblast. If the Proposed Transaction is approved, the Proposed Merged Entity will have:

- a more diversified portfolio of products than that of Mesoblast on a standalone basis.
   The Proposed Merged Entity will have the right to develop the MPC technology for a wider spectrum of applications, including cardiovascular diseases and orthopaedic conditions
- a larger portfolio of products than Mesoblast has as a standalone company. The probability of the Proposed Merged Entity receiving FDA approval for at least one product from a larger portfolio of products will be higher than that for Mesoblast
- access to the market potential within much larger therapeutic markets, being the cardiovascular disease market held by Angioblast
- the ability to operate as one company with a common R&D strategy. The Proposed Merged Entity will have improved ability to consolidate and prioritise R&D efforts and allocate funding towards key products to achieve an optimal outcome for the shareholders to a greater extent than Mesoblast and Angioblast can as separate entities
- the ability to potentially achieve a better bargaining position when conducting commercial negotiations with the major pharmaceutical companies as it will be able to execute a negotiation strategy across the entire range of products.

#### The Proposed Merged Entity will have increased scale

The Proposed Merged Entity is likely to have a market capitalisation in excess of AUD 500 million. The increased market capitalisation of the Proposed Merged Entity and enlarged shareholder base may attract greater analyst coverage and may enhance the profile of the Proposed Merged Entity with institutional investors. These factors should provide increased liquidity and greater trading depth than that currently experienced by the current holders of Mesoblast shares. This may also result in a positive re-rating of shares in the Proposed Merged Entity.

As a result of the increased market capitalisation, the Proposed Merged Entity may have improved access to capital markets on possibly more attractive terms compared with those currently available to Mesoblast.

#### The Proposed Merged Entity should have improved market transparency

Currently, Angioblast is a US based private company with limited disclosure requirements. The limited understanding of and transparency around the operations of Angioblast may have historically limited access to capital for Angioblast. Angioblast has been reliant on Mesoblast to provide the necessary capital for its operations.

Given that its investment in Angioblast is a key asset of Mesoblast, the value of Mesoblast may have been adversely affected by the lack of transparency associated with the investment in Angioblast.

If the Proposed Transaction is approved, the Proposed Merged Entity will be required to meet its continuous disclosure obligations with the ASX, disclosing any major operating activities and clinical trial results, including those of Angioblast. Greater transparency should assist market participants better understand Angioblast's activities, which may enhance the trading price of shares in the Proposed Merged Entity.

# Disadvantages of the Proposed Transaction Professor Itescu's interest in Mesoblast will increase

Currently, the Non-Associated Shareholders hold 76.7% of Mesoblast whilst Professor Itescu holds 22.9% and Mr O'Dwyer holds 0.4% of Mesoblast (on a fully diluted basis).

If the Proposed Transaction is approved, Professor Itescu's shareholding will increase by 11.6% to approximately 34.5% and possibly up to 36.4% (on a fully diluted basis). The increase in Professor Itescu's shareholding of between 11.6% and 13.5% could reduce the likelihood of a potential takeover offer in the future.

However, given Professor Itescu already has a significant interest in Mesoblast before the Proposed Transaction, and his stake in the Proposed Merged Entity will not increase to a control level if the Proposed Transaction is approved, we consider the likelihood of the Proposed Merged Entity receiving a potential takeover offer is not likely to be significantly reduced by the Proposed Transaction.

Further, in this respect, we note that the Proposed Merger Entity may actually be of greater interest to potential acquirers given the consolidation of the MPC technologies within the Proposed Merged Entity (as opposed to previously being held across Mesoblast and Angioblast).

The Non-Associated Shareholders' interest in Mesoblast will be diluted to between approximately 49.7% and 51.9% and shareholders of Angioblast, other than Mesoblast, Professor Itescu and Mr O'Dwyer, will hold approximately 13.1% and 12.8%.

#### Reduced exposure to Mesoblast's portfolio of orthopaedic applications

If the Proposed Transaction is approved, the Non-Associated Shareholders' exposure to Mesoblast's portfolio of orthopaedic application will be reduced as any commercial success of Mesoblast's products will be shared with the current holders of Angioblast shares. However, this is mitigated by the Non-Associated Shareholders gaining exposure to Angioblast's products for cardiovascular diseases.

#### Conclusion of the advantages and disadvantages of the Proposed Transaction

On balance, in our opinion, the advantages of the Proposed Transaction outweigh the disadvantages.

# 12.4 Conclusion

Having regard to all of the above factors, we consider that the Proposed Transaction is:

- fair and reasonable so far as Non-Associated Shareholders are concerned for the purpose of Section 611 of the Corporations Act
- fair and reasonable so far as Non-Associated Shareholders are concerned for the purpose of ASX Listing Rule 10.

# **Appendix 1: Glossary**

| Reference                  | Definition  |
|----------------------------|---|
|                            |   |
| 15% Cash Option            | The cash consideration that Angioblast Shareholders can elect to receive in respect of up to 15% of their shareholdings, with reference to the price of a Mesoblast shares on the date of approval by the Non-Associated Shareholders |
| α                          | alpha, the specific company risk premium  |
| Abbott                     | Abbott Cardiovascular Systems Incorporated  |
| Acuity                     | Acuity Technology Management Pty Limited  |
| AFSL                       | Australian Financial Services Licence   |
| AGSM                       | Australian Graduate School of Management  |
| AHA                        | American Heart Association  |
| AMEX                       | American Stock Exchange   |
| Angioblast                 | Angioblast Systems, Incorporated  |
| Angioblast Shareholders    | Shareholders of Angioblast other than Mesoblast   |
| APESB                      | Accounting Professional and Ethical Standards Board Limited   |
| Arana                      | Arana Therapeutics Corporation Limited  |
| ASIC                       | Australian Securities and Investments Commission  |
| Aswath                     | Aswath Damodaran  |
| ASX                        | Australian Securities Exchange  |
| ASX Listing Rule 10        | Listing Rule 10 of the Listing Rules of the ASX   |
| ATO                        | Australian Taxation Office  |
| AUASB                      | Auditing and Assurance Standards Board  |
| AUD                        | Australian dollars  |
| β                          | Beta, the systematic risk of a stock  |
| bps                        | Basis points  |
| CAPM                       | Capital Asset Pricing model   |
| CEO                        | Chief Executive Officer   |
| CFO                        | Chief Financial Officer   |
| Cephalon                   | Cephalon Incorporated   |
| Chapter 2E                 | Chapter 2E of the Corporations Act 2001   |
| Chapter 6                  | Chapter 6of the Corporations Act 2001   |
| Convertible Noteholders    | The convertible noteholders in Angioblast   |
| Convertible Note Offer     | The invitation made by Mesoblast to Convertible Noteholders to make an offer to tender their convertible notes in Angioblast directly to Mesoblast for purchase   |
| Corporations Act           | The Corporations Act 2001 (Cth)   |
| DGCL                       | Delaware General Corporation Law  |
| Deloitte Corporate Finance | Deloitte Corporate Finance Pty Limited  |
| DMSO                       | Dimethyl sulfoxide, a toxic cryoprotective agent in which MPCs are stored   |

| Reference             | Definition   |
|-----------------------|--|
|                       |  |
| DNA                   | Deoxyribonucleic acid  |
| D/V                   | Proportion of enterprise funded by debt  |
| EBIT                  | Earnings before interest and tax   |
| EBITDA                | Earnings before interest, tax, depreciation and amortisation   |
| EGM                   | Extraordinary general meeting  |
| EMRP                  | Equity Market Risk Premium   |
| E/V                   | Proportion of enterprise funded by equity  |
| EvoGenix              | EvoGenix Limited   |
| FDA                   | US Food and Drug Administration  |
| FICS                  | Financial Industry Complaints Service  |
| FOS                   | Financial Ombudsman Services   |
| FSG                   | Financial Services Guide   |
| FY                    | Financial year   |
| Genzyme               | Genzyme Corporation  |
| GMP                   | Good Manufacturing Practice  |
| GvHD                  | Graft versus host disease  |
| HB 3590               | US Patient Protection and Affordable Care Act  |
| HIV-AIDS              | Human immunodeficiency virus-acquired immune deficiency syndrome   |
| IBIS                  | IBIS World Pty Ltd   |
| IMVS                  | Institute of Medical and Veterinary Science  |
| IND                   | Investigational new drug   |
| Independent Directors | The independent directors of Mesoblast   |
| IP                    | Intellectual property  |
| $K_d$                 | Cost of debt capital   |
| $K_e$                 | Cost of equity capital   |
| Mesoblast             | Mesoblast Limited  |
| Mesoblast Notice of   | A notice of meeting prepared by the Independent Directors containing   |
| Meeting               | the detailed terms of the Proposed Transaction   |
| MIA                   | The merger implementation agreement setting out the obligations of<br>both Angioblast and Mesoblast in relation to implementation of the<br>Proposed Transaction |
| Millennium            | Millennium Pharmaceuticals Incorporated  |
| Models                | The probability adjusted projected cash flows prepared by Acuity   |
| Morningstar           | Morningstar Incorporated   |
| MPC                   | Mesenchymal precursor cells  |
| MSCI Index            | Morgan Stanley Capital International World Index   |
| NASDAQ                | National Association of Securities Dealers Automated Quotation<br>System   |
| NCE                   | New chemical entities  |
| Non-Associated        | The shareholders of Mesoblast that are not associated with Angioblast  |

| Reference               | Definition   |
|-------------------------|--|
|                         |  |
| Shareholders            |  |
| Orphan Drug designation | FDA Orphan Drug designation  |
| Osiris                  | Osiris Therapeutics Incorporated   |
| PAI-1                   | Plasminogen activator  |
| Phase 1b/IIa            | Combined Phase I and Phase II trials when additional indications for<br>the MPCs are being evaluated   |
| Proposed Transaction    | The proposed merger between Angioblast and Mesoblast, whereby<br>Mesoblast will acquire all of the ordinary shares in Angioblast that it<br>does not already own |
| Proposed Merged Entity  | The proposed merged entity after the Proposed Transaction  |
| R&D                     | Research and development   |
| $R_f$                   | Risk free rate of return   |
| $R_m$                   | Expected return on the market portfolio  |
| RNA                     | Ribonucleic acid   |
| Scrip Consideration     | The shares that Mesoblast will issue to acquire all shares from<br>Angioblast Shareholders   |
| SDF-1                   | Stromal-derived factor 1   |
| Section 606             | Section 606 of the Corporations Act 2001   |
| Section 611             | Section 611 of the Corporations Act 2001   |
| SWOT                    | Strengths, weaknesses, opportunities and threats   |
| Takeda                  | Takeda Pharmaceutical Company Limited  |
| $t_c$                   | Corporate tax rate   |
| US                      | United States  |
| USD                     | United States dollar   |
| VWAP                    | Volumed weighted average price   |
| WACC                    | Weighted average cost of capital   |

# **Appendix 2: Discount rate**

## Introduction

In this section, we have determined the appropriate discount rates for Mesoblast, Angioblast and the Proposed Merged Entity.

Deloitte Corporate Finance engaged Acuity to independently prepare cash flow projections for Mesoblast and Angioblast. The projected cash flows have been prepared on a USD pre-tax basis. Accordingly, we have adopted a US denominated discount rate to apply to the projected cash flows.

The discount rate used to equate the future cash flows to their present value reflects the risk adjusted rate of return demanded by a hypothetical investor for the asset or business being valued.

Selecting an appropriate discount rate is a matter of judgement having regard to relevant available market pricing data and the risks and circumstances specific to the asset or business being valued.

Whilst the discount rate is in practice normally estimated based on a fundamental ground up analysis using one of the available models for estimating the cost of capital (such as the Capital Asset Pricing Model (CAPM)), market participants often use less precise methods for determining the cost of capital such as hurdle rates or target internal rates of return and often do not distinguish between investment type or region or vary over economic cycles.

For ungeared cash flows, discount rates are determined based on the cost of an entity's debt and equity weighted by the proportion of debt and equity used. This is commonly referred to as the weighted average cost of capital (WACC).

The WACC can be derived using the following formula:

The components of the formula are:

$$WACC = \left(\frac{E}{V} * K_e\right) + \left(\frac{D}{V} * K_d (1 - t_c)\right)$$

 $K_e$  = cost of equity capital

 $K_d$  = cost of debt

 $t_c$  = corporate tax rate

E/V = proportion of enterprise funded by equity

D/V = proportion of enterprise funded by debt

The adjustment of  $K_d$  by (1-  $t_c$ ) reflects the tax deductibility of interest payments on debt funding.

In selecting an appropriate range of discount rates and in applying the selected discount rates to the cash flow projections of Mesoblast and Angioblast, we have considered the following:

- the projected cash flows have been probability adjusted to reflect the statistical likelihood of technical success. However, this does not necessarily capture the likelihood of commercial success, although it is usual for approved therapeutic products to also succeed commercially due to lack of competition. The FDA approval process is binary, in that the project will either succeed (low probability) or not succeed (high probability)
- the companies' R&D programs require them to incur a certain level of future costs, which may or may not result in a project progressing to the next stage of development, i.e., at each stage the risk of technical success is independent of the R&D costs incurred
- the patent products of Mesoblast and Angioblast are at an early development stage, such as pre-clinical trial or Phase I/early Phase two clinical trials, and there is significant work to be undertaken to progress the projects through the required trial phases, which may take longer and cost more than currently envisaged
- even if Mesoblast and/or Angioblast overcome the technical and commercial hurdles, the timing and quantum of the royalties received by each company will vary from the projected royalties, perhaps significantly
- there are a number of other competing projects currently under research and there may be a similar product which reaches the market earlier (first mover advantage), or be more effective in treating patients. The opposite may also be true.

We expect the discount rate for Mesoblast and Angioblast to be similar based on the following factors:

- both companies use the same core MPC technology, although the focus of the technology's applications is different
- currently, both companies have a number of patented products at the pre-clinical development and Phase Ib/IIa human clinical trial stages. There is no product in Phase III clinical trials
- the value and scale of the companies is broadly similar.

We consider it appropriate to select a lower discount rate for the Proposed Merged Entity than that selected for Mesoblast and Angioblast. This is driven by the following factors:

- the Proposed Merged Entity will have an increased value and scale
- the Proposed Merged Entity will have a more diversified portfolio of products, including products for cardiovascular and orthopaedic applications
- the Proposed Merged Entity will have an improved likelihood of an application passing clinical trials and obtaining FDA approval, reflecting the Proposed Merged Entity's ability to optimise capital allocation to focus on applications with the higher perceived probability of succeeding.

Based on the above, we consider it appropriate to adopt the same discount rates for both Mesoblast and Anigoblast and a comparatively lower discount rate for the Proposed Merged Entity.

# Cost of equity capital (K<sub>e</sub>)

The cost of equity, Ke, is the rate of return that investors require to make an equity investment in a firm.

We have used the CAPM to estimate the Ke for the companies. CAPM calculates the minimum rate of return that the company must earn on the equity-financed portion of its capital to leave the market price of its shares unchanged. The CAPM is the most widely accepted and used methodology for determining the cost of equity capital.

The cost of equity capital under CAPM is determined using the following formula:

$$K_e = R_f + \beta (R_m - R_f) + a$$

The components of the formula are:

 $K_e$  = required return on equity

 $R_f$  = the risk free rate of return

 $R_m$  = the expected return on the market portfolio

 $\beta$  = beta, the systematic risk of a stock

 $\alpha$  = specific company risk premium

Each of the components in the above equation is discussed below.

## Risk free rate (R<sub>f</sub>)

The risk free rate compensates the investor for the time value of money and the expected inflation rate over the investment period. The frequently adopted proxy for the risk free rate is the long-term government bond rate.

In determining Rf we have taken the 5-day average of the zero coupon 30-year US Government bond rate for the five-trading day period of 6 July 2010 to 12 July 2010 of 4.34%. The 30-year bond rate is a widely used and accepted benchmark for the risk free rate in the US. This rate represents a nominal rate and thus includes inflation.

## **Equity market risk premium (EMRP)**

The EMRP  $(R_m - R_f)$  represents the risk associated with holding a market portfolio of investments, that is, the excess return a shareholder can expect to receive for the uncertainty of investing in equities as opposed to investing in a risk free alternative. The size of the EMRP is dictated by the risk aversion of investors – the lower (higher) an investor's risk aversion, the smaller (larger) the equity risk premium.

The EMRP is not readily observable in the market and therefore represents an estimate based on available data. There are generally two main approaches used to estimate the EMRP, the historical approach and the prospective approach, neither of which is theoretically more correct or without limitations. The former approach relies on historical share market returns relative to the returns on a risk free security; the latter is a forward looking approach which derives an estimated EMRP based on current share market values and assumptions regarding future dividends and growth.

In evaluating the EMRP, we have considered both the historically observed and prospective estimates of EMRP.

#### Historical approach

The historical approach is applied by comparing the historical returns on equities against the returns on risk free assets such as Government bonds, or in some cases, Treasury bills. The historical EMRP has the benefit of being capable of estimation from reliable data; however, it is possible that historical returns achieved on stocks were different from those that were expected by investors when making investment decisions in the past and thus the use of historical market returns to estimate the EMRP would be inappropriate.

It is also likely that the EMRP is not constant over time as investors' perceptions of the relative riskiness of investing in equities change. Investor perceptions will be influenced by several factors such as current economic conditions, inflation, interest rates and market trends. The historical risk premium assumes the EMRP is unaffected by any variation in these factors in the short to medium term.

Historical estimates are sensitive to the following:

- the time period chosen for measuring the average
- the use of arithmetic or geometric averaging for historical data
- selection of an appropriate benchmark risk free rate
- the impact of franking tax credits
- exclusion or inclusion of extreme observations.

The EMRP is highly sensitive to the different choices associated with the measurement period, risk free rate and averaging approach used and as a result estimates of the EMRP can vary substantially.

We have considered the most recent studies undertaken by the Centre for Research in Finance at the Australian Graduate School of Management (AGSM), Morningstar Incorporated (Morningstar), ABN AMRO/London Business School and Aswath Damodaran (Damodaran). These studies generally calculate the EMRP to be in the range of 5% to 8%.

#### Prospective approach

The prospective approach is a forward looking approach that is current, market driven and does not rely on historical information. It attempts to estimate a forward looking premium based on either surveys or an implied premium approach.

The survey approach is based on investors, managers and academics providing their long term expectations of equity returns. Survey evidence suggests that the EMRP is generally expected to be in the range of 6% to 8%.

The implied approach is based on either expected future cash flows or observed bond default spreads and therefore changes over time as share prices, earnings, inflation and interest rates change. The implied premium may be calculated from the market's total capitalisation and the level of expected future earnings and growth.

#### **Selected EMRP**

We have considered both the historically observed EMRP and the prospective approaches as a guideline in determining the appropriate EMRP to use in this report. Australian studies on the historical risk premium approach generally indicate that the EMRP would be in the range of 5% to 8%.

In recent years it has been common market practice in Australia in expert's reports and regulatory decisions to adopt an EMRP of 6%.

Having considered the various approaches and their limitations, we consider an EMRP of 6.0% to be appropriate.

#### Beta estimate (β)

#### **Description**

The beta coefficient measures the systematic risk or non-diversifiable risk of a company in comparison to the market as a whole. Systematic risk, as separate from specific risk as discussed below, measures the extent to which the return on the business or investment is correlated to market returns. A beta of 1.0 indicates that an equity investor can expect to earn the market return (i.e. the risk free rate plus the EMRP) from this investment (assuming no specific risks). A beta of greater than one indicates greater market related risk than average (and therefore higher required returns), while a beta of less than one indicates less risk than average (and therefore lower required returns).

Betas will primarily be affected by three factors which include:

- the degree of operating leverage employed by the firm in that companies with a relatively high fixed cost base will be more exposed to economic cycles and therefore have higher systematic risk compared to those with a more variable cost base
- the degree of financial leverage employed by a firm in that as additional debt is employed by a firm, equity investors will demand a higher return to compensate for the increased systematic risk associated with higher levels of debt
- correlation of revenues and cash flows to economic cycles, in that companies that are more exposed to economic cycles (such as retailers), will generally have higher levels of systemic risk (i.e. higher betas) relative to companies that are less exposed to economic cycles (such as regulated utilities).
- the betas of various Australian industries listed on the ASX are reproduced below and provide an example of the relative industry betas for a developed market.

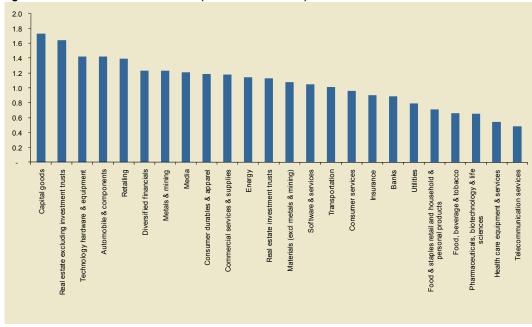


Figure 10: Betas for various industries (as at 31 March 2010)

Source: AGSM Risk Management Service

The differences are related to the business risks associated with the industry. For example, the above diagram indicates transportation companies are more correlated to overall market returns with a beta close to 1.0 whereas telecommunications services companies (in particularly those that are regulated) typically have betas lower than 1.0.

The geared or equity beta can be estimated by regressing the returns of the business or investment against the returns of an index representing the market portfolio, over a reasonable time period. However, there are a number of issues that arise in measuring historical betas that can result in differences, sometimes significant, in the betas observed depending on the time period utilised, the benchmark index and the source of the beta estimate. For unlisted companies it is often preferable to have regard to sector averages or a pool of comparable companies rather than any single company's beta estimate due to the above measurement difficulties.

#### Market evidence

In estimating an appropriate beta for the companies and the Proposed Merged Entity we have considered the betas of listed companies that are comparable to both Angioblast and Mesoblast. These betas, which are presented below, have been calculated based on weekly returns, over a two year period, and monthly returns, over a four year period, compared to the Morgan Stanley Capital International World Index (MSCI Index).

Table 37: Analysis of betas for listed companies with comparable operations to Mesoblast and Angioblast

|                                  |              | Enterprise value <sup>1</sup> | Historical sales | Historical<br>EBIT | Unleve | red beta |
|----------------------------------|--------------|-------------------------------|------------------|--------------------|--------|----------|
| Company                          | Currency     | (million)                     | (million)        | (million)          | Weekly | Monthly  |
| Mesoblast                        | AUD          | 275.6                         | 0.9              | (9.4)              | 0.89   | 0.86     |
| Australian biotechnology compa   | nies         |                               |                  |                    |        |          |
| Pharmaxis Limited                | AUD          | 377.5                         | 0.6              | (40.9)             | 0.78   | 1.27     |
| Acrux Limited                    | AUD          | 291.4                         | 1.3              | (9.9)              | 0.82   | 1.39     |
| Starpharma Holdings Limited      | AUD          | 103.7                         | 9.8              | (4.3)              | 0.67   | 0.76     |
| Bionomics Limited                | AUD          | 81.3                          | 4.6              | (6.6)              | 0.78   | 0.99     |
| Chemgenex Limited                | AUD          | 71.9                          | 0.2              | (25.2)             | 0.74   | 1.32     |
| Living Cell Technologies         |              |                               |                  |                    |        |          |
| Limited                          | AUD          | 57.5                          | 0.8              | (7.2)              | 1.22   | 1.56     |
| Clinuvel Pharmaceuticals         | ALID         | 41.0                          | 2.0              | (15.4)             | 0.50   | 1.01     |
| Limited                          | AUD          | 41.8                          | 2.9              | (15.4)             | 0.58   | 1.01     |
| Prana Biotechnology Limited      | AUD          | 27.9                          | 0.4              | (8.3)              | 0.74   | 1.02     |
| Circadian Technologies Limited   | AUD          | 0.0                           | 3.1              | (8.1)              | 0.65   | 0.91     |
| Average                          |              |                               |                  |                    | 0.78   | 1.14     |
| Median                           |              |                               |                  |                    | 0.74   | 1.02     |
| US biotechnology companies - s   | tem cell and | regenerative 1                | medicine com     | panies             |        |          |
| Geron Corporation                | USD          | 373.5                         | 1.7              | (70.2)             | 1.27   | 0.82     |
| Cytori Therapeutics Incorporated | USD          | 150.4                         | 14.7             | (17.9)             | 1.28   | 1.55     |
| Osiris Therapeutics Incorporated | USD          | 112.1                         | 44.5             | (27.5)             | 0.79   | $nm^2$   |
| StemCells Incorporated           | USD          | 87.9                          | 1.0              | (28.0)             | 1.27   | nm       |
| Athersys Incorporated            | USD          | 46.0                          | 2.2              | (15.6)             | 1.61   | nm       |
| Opexa Therapeutics Incorporated  | USD          | 23.4                          | n/a              | (4.3)              | 0.80   | 1.36     |
| Pluristem Therapeutics           |              |                               |                  |                    |        |          |
| Incorporated                     | USD          | 22.2                          | n/a              | (6.6)              | 0.82   | nm       |
| Aastrom Biosciences              | Hab          | 10.7                          | 0.2              | (1.6.0)            | 0.02   |          |
| Incorporated                     | USD          | 19.7                          | 0.2              | (16.2)             | 0.93   | nm       |
| Average                          |              |                               |                  |                    | 1.10   | 1.24     |
| Median                           |              |                               |                  |                    | 1.10   | 1.36     |
| Overall high                     |              |                               |                  |                    | 1.61   | 1.56     |
| Overall low                      |              |                               |                  |                    | 0.58   | 0.76     |
| Overall average                  |              |                               |                  |                    | 0.93   | 1.16     |
| Overall median                   |              |                               |                  |                    | 0.80   | 1.15     |

Source: Capital IQ and Deloitte Corporate Finance analysis

Note:

<sup>1.</sup> Enterprise value as at 7 July 2010

 $<sup>2. \</sup>hspace{0.5cm} nm-not\ meaningful.$ 

Descriptions for each of the above companies are provided in Appendix 3.

The observed beta is a function of the underlying risk of the cash flows of the company, together with the capital structure and tax position of that company. This is described as the levered beta.

The capital structure and tax position of the entities in the table above may not be the same as those of Mesoblast, Angioblast and the Proposed Merged Entity. The levered beta is often adjusted for the effect of the capital structure and tax position. This adjusted beta is referred to as the unlevered beta. The unlevered beta is a reflection of the underlying risk of the pre-financing cash flows of the entity.

We have selected a range of betas as follows:

- a beta range for Mesoblast and Angioblast
- a beta range for the Proposed Merged Entity.

#### Selected beta for Mesoblast and Angioblast

In selecting an appropriate beta for Mesoblast and Angioblast we have considered the following:

- share trading in a number of the selected comparable companies is illiquid, which may affect the observed beta
- the selected comparable companies have no significant revenues and are loss making. The average debt to enterprise value ratio is nil
- the selected international based biotechnology companies are considered comparable to Mesoblast and Angioblast, on the basis that their primary research focuses are related to stem cells or regenerative medicine. The average unlevered beta for these international based companies is 1.10 based on weekly returns and 1.24 based on monthly returns
- the selected Australian biotechnology companies are considered less comparable to
  Mesoblast and Angioblast, given that none of these companies are involved in stem
  cell related research. These companies' research focus varies from the development
  of drugs for cancer treatment to the development of nanotechnology products for
  pharmaceutical and life science applications. The average unlevered beta for the
  selected Australian biotechnology companies is 0.78 based on weekly returns and
  1.14 based on monthly returns
- we considered the most comparable company to both Mesoblast and Angioblast to be Osiris, which is involved in the development of adult stem cell products for the treatment and functional restoration of damaged tissues. Osiris currently has one product in Phase III clinical trials for three indications, including steroid refractory GvHD, newly diagnosed acute GvHD and also Crohn's disease. Osiris also has a second product currently in Phase II clinical trials, which is directed at the regeneration of the meniscus and prevention of osteoarthritis in the knee. The unlevered beta for this company is 0.79 based on weekly returns.

We consider Osiris to be of lower risk profile than that of Mesoblast and Angioblast, reflecting the fact that Osiris has one adult stem cell product in Phase III clinical trials and the risks associated with the development and commercialisation of this product have accordingly declined. Therefore, we expect the unlevered beta for Mesoblast and Angioblast to be higher than the unlevered beta for Osiris

• other international companies involved in the development of stem cell products including StemCells Incorporated, Aastrom Biosciences Incorporated, Athersys

Incorporated and Pluristem Therapeutics Incorporated are also considered broadly comparable to Mesoblast and Angioblast. The products developed by these companies are currently at various pre-clinical and clinical trial stages. The average unlevered beta of these companies is 1.16 based on weekly returns

• we consider an appropriate debt to enterprise value ratio for Mesoblast and Angioblast to be zero percent.

We have selected a levered beta of 1.2 to 1.3 for both Mesoblast and Angioblast.

#### Selected beta for the Proposed Merged Entity

We do not consider the systematic risks and the risk of the underlying cash flows of the Proposed Merged Entity to be different to those of Mesoblast and Angioblast. On this basis we have selected a levered beta of 1.2 to 1.3 for the Proposed Merged Entity.

## Specific company risk premium (α)

The specific company risk premium adjusts the cost of equity for company specific factors, including unsystematic risk factors such as:

- company size (which we discuss in detail below)
- depth and quality of management
- reliance on one key individual or a few key members of management
- reliance on key customers
- reliance on key suppliers
- product diversity (limits on potential customers)
- geographic diversity
- labour relations, quality of personnel (union/non-union)
- capital structure, amount of leverage
- existence of contingent liabilities.

The CAPM assumes, amongst other things, that rational investors seek to hold efficient portfolios, that is, portfolios that are fully diversified. One of the major conclusions of the CAPM is that investors do not have regard to specific company risks (often referred to as unsystematic risk).

There are several empirical studies that demonstrate that the investment market does not ignore specific company risks. In particular, studies show that:

- on average, smaller companies have higher rates of return than larger companies (often referred to as the size premium)
- on average, early stage companies have higher rates of return than mature companies.

These are discussed separately below.

#### Size premium

The following table summarises the returns for different size categories from 1926 to 2009 for companies on the New York Stock Exchange (NYSE), the American Stock Exchange (AMEX) and the National Association of Securities Dealers Automated Quotation System (NASDAQ).

Table 38: Evidence of size premium

|                                     |  | Summary statistics of annual returns |  |  |
|-------------------------------------|--|--------------------------------------|--|--|
| Decile                              | Market capitalisation of largest company in group <sup>2</sup> (US \$ million) | Arithmetic mean<br>return³<br>(%)    | Size premium (return<br>in excess of CAPM) <sup>1</sup><br>(%) |  |
|                                     |  |                                      |  |  |
| Largest (1st decile)                | 329,725  | 10.90                                | (0.37)   |  |
| Large (2nd decile)                  | 14,691   | 12.81                                | 0.74   |  |
| Mid-cap (3rd – 5th decile)          | 5,936  | 13.36                                | 0.85   |  |
| Low-cap (6th – 8th decile)          | 1,600  | 14.81                                | 1.73   |  |
| Micro-cap (9th – 10th decile)       | 431  | 17.01                                | 2.85   |  |
| Smallest (10th decile) <sup>4</sup> | 214  | 20.85                                | 6.28   |  |

Source: Market Results for Stocks, Bonds, Bills, and Inflation 2010 Yearbook, Ibbotson SBBI Notes:

- 1. Size premium was calculated as the difference between the actual return and the return calculated using the CAPM
- 2. Market capitalisation was calculated as at 31 December 2009
- 3. Ibbotson use the 20 year Government bond rate in determining the risk free rate
- 4. Ibbotson provide a further breakdown of the 10th decile, noting that the size premium for the upper half of the 10th decile (decile 10a) was 4.45%, whereas the size premium for the lower half of the 10th decile (decile 10b) was 10.01%. However care must be taken in considering decile 10b due to the volatility of companies in this segment of the market.

#### Early stage companies

Both Mesoblast and Angioblast are early stage businesses seeking to expand rapidly. Investors in early stage companies often require higher rates of return than investors in mature companies. Venture capitalists are a common source of equity capital for early stage investments. The Australian Venture Capital Guide provides the following indicative guidelines for their required rate of return.

Table 39: Venture capital required rates of return

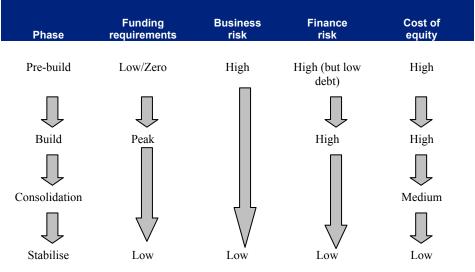
| Methodology                        | Required rate of return |
|------------------------------------|-------------------------|
| Starting a new business            | 30.0% to 40.0%          |
| Expanding a business, MBOs or MBIs | 20.0% to 30.0%          |

Source: Australian Venture Capital Guide 2007

These rates of return are significantly higher than those required for mature listed companies. The reason that the discount rate required for an early stage company is different to that required for a mature company is because the relationship between business risks, finance risks and the cost of equity changes as a company progresses from an early stage company to a mature company.

The relationship between business risk, finance risk and cost of equity is illustrated in the following figure.

Figure 11: Business risks, finance risks and cost of equity



Source: Adapted from The Valuation of Businesses, Shares and Other Equity, 3rd edition, W Lonergan

#### Selection of specific company risk premium for Mesoblast and Angioblast

We have selected a specific company risk premium in the range of 4.0% to 4.5% for Mesoblast and Angioblast. In determining this amount we have had regard to the following:

- the small size of operations of Mesoblast and Angioblast
- the uncertainty associated with the underlying projected cash flows for Mesoblast and Angioblast
- the applications under development by Mesoblast and Angioblast are at an early stage of development and require significant capital during the R&D phases
- individually, the companies have limited access to capital. To date, Mesoblast has raised capital through on-market capital raisings, which have also supported Angioblast's capital demands. Neither of the companies has access to debt, given early stage biotechnology companies are likely to have a higher risk profile than established, manufacturing pharmaceutical companies and therefore are less likely to secure debt funding
- Mesoblast and Angioblast each have a portfolio of applications which are individually focussed on orthopaedic and cardiovascular applications, respectively. If an application is not successful within each of Mesoblast and Angioblast's portfolio, this may have a significant effect on the value of Mesoblast and Angioblast.

We have also had regard to the considerations discussed in the introduction of this appendix.

#### Selection of specific company risk premium for the Proposed Merged Entity

After the Proposed Transaction, the Proposed Merged Entity will continue to develop cardiovascular and orthopaedic applications using the MPC technology and these applications are still at an early stage of development. Therefore, we consider it appropriate to include a specific company risk premium in the calculation of the Proposed Merged Entity's cost of equity.

We have selected a lower specific company risk premium in the range of 3.0% to 3.5% for the Proposed Merged Entity compared with Mesoblast and Angioblast based on the following:

- if the Proposed Transaction is approved, the Proposed Merged Entity will be larger than Mesoblast and Angioblast as separate entities, and will be broadly two to three times the size of Mesoblast's current value of USD 293 million. Based on Ibbotson's size premium analysis, as shown in Table 38, small companies historically have higher required rates of return than large companies. Empirical evidence shows the difference in the required rate of return between a company with a market capitalisation of USD 214 million and a company with a market capitalisation of USD 431 million is approximately 3%. Therefore, we would expect the Proposed Merged Entity to have a lower specific company risk premium than Mesoblast and Angioblast
- the Proposed Merged Entity will have the opportunity to allocate capital towards applications with more promising clinical trial results, away from applications with a lower risk of successfully receiving FDA approval, to a greater extent than would be the case for Mesoblast and Angioblast
- the Proposed Merged Entity will have greater opportunity to realise value given the increased number of applications in its portfolio compared with Mesoblast and Angioblast
- the Proposed Merged Entity will benefit from diversification across its portfolio of other non-orthopaedic (including cardiovascular) and orthopaedic applications and will therefore have reduced its exposure to a focussed group of applications compared with Mesoblast and Angioblast.

# **Dividend imputation**

Dividends paid by Australian corporations may be franked, unfranked, or partly franked. A franked dividend is one that is paid out of company profits which have borne tax at the company rate, currently 30%. Where the shareholder is an Australian resident individual or complying superannuation fund, it will generally be entitled to a tax credit (called an imputation credit) in respect of the tax paid by the company on the profits out of which the dividend was paid. If the recipient of the dividend is another company, the dividend will give rise to a credit in that company's franking account thereby increasing the potential of the company to pay a franked dividend at a later stage.

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<sup>&</sup>lt;sup>22</sup> As at 21 July 2010

We have not adjusted the cost of capital or the projected cash flows for the impact of dividend imputation due to the diverse views as to the value of imputation credits and the appropriate method that should be employed to calculate this value. Determining the value of franking credits requires an understanding of shareholders' personal tax profiles to determine the ability of shareholders to use franking credits to offset personal income. Furthermore, the observed EMRP already includes the value that shareholders ascribe to franking credits in the market as a whole. In our view, the evidence relating to the value that the market ascribes to imputation credits is inconclusive.

### **Conclusion on cost of equity**

Based on the above factors we arrive at a cost of equity, Ke, as follows:

#### Cost of equity for Mesoblast and Angioblast

Table 40:  $K_e$  applied to valuation of Mesoblast and Angioblast

| Input                             | Low   | High  |
|-----------------------------------|-------|-------|
| Diele free vote (9/)              | 4.34  | 4.34  |
| Risk free rate (%)<br>EMRP (%)    | 6.00  | 6.00  |
| Beta                              | 1.20  | 1.30  |
| Specific company risk premium (%) | 4.00  | 4.50  |
| $K_e$ – calculated                | 15.54 | 16.64 |
| $K_e$ – selected                  | 15.50 | 16.50 |

Source: Deloitte Corporate Finance analysis

#### Cost of equity for the Proposed Merged Entity

Table 41: Ke applied to valuation of the Proposed Merged Entity

| Table 117 regulption to variation of the 170 poole mon |       |       |
|--|-------|-------|
| Input  | Low   | High  |
|  |       |       |
| Risk free rate (%)                                     | 4.34  | 4.34  |
| EMRP (%)   | 6.00  | 6.00  |
| Beta   | 1.20  | 1.30  |
|  |       |       |
| Specific company risk premium (%)                      | 3.00  | 3.50  |
|  |       |       |
| $K_e$ – calculated                                     | 14.54 | 15.64 |
|  |       |       |
| $K_e$ – selected                                       | 14.50 | 15.50 |
|  |       |       |

Source: Deloitte Corporate Finance analysis

# Debt and equity mix

Based on our analysis, early stage biotechnology companies generally have no debt. Accordingly, we have adopted a target debt to enterprise value ratio of zero percent for both the calculation of the WACC for Mesoblast and Angioblast and for the Proposed Merged Entity.

# **Conclusion on WACC**

Based on the above, we have assessed the nominal post-tax WACC for Mesoblast and Angioblast to be in the range of 15.50% and 16.50%, and for the Proposed Merged Entity to be in the range of 14.50% and 15.50%.

# **Appendix 3: Comparable entities**

We provide the descriptions for each of the above comparables as follows:

#### **Pharmaxis Limited**

Pharmaxis Limited is a pharmaceutical company involved in the research, development and commercialisation of therapies used in the treatment of respiratory diseases such as cystic fibrosis, bronchiectasis, asthma, chronic bronchitis and pulmonary fibrosis. One of the company's products has been approved for sale in Australia, major European countries and Korea, while a second product has completed the first regulatory Phase III clinical trials in both cystic fibrosis and bronchiectasis.

#### **Acrux Limited**

Acrux Limited derives its revenue from the development and commercialisation of drug products which are administered through the skin. The company currently has one product in Phase III development which is applied to the armpit in much the same way as deodorants or antiperspirants and is indicated for the treatment of low testosterone in men

#### **Starpharma Holdings Limited**

Starpharma Holdings Limited develops, manufactures and supplies a range of nanotechnology products for pharmaceutical and life science applications, including gelbased formulations for the prevention of sexual diseases and several vaginal microbicides for the prevention of sexually transmitted infections, including human immunodeficiency virus/acquired immune deficiency syndrome (HIV-AIDS) and genital herpes. Its flagship product is currently at the Phase IIa stage of clinical development and has been granted Fast Track status by the FDA.

#### **Bionomics Limited**

Bionomics Limited is involved in the identification and development of therapies to treat cancer and conditions of the central nervous system, including anxiety, multiple sclerosis and epilepsy. The company currently has two drug candidates in Phase II clinical trials for the treatment of cancer and the treatment of acute and generalised anxiety disorders.

#### **Chemgenex Limited**

Chemgenex Limited is a biopharmaceutical development company that develops cancer treatments by identifying and targeting the genetic components of a range of cancer types. The company currently has two molecules in clinical trials for the purposes of treating chronic myelogenous leukaemia, acute myelogenous leukaemia and hormone refractory prostate cancer.

#### **Living Cell Technologies Limited**

Living Cell Technologies Limited is a biotechnology company involved in the clinical development of cell-based therapeutics for the treatment of diabetes, neurological disease and haemophilia. The company is primarily focused on the commercialisation of pig cell therapeutics, with one therapy (for the treatment of type 1 diabetes) currently in Phase IIa trials.

#### **Clinuvel Pharmaceuticals Limited**

Clinuvel Pharmaceuticals Limited develops and markets a preventative photoprotective agent used for treating various ultraviolet-related skin disorders. Its core product, afamelanotide, is a chemical analogue of the alpha-melanocyte stimulating hormone, a naturally occurring peptide hormone which is released by skin cells in response to the stimulation by ultraviolet radiation. This hormone aids the production of melanin which is known for its photoprotective effect. The company is currently in Phase II and Phase III clinical trials of applications associated with this product.

#### **Prana Biotechnology Limited**

Prana Biotechnology Limited is engaged in the development of disease modifying therapeutics for the treatment of common neurological disorders, with a focus upon Alzheimer's, Parkinson's and Huntington's diseases. Through the development of its library of Metal-Protein Attenuating Compounds, the company has entered one of its core therapies into clinical trials where it is expected to commence Phase IIb in the case of moderate Alzheimer's Disease.

#### **Circadian Technologies Limited**

Circadian Technologies Limited develops and commercialises therapies primarily used in the treatment of cancer. The company's focus is on a specific class of proteins that play a critical role in regulating tumour blood supply with its most advanced program expected to enter clinical trials in 2011.

#### **Geron Corporation**

Geron Corporation, a biopharmaceutical company, discovers and develops therapeutic and diagnostic products to treat cancer and other age-related degenerative diseases using its three patented core technologies: telomerase<sup>23</sup>, human embryonic stem cells and nuclear transfer (i.e. genetic cloning). Using the telomerase-based technology, Geron has two oncology-related products in the latter stages of Phase I and Phase II respectively, while the majority of Geron's four stem cell-based technologies (directed at the treatment of a range of diseases, including cancer, cardiovascular and bone diseases) remain in the research phase. Geron has no products derived from its nuclear transfer technology in development.

#### **Cytori Therapeutics Incorporated**

Cytori Therapeutics Incorporated is primarily engaged in the marketing of its biopharmaceutical tools used in the preparation of fat grafts and tissue collection. In order to further its Tissue Processing System, Cytori is currently sponsoring two clinical trials that evaluate the use of adipose-derived stem<sup>24</sup> and regenerative cells to treat acute myocardial infarction and chronic myocardial ischemia. Both of these trials are currently in Phase I.

<sup>&</sup>lt;sup>23</sup> Telomerase are enzymes located at the ends of chromosomes, the presence of which has been shown by Geron Corporation to enable cancer cells to maintain telomere length, thus providing them with indefinite replicative capacity. Geron Corporation's anti-cancer therapies are focusing on the inhibition of telomerase activity in cancer cells and a telomerase-based vaccine specific to cancer cells.

Adipose-derived stem cells are similar to MPCs in that they are multipotent, meaning they are restricted in the types of cell they can become. Adipose cells are derived from tissue mainly made up of fat cells.

#### **Osiris Therapeutics Incorporated**

Osiris researches and develops therapeutic products for the regeneration of human connective tissues. The company is focusing its initial product development efforts on the regeneration of bone marrow stroma following high-dose cancer chemotherapy and on the regeneration of bone in long bone and spinal defects. Osiris currently has one product, Prochymal<sup>R,25</sup>, in Phase III clinical trials and a second product, Chondrogen<sup>R</sup>, currently in Phase I/II clinical trials for the regeneration of the meniscus and prevention of osteoarthritis in the knee.

#### **StemCells Incorporated**

StemCells Incorporated is a biotechnology company. The company discovers, develops and commercialises stem cell-based therapies to treat diseases of the central nervous system, liver and the pancreas using its purified human neural stem cells<sup>26</sup> technology. Its technology is currently being investigated in two neurodegenerative disorders<sup>27</sup>, both of which are in Phase I

#### **Athersys Incorporated**

Athersys Incorporated discovers and develops stem cell-based and synthetic pharmaceutical products, among which includes a patented stem cell product that is being developed in three clinical trials. The treatments directed at acute myocardial infarction and bone marrow transplantation are currently in Phase I, while Athersys Incorporated's treatment directed at ischemic stroke has recently passed the pre-clinical phase. Athersys Incorporated's synthetic pharmaceutical products are focused on the obesity and cognitive areas and are in pre-clinical phases.

#### **Opexa Therapeutics Incorporated**

Opexa Therapeutics Incorporated is a biopharmaceutical company developing autologous cellular therapies with the potential to treat major illnesses, including multiple sclerosis and diabetes. Opexa currently has a T-cell derived therapeutic vaccine, Tovaxin<sup>R</sup>, in Phase II clinical development for the treatment of MS and has developed an adult stem cell technology to produce a stem cell variant from blood which is yet to progress to the development stage.

#### **Pluristem Therapeutics Incorporated**

Pluristem Therapeutics Incorporated is engaged in developing and commercialising cell therapy production technologies and products derived from human placenta, an adult mesenchemyl stromal cell source<sup>28</sup>. Using this technology, Pluristem has one application, an allogeneic therapeutic product to treat critical limb ischemia, currently in Phase I.

#### **Aastrom Biosciences Incorporated**

Aastrom Biosciences Incorporated develops autologous stem cell products for the repair and regeneration of tissues based on its Tissue Repair Cell adult stem cell technology. Its technology is currently being assessed in a number of clinical trials, however only three<sup>29</sup> of the applications are beyond the pre-clinical phase.

<sup>&</sup>lt;sup>25</sup> Prochymal<sup>R</sup> is being directed at the treatment of steroid refractory acute GvHD and Chrohn's disease, and is also being evaluated for cardiovascular applications. GvHD is a life-threatening immune reaction that can occur in patients following bone marrow transplantation. Steroids are typically used to control the disease, however they are often ineffective. In patients that fail to respond to steroids, mortality can reach 85%

Human neural stem cells are multipotent and are generally derived from various areas of the adult brain

<sup>&</sup>lt;sup>27</sup> Neuronal Ceroid Lipofuscinosis and Pelizaeus-Merzbacher Disease

<sup>&</sup>lt;sup>28</sup> Mesenchymal stromal cells are multipotent stem cells that have been isolated from a variety of anatomical locations including the bone marrow, peripheral blood, and placenta.

wo treatments directed at congestive cardiomyopathy (which can in result congestive heart failure), and one treatment directed at critical limb ischemia (all in Phase I/II).

# **Appendix 4: Acuity Technical Expert's Report**

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6 July 2010

Mr Stephen Reid Director Deloitte Corporate Finance Pty Limited GPO Box 78 Melbourne, VIC 3001

Dear Sirs

#### Independent Industry Report - Mesoblast Limited

This report has been prepared at the request of Deloitte Corporate Finance Pty Limited (Deloitte Corporate Finance) for inclusion in an independent expert's report to be addressed to the Directors of Mesoblast Limited (Mesoblast or the Company). We understand that the independent expert's report will be dated on or about 115 May 2010 and will be included in a Statement to be provided to Mesoblast shareholders in relation to the proposed acquisition of Angioblast Systems, Inc (Angioblast) (the Proposed Transaction).

Mesoblast and Angioblast share a common significant shareholder in Professor Silviu Itescu; common Directors, Silviu Itescu and Donal O'Dwyer; and Mesoblast is a significant shareholder in Angioblast. The non-associated shareholders in Mesoblast will be required to vote on the acquisition of all outstanding shares in Angioblast in a merger of the two entities and Deloitte Corporate Finance's report will provide a comment as to whether the price is fair and reasonable to non-associated shareholders.

Mesoblast is a company listed on the Australian Stock Exchange (ASX) with defined rights to patents applicable to the development and exploitation of Mesenchymal Precursor Cell (MPC) in orthopaedic indications. Mesoblast has advanced the initial discoveries and, sometimes in collaboration with Angioblast, implemented clinical trials to evaluate the Intellectual Property (IP) in treating bone and cartilage conditions.

The initial MPC patents were taken out by South Australia's Institute of Medical and Veterinary Science (IMVS) and subsequently assigned to Angioblast excluding the field of orthopaedic medicine. Angioblast is a US-based company targeting use of MPC in the treatment of cardiovascular and eye diseases, and diabetes.

In addition to the IMVS patents, Angioblast has a licence to certain patents owned by Columbia University in New York. Angioblast has applied for patents in its own right which aim to provide additional protection to MPC in specific medical indications.

Acuity Technology Management Pty Ltd (Acuity) has been requested by Deloitte Corporate Finance to review the technology, patents, licence agreements and clinical trials approvals held by Mesoblast and Angioblast, and to provide financial projections for the companies. These projections will form the basis of a valuation to be undertaken by Deloitte Corporate Finance.

Specifically, Acuity was requested to provide the following:

- An overview of Mesoblast and Angioblast and their IP, including all the patents;
- Analysis of the potential markets for the IP of both companies;
- An analysis of the possible routes to market for the IP;
- An assessment of the technical and commercial risks for the IP, together with an assessment of probabilities of successful development;
- An assessment of the potential market size, market penetration and time to market for the IP;
- Details of the likely costs Mesoblast and Angioblast will have to incur in exploiting the IP; and
- A general summary of the likely revenues and expenditures that Mesoblast and Angioblast are expected to incur over the forecast period.



Based on our analysis, Acuity was required to prepare a probability adjusted pre-tax cash flow forecast (or series of forecasts) for the Mesoblast and Angioblast IP.

The current review follows earlier reports prepared for Deloitte Corporate Finance in September 2006, June 2008 and June 2009. It, as previously, is based on discussions with and documents provided by Mesoblast and Angioblast, online database searches through the internet and subscription services, and Acuity's own experience in financial modelling of drug development programs. Details of specific documents provided under confidentiality are provided at the end of this report. Other, publicly accessible references are footnoted throughout the report.

#### 1. The Companies

Mesoblast Limited was founded by Professor Itescu in 2001 and listed on the ASX in 2004 raising approximately \$21 million at the time. Subsequent raisings in 2006, 2007 and 2009 raised \$17 million, \$13 million and \$11 million respectively.

Mesoblast is developing stem cell-based treatments for orthopaedic conditions based on IMVS's discoveries and has worldwide exclusive rights to the patents assigned to Angioblast in the specified field. The Company's focus is to progress its IP through clinical trials and regulatory approvals in the major global healthcare markets with the USA being the initial focus.

Mesoblast acquired a 33% interest in Angioblast in 2004 following the former's initial public offering (IPO) and has subsequently increased this to 38.4% (undiluted basis). The initial equity investment was subject to Angioblast meeting certain milestones related to the development of MPC technology including the filing of an Investigational New Drug (IND) Application with the US Food and Drug Administration (FDA). The milestones were of mutual interest to both Mesoblast and Angioblast, being complementary to bone and cartilage, and cardiovascular applications. Much of the development to date has been jointly funded.

Additional shareholders in Angioblast include The Trustees of Columbia University in the City of New York and Abbott Cardiovascular Systems, Inc. (Abbott). In December 2007, Angioblast entered into an agreement with Abbott which included the issue of a convertible note to Abbott for US\$5.0 million at a conversion rate of USD75.61 per common stock.

The companies have a common goal of creating early collaborations with diverse corporate partners to enable rapid penetration in each market by product and geography.

#### 2. The Technology and Products

#### 2.1 Background to the Technology

Mesoblast and Angioblast have a number of applications of the MPC platform in development, the primary and most advanced of which is the treatment of cardiovascular diseases and certain bone related conditions.

Two other technologies are available to Angioblast, a peptide therapeutic stromal-derived factor 1 and drug eluting stents based on RNA silencing technology with the lead candidate targeting plasminogen activator inhibitor 1. In preparing cash flow projections for the companies, we have concentrated solely on the MPC technology as plans for its further development and commercialisation are the most advanced.

A considerable amount of research on MPC and their medical use has been completed by Mesoblast and Angioblast in collaboration with the IMVS and others. The basic research to identify the appropriate MPC population and develop technology to isolate these cells, and other necessary information essential for supporting the early patent applications has been finalised.

Through collaborations with Cell Therapies Pty. Ltd. (a Melbourne company part-owned by the Peter MacCallum Cancer Centre which has access rights to the Centre's regulatory compliant clinical suites), Cambrex, Inc. (USA) and Avid Biosciences, Inc. (USA) the companies have completed development of antibody production and MPC handling processes to Good Manufacturing Guidelines (GMP) standards for both autologous and allogeneic



application<sup>1</sup>. The company has contracted Lonza, Inc. (USA), which acquired Cambrex in 2006, to manufacture cells for use in clinical trials.

A number of studies have been undertaken in sheep looking at safety of allogeneic MPC, suitable dosage levels and delivery method. These studies were conducted at independent sites in Australia and the USA. A Phase Ib human autologous trial has been completed evaluating safety of the manufacturing process and the administration to humans of cultured MPC. The trial involved patients with myocardial ischemia and was conducted at the John Hunter Hospital in Newcastle under the Australian Clinical Trials Notification (CTN) Scheme.

The FDA requires a sponsor company to lodge an IND for approval prior to the commencement of human clinical trials in the USA. Angioblast lodged its first IND with the intention of conducting a Phase Ib/IIa<sup>2</sup> dose escalating trial using allogeneic MPC for heart failure. This study commenced in early 2009. The IND cited results of the autologous human study in Australia and the allogeneic studies in sheep. It was the first study demonstrating safety of allogeneic MPC in humans and was pivotal to the commercial success of both companies.

The companies have further advanced the MPC technology by:

- Demonstrating production to clinical quality of the two vital components, being (i) the hybridoma derived monoclonal antibodies, and (ii) the MPC isolation (using the monoclonal antibodies), storage, expansion and administration. Both components are being produced under current GMP guidelines and the cell therapies component is adequate for both autologous and allogeneic treatments;
- Proving efficacy in animal models of congestive heart failure (CHF) and acute myocardial infarction (AMI) or heart attack;
- Completing clinical trials in Australia as an autologous treatment for AMI. This study aimed at proving safety but, because it was administered to patients who have suffered a heart attack, also provided early human efficacy data. All patients treated showed improvement in either symptoms of heart failure or heart function and no cell related adverse events;
- Lodging an IND with the US FDA and received approval to proceed with a Phase II study using allogeneic MPC in heart attack patients. Clinical investigators are currently part way through patient recruitment;
- On 5 June 2008 announcing approval by the FDA of its IND submission to conduct a Phase Ia/IIb trial in CHF. This study involves three groups of patients receiving allogeneic cells at different dosage as well as a placebo group. The trial is testing the safety and effectiveness of MPC, trademarked Revascor<sup>TM</sup>, injected into damaged heart muscle using the NOGA MyoStar<sup>TM</sup> catheter technology system provided through a collaborative agreement with Johnson & Johnson subsidiary, Cordis Corporation. Published results of the initial cohort of 20 patients found no treatment-related adverse events at the six month follow-up point and those with the most severely compromised hearts showed greatest improvement. A second 20 patient cohort at a higher dose has also completed and the highest dose group is currently part way through recruitment.
- Angioblast has initiated a Phase II trial to evaluate the safety and effectiveness of Revascor™ for improving heart muscle function in patients with the most severe, or class IV, end-stage form of heart failure. The clinical trial, being conducted in multiple centres in the US, will involve 80 patients who are waiting to receive a heart transplant from an appropriate donor and are being kept alive temporarily by a Left Ventricular Assist Device (LVAD). The trial will evaluate whether injections into the damaged heart of either of two increasing doses improve heart muscle function compared with control injections over a 60-90 day period, potentially enabling the patient to have the LVAD removed and avoid a heart transplant.

"Allogeneic" means that cells and are obtained from a donor and then used to treat one or a multitude of unrelated recipients.

<sup>&</sup>lt;sup>1</sup> "Autologous" means that cells from a patient are obtained, expanded, and then used to treat the donating patient only. Autologous treatment with another form of precursor cells, haematopoietic cells, is routine practice for patients undergoing ablative radiotherapy for cancer.

<sup>&</sup>lt;sup>2</sup> Generally, the evaluation of a novel drug goes through three phases, I to demonstrate safety usually in healthy individuals, II to show efficacy and determine appropriate dose level in the targeted medical condition, and III a large study at chosen dosage. Often it is unethical to test safety in healthy individuals and a Phase Ib/IIa study looks for both adverse events and effectiveness.



- Initiating under IND a Ib/IIa trial with patients undergoing bone marrow transplantation (BMT) for insufficient haematopoietic stem cell production in patients with haematologic malignancies who have failed treatment with conventional chemotherapy.
- Completing a non-human primate trial for macular degeneration and diabetic retinopathy. Results showed that combining MPC with a vascular endothelial growth factor (VEGF) inhibitor, such as Lucentis®, may lead to improved vision and a reduction in the frequency of subsequent anti-VEGF injections into the eye. Angioblast can now move to file an IND for human studies.
- Mesoblast has completed a human study with autologous MPC in delayed healing long bone fractures at the Royal Melbourne Hospital under CTN. Ten patients with a total of 11 non-healing fractures of the long bones in the legs received MPC. Eight, who had a non-union fracture for up to 40 months with a median of 10 months prior to treatment, achieved complete bony union. The remaining two had complex road trauma fractures which required reoperation. No adverse events were reported. This study, which supports efficacy of MPC in the condition, and others demonstrating safety of allogeneic cells, paves the way for a US IND filing.
- In July last year, the Company commenced the formal process of obtaining approval through the TGA to manufacture autologous cells in Australia, with Cell Therapies Pty. Ltd., and treat fracture repair.
- Effectiveness of MPC for preventing osteoarthritis (OA) of the knee has been shown in a large animal model where MPC were injected into the knee joint shortly after knee surgery. A Phase II clinical trial of the product referred to as RepliCart<sup>TM</sup> has commenced in Australia aimed at slowing or preventing the development of OA after reconstruction of ruptured anterior cruciate ligament.
- A pre-clinical large animal study for degenerative disc disease has been completed and an IND submission
  for Phase IIa trial is under preparation. The injection of MPC into severely damaged intervertebral discs in
  sheep resulted in reversal of the degenerative process, regrowth of disc cartilage, and sustained normalization
  of disc pathology, anatomy and function.
- Mesoblast is evaluating MPC in lumbar and cervical interbody fusion. A single centre Phase Ib/IIa study of NeoFuse<sup>TM</sup> alone has been completed and an FDA approved, multicentre, Phase II study for lumber fusion using NeoFuse with autograft (patient's own hip bone) is currently in progress. A multicentre Phase II study in cervical fusion, comparing NeoFuse with autograft, has started in Australia.
- In an animal model of diabetes, the streptozotocin induced diabetic mouse, MPC injection resulted in a significant increase in blood insulin levels and sustained reduction in blood glucose levels over the three week study period. Treated animals had restored balance between insulin-producing beta cells and glucagon-producing alpha cells.

In summary, the companies between them have demonstrated safety of their allogeneic stem cells in preclinical studies and several recent human studies in a range of conditions. Human clinical efficacy has been demonstrated in CHF, BMT, long bone fracture and spinal fusion.

Combining data from all of these studies will allow the companies to by-pass Phase I studies in other indications. It is reasonable to assume that the evaluation of MPC for additional indications will commence with a Phase I/II trial. In most indications, studies will then progress directly to a Phase III or Pivotal Study which generates the data required by a regulatory agency to decide whether or not to approve the treatment.

#### 2.2 Mesenchymal Stem Cells

Stem cell therapy is emerging as a important modality for treating and potentially curing human disease. It involves the use of living cells to replace and initiate the production of other cells that are missing or damaged due to disease or injury.

Adult stem cells, including MPC, are restricted in their ability to differentiate into other cell types. Embryonic stem cells, on the other hand, can generate a greater variety of tissue types and have been viewed by many as the ideal starting point for repair and replacement of tissue and organs. It is currently difficult to regulate and direct



embryonic stem cells into particular cell types and, as a consequence, there have been concerns about cancer formation should such cells proliferate uncontrollably. Access to sufficient numbers of embryonic stem cells has raised ethical concerns as the current sources are early stage human embryos or through therapeutic cloning and, as a consequence, mainstream pharmaceutical and medical device companies may find it difficult to commercialise embryonic stem cell technologies.

Current medical treatment with stem cells is focused on the use of haematopoietic (blood) stem cells to regenerate healthy, functioning bone marrow to establish and maintain the blood and immune system, often as an adjunct to cancer therapy. Haematopoietic precursor cells have been used in myeloblative cancer therapy for over 40 years with 40,000 to 50,000 procedures currently performed annually.

Mesoblast's and Angioblast's platform is built upon the discovery of a particular class of adult-derived mesenchymal stem cells and the development of methods to isolate and accurately identify these cells. The IP, owned by Angioblast, covers tools for the purification of MPC from bone marrow aspirates and other tissue, and further defines the MPC by surface markers. Additional IP relates to the application of MPC to treat specific medical conditions.

Mesenchymal, or human stromal stem cells, are non-hematopoietic bone marrow-derived progenitor cells with the ability to transform into a variety of structural tissue when provided with the right stimuli. Although the precise signals necessary to direct cell differentiation to specialised cells are not known, placement of a precursor cell into the appropriate environment is often all that is necessary to achieve the desired outcome. The surrounding cells provide the relevant chemical signals. Thus placement of mesenchymal stem cells into cardiac muscle will cause them to differentiate into myocardium or heart muscle cells. Mesenchymal stem cells may also evolve into cartilage, bone, skeletal muscle, tendon, ligament, fibrous connective tissue, blood and lymphatic vessels, and fat.

One of the most important features of MPC is that they do not initiate an immune response in a recipient when harvested from another individual. MPC can therefore be "bulked-up" in a manufacturing facility for delivery to many patients. The potential is for MPC to be produced from a limited number of donor sources and supplied to large numbers of unrelated patients. Such a business model is more aligned to pharmaceutical production and supply than to cell therapies as being practiced with haematopoietic stem cells or under development by other stem cell companies.

Unlike pharmaceuticals which are generally used to treat a single disease or condition MPC can be used in a broad range of indications where replacement of damaged tissue is required. As a consequence, such cells could prove beneficial in treating bone fractures, for cartilage replacement, heart muscle and blood vessel restoration, and many other applications.

#### 2.3 Intellectual Property

Angioblast has an assignment of patents lodged initially in the name of Adelaide's IMVS. Mesoblast has a separate agreement with IMVS, through the latter's commercial arm, Medvet Science Pty Ltd, for orthopaedic, bone and cartilage applications. The assigned patents aim to provide an exclusive and protected position for MPC composition-of-matter, methods for MPC isolation, and several use indications for cell therapy. Two of these patents have recently been granted in the US.

The composition-of-matter claims derive from the identification of unique markers on the surface of adult MPC which underpin claims to a novel cell type. The patents cannot preclude competitors and medical practitioners from using crude bone marrow aspirates containing cells with the "proprietary" markers, but these parties will not be able to purify or concentrate MPC without infringing patents. Consequently, others will be restricted to cell mixtures containing exceedingly low numbers of MPC which, by definition, will be significantly less effective than the defined MPC products and possibly unsuitable for allogeneic administration.

The methodology for MPC isolation involves use of proprietary marker-specific monoclonal antibodies. Alternative methods for stromal stem cell separation have been developed, and in some cases patented, by other companies. Mesoblast has shown that its cells differ from cultured competitor products by their surface characteristics and genetic phenotype. Consequently, Mesoblast and Angioblast have complete freedom to operate with respect to these particular cells.



Additional international patent applications have been lodged claiming the use of MPC in the treatment of excessive neovascularisation and ocular disease, and the use of MPC as immunosuppressive agents. This year a further application was lodged claiming the use of MPC in treating diabetes. These further strengthen the technology's protection and extend the market monopoly.

Our examination of the technology included application to congestive heart failure, acute myocardial infarct and bone marrow transplantation which are the subjects of claims in the earlier patents; age related macular degeneration and diabetic macular oedema, which applications are afforded additional coverage by the "neovascularisation" and "ocular disease" patents; and diabetes type 2.

#### 2.4 Route to Market

The usual route to market for small-cap biotechnology companies is to out-license IP at an advanced stage of development to a large pharmaceutical, medical device or biotechnology company. Licensing is attractive because it provides access to the resources and skills of the larger partner in production and distribution, marketing and regulatory affairs. It brings products to market more rapidly and provides maximum market impetus. It also reduces the financial burden on often under-capitalised companies and greatly reduces risks.

It is clear that both Mesoblast and Angioblast have a common desire to progress development of lead products for as long as possible prior to licensing and to retain independence from a major pharmaceutical or medical device company. They may seek a trade sale, sale of individual clinical applications, or joint venture rather than license-out products, or they may complete development and registrations with appointment of distributors of the products. The advantage to the companies of deferring a deal is that they can seek a larger slice of the pie in the form of a sale price, up-front payments and/or royalties. The concerns are that they carry all the development risks, or at least those risks that are encountered prior to licensing or collaborating, with the possibility of failure leaving shareholders with very little; and the continuously escalating costs of development as products progress down the trials and approvals route.

Mesoblast and Angioblast have not publicly indicated a specific licensing point or, for that matter, a preferred route to commercialisation. For the purposes of our modelling, we have assumed that the Company can fund R&D to the point of receipt of marketing approvals in the USA and that it will receive a percentage of pre-tax profits on the sale of products or the equivalent percentage as royalty.

#### 2.5 Key Collaborations and Agreements

The terms of the assignment of patents to Angioblast by Medvet Science requires payments on the achievement of defined milestones, payable for each medical indication, and a royalty on sales by Angioblast or a sub-licensee. Mesoblast is also required to make milestone and royalty payments.

In November 2005, Angioblast entered into a formal non-exclusive collaborative agreement with Cordis Corporation. Cordis is a worldwide leader in developing and manufacturing interventional vascular technology including the drug eluting Cypher® stent. Cordis's latest generation heart catheter system has been specifically developed to deliver cells or other biological products directly into the heart. The catheter system received its first worldwide test in patients in conjunction with MPC during the autologous MPC clinical trial.

In December 2007, Angioblast entered into an agreement with Abbott Cardiovascular Systems for the collaborative development and commercialisation of Angioblast's catheter-based cell therapy product for heart failure. The transaction included the issue of a convertible note to Abbott.

In February 2009, Mesoblast initiated a broad-based collaborative clinical program with one of Singapore's leading private healthcare providers, Parkway Group Healthcare Pte Ltd, a subsidiary of Parkway Holdings Limited. Parkway Independent Ethics Committee approved Mesoblast's first registry trial of RepliCart<sup>TM</sup>, its adult stem cell product for patients with knee osteoarthritis.

Mesoblast has joined with Cell Therapies Pty. Ltd. in applying for approval from the TGA to market autologous MPC for treating bone fractures. Melbourne-based Cell Therapies will manufacture and supply cells to clinicians.



#### 3. Cash Flow Models

#### 3.1 Approach to Modelling

For each targeted clinical indication cash flows have been prepared using incidence and prevalence data for specific diseases and conditions, where appropriate, along with hospital discharge rates, where available, for surgical procedures. MPC market penetration is based on consideration of sub-groups of patients with a particular condition who are likely to benefit from stem cell therapy as well as current and in-development competition. In the case of CHF, consideration was given to the number of interventional cardiologists as being the bottleneck in effective delivery of the treatment.

The CHF, Diabetes type 2 and Knee Osteoarthritis models differs from the others in that pre-existing patients (based on prevalence data), and not just newly diagnosed (based on incidence data), represent a major group in need of treatment. The models are epidemiology-style analyses in which prevalence is based on current prevalence less deaths and those treated by competition and MPC, to which is added those newly diagnosed patients who do not receive immediate treatment or do not die. As a consequence, once effective treatments become available prevalence numbers decline.

The models are based on USA disease statistics only as this is the primary market for both companies. A global analysis would result in significantly greater cash flows.

Wherever possible, an estimated average selling price (ASP) has been benchmarked against product and procedure charges applicable to current treatments for the particular condition with, in some cases, consideration given to the fact that MPC treatment may be more efficacious, or on US Current Procedural Terminology (CPT) codes as used by insurers or Healthcare Common Procedure Coding System (HCPCS) numbers as used by US Medicare, published hospital cost data or cost-effectiveness studies.

Clinical development schedules have been made available for our analysis by both companies including estimates of numbers of patients and the per-patient costs. We have retained figures in most instances, crosschecked patient numbers against other studies into the same medical condition as available through the US National Institutes of Health clinical trials web site (http://.clinicaltrials.gov), while tending to take a more conservative view to development times.

Additional expenses have been included for pre-clinical development where required, regulatory dossier preparation and fees, and post-market surveillance. It is assumed that Mesoblast and Angioblast are responsible for these costs.

The cash flows have been developed such that Deloitte Corporate Finance may provide project valuations using a probability adjusted net present value (PANPV) approach.<sup>3</sup> The preferred methodology for valuing in-process research and development (IPR&D) is to use expected cash flows arrived at using decision analysis techniques and probability analysis.<sup>4</sup> The resulting cash flows may then be discounted at a rate close to the cost of capital as the risks are deemed to have been dealt with in the probability analysis.

### 3.2 Likelihoods of Success

In pharmaceutical development the risks are generally well defined, starting from the candidate molecule and progressing through preclinical development, Phase I, Phase II and Phase III trials.<sup>5, 6, 7, 8</sup> A number of sources provide statistics on transitional probabilities. However, stem cell therapies have as yet to receive market approval in numbers sufficient to allow meaningful statistics. We have conservatively applied probabilities that are lower

<sup>&</sup>lt;sup>3</sup> Bogdan B & Villager R. Valuation in Life Sciences: A Practical Guide. Springer Verlag (Berlin), 2007.

<sup>&</sup>lt;sup>4</sup> "Assets Acquired in a Business Combination to be used in Research and Development Activities: A Focus on Software, Electronic Devices, and Pharmaceutical Industries." AICPA, New Jersey. 2002.

<sup>&</sup>lt;sup>5</sup> Abrantes-Metz RM, *et al.* Pharmaceutical Development Phases: A Duration Analysis. Bureau of Economics, Working Paper No. 274, October 2004

<sup>&</sup>lt;sup>6</sup> Reichert JM & Wenger JB. Development Trends for New Cancer Therapeutics and Vaccines. Drug Disc Today 13(1/2):30, 2008.

<sup>&</sup>lt;sup>7</sup> Pavlou AK & Reichert JM. Recombinant Protein Therapeutics – Success Rates, Market Trends and Values to 2010. Nature Biotechnology 22(12):1513, 2004.

<sup>&</sup>lt;sup>8</sup> Kola I & Landis J. Can the Pharmaceutical Industry Reduce Attrition Rates? Nature Reviews: Drug Disc. 3:711, 2004.



than those published for new chemical entities or biologicals. In particular, we have reduced the likelihood of receiving market approval significantly as the guidelines for approvals are continuing to be formulated.

Each probability factor is applied at the time at which the risk hurdle is encountered and it applies a linear discount, in proportion to the cumulative risk, to all future cash flows beyond that time point. Subsequent risk factors apply further compounded linear discounts. Revenues received prior to a risk occurring, such as a milestone payment, are unaffected by a future risk.

#### 4. Markets & Competition

#### 4.1 The Pharmaceutical Industry - Overview

The global prescription pharmaceutical market was US\$712 billion in 2007, up 6.4% on the previous year. Cardiovascular disease is a leading therapeutic category worth over US\$141 billion in 2007. The US posted the highest sales, at US\$50.5 billion, although this was a decline of 6.6% as compared to 2006. This broad-based group includes treatments for heart attacks, hypertension, angina, arrhythmia, and elevated cholesterol levels. Cardiac therapies and cardiovascular agents constituted US\$12.3 billion in sales.

In 2008, revenues generated by sales of orthopaedic products worldwide neared US\$36 billion, an increase of just under 10% over 2007 global revenues. <sup>10</sup> The US, Europe and Japan accounted for 80% of the marketplace. In the fracture repair market, US sales were \$2.6 billion and US\$2.3 billion in the rest of the world.

Pearldiver, Inc's analysis of the market for 2008 was that there were global sales of US\$30.9 billion in 2008 comprising: 11

| Segment      | 2008 Sales<br>(\$' billions) | Segment         | 2008 Sales<br>(\$' billions |
|--------------|------------------------------|-----------------|-----------------------------|
| Spine        | 8.1                          | Sports medicine | 2.8                         |
| Knees        | 6.7                          | Orthobiologics  | 2.5                         |
| Hips         | 5.5                          | Extremity       | 0.9                         |
| Trauma       | 4.7                          |                 |                             |
| Total Market | 30.9                         |                 |                             |

Table 1: Global Orthopaedic Product Revenues 2008

The world market for cell-based therapies, although in their infancy, is currently estimated at US\$600 million with the US accounting for about 90% of the world market. Cell therapies were approximately 50% of this figure with the remainder cord blood banking services. Business Insights estimates that the market for stem cells will grow at a rate in excess of 40% per annum as new products become available, growing to US\$5.1 billion in 2014. Stem cell products in advanced clinical development, and expected to be approved for marketing in the near term, include Prochymal<sup>TM</sup> (Osiris Therapeutics ,Inc.) for acute graft versus-host disease, and Chondrogen<sup>TM</sup>, also from Osiris, for repair of knee cartilage.

Mesoblast's MPC may also fall into the orthopaedic market segment known as orthobiologics. This refers to products that incorporate biology and/or biochemistry for the repair, replacement or regeneration of musculoskeletal structures. Products include bone and soft tissue substitutes, allograft bone/tissue, tissue engineered substances, growth factors/bone proteins, stem cells, hyaluronic acids, etc. In 2008, revenues generated by the sale or distribution of orthobiologics approached US\$3.7 billion, an increase of nearly 10% from 2007. 10

In the following sections, we discuss markets for specific therapeutic areas.

<sup>12</sup> Advances in the Stem Cell Industry. Business Insights Ltd (UK). 2009.

<sup>&</sup>lt;sup>9</sup> The Cardiovascular Market Outlook to 2013. Business Insights Ltd (UK), 2008.

<sup>&</sup>lt;sup>10</sup> The Orthopaedic Industry Annual Report: For Year ended June 15, 2009. Orthoworld Inc.

<sup>11</sup> Market Landscape. Pearldiver, Inc. www.pearldiverinc.com/pdi/markets.jsp



#### 4.2 Indications Targeted by Angioblast

#### Heart Disease

The American Heart Association and the National Heart, Lung, and Blood Institute have estimated that cardiovascular disease and stroke will cost the USA US\$448.5 billion in 2008, and the burden continues to grow as the population ages. The principle aims of cardiovascular therapies are to reduce morbidity and mortality from heart attacks, strokes and other blood vessel related disease. Hence, an emphasis on lowering blood pressure and plaque and emboli formation through lowering cholesterol levels. The markets for treating CHF and the consequences of heart attack are currently poorly serviced.

The delivery of stem cells to a patient for therapeutic purposes is a new approach to therapeutic intervention and there are, as yet, no products approved for sale. An effective cell therapy that helps in repairing the heart would have a significant market. If such a treatment became the standard of care for heart attack survivors or CHF sufferers, revenues of many tens of billions of dollars annually would be possible. At this stage, however, as no therapy has progressed beyond clinical trials, it is unlikely that substantial revenues from these therapies will be generated before the year 2012.

Angioblast's product development programs are aimed at several cardiovascular conditions, including CHF, AMI and peripheral arterial disease.

Almost 10% of the adult population of the US has some form of cardiovascular disease. Heart failure affects between five and six million people in America, ten million in Europe and as many as 20 million worldwide. <sup>14</sup> There are 550,000 new cases per year in the US, growing at 10% per annum, and almost one million hospitalizations every year. Mortality among CHF patients is 7% pa contributing to or causing 300,000 American deaths annually. As many as 20 million people may have undiagnosed heart failure and are likely to develop symptoms within five years.

CHF is a chronic condition characterized by an enlarged heart and insufficient blood flow to the extremities of the body. The condition develops over time and can be caused by many factors that put an excess demand on the heart muscle, including high blood pressure, incompetent valves, infections of the heart muscle or valves, or congenital heart problems. The incidence of CHF in people with hypertension is double that of people with normal blood pressure. Whatever the initial cause, CHF results from the death of cardiomyocytes, the cells that form the heart muscle.

Twenty percent of CHF sufferers die in the first year. From the Framingham Heart Study, median survival after the onset of heart failure was 1.7 years in men and 3.2 years in women. Overall, one-year and five-year survival rates were 57% and 25% in men and 64% and 38% in women, respectively. Although patients are initially treated with drug therapy, the only method of treating end-stage disease currently is a heart transplant. Over 3,000 heart transplants are performed annually in the US.

CHF is currently treated primarily with drugs that increase blood flow. Diuretics, digoxin, acetylcholinesterase inhibitors, and beta-blockers are useful in treating symptoms of heart failure, but do nothing to reverse the damage. They do not regenerate heart muscle or rebuild heart tissue.

MPC are thought to be of benefit in rebuilding damaged heart by two mechanisms which are not available from existing therapies. Firstly the formation of arterioles may increase blood supply to damaged heart muscle and, secondly, MPC may directly induce new heart muscle cells to regenerate and grow.

Acute MI, or heart attack, occurs when the blood supply to part of the heart muscle is severely reduced or stopped. This happens when one of the heart's arteries is blocked by an obstruction, such as a blood clot that has formed on atherosclerotic plaque. If the blood supply is cut off drastically or for a long time, heart muscle cells suffer irreversible injury and die. The aim of stem cell treatment is to prevent the onset of heart failure after heart attack.

<sup>&</sup>lt;sup>13</sup> Stem Cell Therapies & Regenerative Medicine - Current Applications & Future Possibilities. Business Communication Company, Inc. MA. December 2005.

<sup>&</sup>lt;sup>14</sup> RS McKelvie. The CHARM Program: The Effects of Candesartan for the Management of Patients with Chronic Heart Failure. Expert Rev Cardiovasc Ther 7(1):9, 2009.



Treatments for heart attack are relatively ineffective in preventing heart failure and none of them is capable of increasing the formation of blood vessels or inducing cardiac repair. The medications used in patients with MI can be categorized in terms of those used acutely at the time of infarction and those used more chronically to prevent the later complications. The initial goal of treatment is restoration of blood flow to minimise progressive scarring of the heart and muscle cell death. This is achieved either through the combined use of aspirin, heparin, thrombolytic agents such as tissue plasminogen activator, and agents that inhibit platelet activation, or through mechanical approaches such as angioplasty or emergency bypass surgery. After the immediate crisis has passed, patients are maintained on a variety of medications, each of which has been shown to have only modest effect. These include cholesterol lowering drugs, beta-blockers and angiotensin converting enzyme inhibitors. These therapies may alleviate heart failure symptoms such as shortness of breath and fatigue but CHF is inevitable.

Approximately 7.3 million American adults have had at least one MI with over 1.1 million incidences each year. About 80% now survive the initial heart attack, mostly by undergoing an early angioplasty procedure of the blocked artery accompanied by implantation of a metal stent to keep the artery patent long-term. However, despite this success with early survival nearly half of the surviving patients become disabled with heart failure over the ensuing six years. Ultimately, over half a million people in the US die each year as a result of a heart attack, either due to the acute event itself or due to heart failure in the wake of a past heart attack. This makes heart attacks the single biggest killer of Americans.

Studies have shown that methods which increase the amount of blood vessels present in healthy heart muscle adjacent to the heart attack area can induce cardiac regeneration and effectively prevent heart failure after a heart attack. The larger that blood vessels can be created, the greater the preventative effect on post-infarct heart failure.

Angioblast's allogeneic MPC have been shown to induce sustainable large blood vessel formation and protect heart muscle against progression to heart failure. The company has developed a successful protocol to infuse the allogeneic MPC directly into the affected coronary artery after removing an initial obstruction. In animal models this simple mode of MPC delivery significantly prevented the heart function that otherwise occurred in controls. The company envisages that coronary artery infusion of MPC by a standard catheter immediately after angioplasty and stent implantation could become a routine procedure to improve cardiac function, enhance quality of life, and reduce the likelihood of heart failure following a heart attack.

#### Macular Degeneration

Blindness afflicts an estimated 40 to 45 million individuals worldwide (0.7% of people), while another 110 million have vision impairment some of which will progress to total blindness. There are many causes of blindness including genetic or hereditary, infection and disease, and trauma. By far the greatest cause, more than 50% among peoples of developed nations, is due to age-related macular degeneration (AMD). It is estimated that over eight million individuals in the US have AMD, and the incidence of AMD is expected to rise as the elderly population continues to increase throughout the western world.

There are two forms of AMD, commonly referred to as "wet" and "dry" AMD. The dry form of AMD may result from the aging and thinning of macular tissues, deposition of pigment or drusen in the macula, or a combination of the two processes. With wet AMD, also referred to as "neo-vascular" AMD, new blood vessels grow beneath the retina and leak fluid which in turn causes retinal cells to die.

While only about 10-15% of AMD cases are of the wet form it accounts for 90% of severe vision loss caused by AMD. The bulk of AMD is dry. This form of the disease is more slowly progressive with about 7% of sufferers ultimately becoming totally blind. In the US alone, there are about 2 million people suffering from the wet form of AMD associated with abnormal blood vessels and there over 200,000 new cases per year.

Angiogenesis (or neovascularisation) is the formation of new blood vessels. The process is generally absent in healthy adult or mature tissue but in many serious disease states the body loses control over angiogenesis. Excessive angiogenesis occurs in cancer, macular degeneration, diabetic retinopathy, arthritis, and psoriasis. In these conditions, new blood vessels feed diseased tissues and destroy normal tissues.

Studies by Angioblast have demonstrated that its stem cells can be used to treat or prevent angiogenesis related ocular diseases. Rodent and monkey studies have demonstrated that there are no adverse consequences of the



procedure and indications are that one hundredth of the dosage of cells used in the cardiovascular indications may be required. Human safety studies may, therefore, be unnecessary.

Current treatments for AMD include anti-VEGF therapy. Pegaptanib (approved in 2004 and marketed as Macugen<sup>™</sup> by Eyetech Pharmaceuticals and Pfizer Inc.) is beneficial in approximately 4% to 6% of patients but the majority of patients continue to lose vision. The other anti-VEGF is an antibody fragment, ranibizumab (approved in 2006 and marketed as Lucentis<sup>™</sup> by Genentech, Inc. and Novartis Ophthalmics) with US sales of US\$875 million in 2008. Patients may require intra-ocular injections of Lucentis as often as once a month for six to 24 months at a cost of approximately US\$2,000 per injection.

The Angioblast technology could be complementary to anti-VEGF treatment, particularly if the potential to restore eyesight is proven. A treatment that avoided repeated intravitreal injections would have a major market advantage.

#### Diabetic Macular Oedema

The most common cause of visual loss in diabetics is due to a condition called diabetic macular oedema or oedema (DME) which complicates underlying diabetic eye disease. The primary cause of diabetic eye disease is thought to be excessive and abnormal capillary growth and proliferation due to loss of inhibitory regulatory signals normally provided by endogenous MPC-like cells normally present in the eye and which coat the capillaries. The endogenous MPC-like cells are selectively lost in the eye due to toxic effects of glucose and other metabolic abnormalities associated with diabetes.

The macula is the central portion of the retina, a small area rich in cones, the specialized nerve endings that detect colour and upon which daytime vision depends. As macular oedema develops, swelling of the retina occurs resulting in blurring in the middle or just to the side of the central visual field. Visual loss from DME can progress over a period of months and make it impossible to focus clearly.

The prevalence of DME among US diabetics approaches 30% in adults who have had diabetes for 20 years or more, and varies with the stage of diabetic retinopathy. It can occur at any stage of diabetes and can predate the appearance of other findings of diabetic retinopathy. The estimated annual incidence of new cases of DME is 75,000.

Current treatments include photocoagulation, which prevents ongoing damage but will not restore lost eyesight, anti-VEGF therapy (monoclonal antibodies such as Lucentis<sup>TM</sup> and Avastin<sup>TM</sup>) although definitive studies have yet to be completed, and corticosteroids. The market for treating DME has been estimated at 335,000 procedures each year in the US increasing at a 2.8% rate p.a.

#### Haematopoietic Stem Cell Transplantation

In bone marrow transplantation (BMT), marrow is removed from a bone in a patient about to undergo chemo- or radiation-therapy. Stem cells are extracted from the marrow, stored and expanded in culture before reinfusion to the patient following the cancer treatment to replenish haematopoietic stem cells (HSC) which are destroyed by the therapy. With the availability of the stem cell growth factors GM-CSF and G-CSF, most HSC transplantation procedures are now performed using stem cells collected from the peripheral blood, rather than from the bone marrow.

Autologous haematopoietic stem and progenitor cells are obtained by mobilising bone marrow elements using drugs and then collecting the mobilised cells from the bloodstream by apheresis. Unfortunately, cancer patients often have poor bone marrow responses to mobilisation protocols, and a large number of these procedures fail to generate enough hematopoietic precursors for successful BMT resulting in the need for multiple repeat apheresis and mobilisation procedures.

Allogeneic HSC therapy involves a healthy donor with a tissue type that matches the recipient. It is a risky procedure with potential for graft-versus-host disease and other adverse consequences. At present only about 30% of patients who could benefit from an allogeneic BMT procedure have a genetically matched sibling. Consequently, two-thirds of the approximately 55,000 BMT procedures currently performed worldwide are autologous. The patient waiting lists are considerably in excess of this number.



Umbilical cord blood is a preferred source of allogeneic HSC because it has a reduced likelihood of causing graft-versus-host disease compared with cells from an unrelated adult. The major limitation to cord blood use in adults is the limited number of hematopoietic stem and progenitor cells compared with bone marrow obtained from an adult. This often results in delay or inability to achieve satisfactory bone marrow reconstitution, resulting in increased rate of graft failure, infections, bleeding, and death.

Consequently, there is a major need to develop therapies in the BMT field to accomplish the following:

- reduce the number of failed apheresis procedures carried out for autologous BMT; and
- increase the number of safe and successful allogeneic BMT procedures carried out.

Central to both of these clinical outcomes is the ability to expand a starting pool of HSC, whether from autologous or allogeneic sources. Clearly, successful outcomes around the second objective, namely increasing the number of safe and effective allogeneic BMT procedures, will, over time, shift the total number of procedures performed from autologous to allogeneic, with the total number of annual BMT procedures estimated to increase to over 75,000.

Research by Angioblast and others indicates that infusing the marrow with added MSC can increase the transplant success rate. Angioblast's MPC have also been shown to support the expansion of HSC *in vitro* and improve their ability to graft following transplantation. MPC provide a source of growth factors capable of inducing over 20-fold expansion of haematopoietic stem and progenitor cells within several days of co-culture.

Angioblast has been granted Orphan Drug Designation from the FDA to develop its MPC technology for treating patients with hematologic malignancies requiring increased hematopoietic stem and progenitor cell production.

#### Diabetes Type 2

An estimate by the World Health Organisation is that there were 171 million diabetes sufferers worldwide and that the number will grow to 366 million in 2030. The US prevalence is 17.9 million with a further 5.7 million undiagnosed. The total (direct and indirect) spending on diabetes in the US is currently estimated at US\$174 billion or one of every 10 health care dollars spent. The direct medical cost is US\$116 billion having doubled over the past five years. The average annual medical spending for a diabetic in the USA is more than US\$15,000.

The global diabetes market was worth US\$27.3 billion in 2008, led by insulin analogues with 45% of the market, followed by glitazones with 22.8%. <sup>17</sup> Anti-diabetic drug sales in the USA in 2008 were US\$12.9 billion. The sale of glitazones, globally US\$6.2 billion, are in decline due to safety issues. Newer antidiabetic agents, dipeptidyl peptidase IV inhibitors (DPP-IV), are gaining market share with Merck's Januvia<sup>TM</sup> recording sales of US\$1.3 billion in 2008. Exenatide (Byetta<sup>TM</sup>, Eli Lilly) is the first of a new class of drug, glugagon-like peptide- agonists (GLP-1), which are expected to become the most prescribed antidiabetic agent for type 2 diabetes within 5 years. Business Insights forecasts sales of almost US\$7.0 billion in 2014.

Angioblast has demonstrated the effectiveness of its MPC in an animal model. Animals were given a single intravenous dose of 2.5 million cells following chemical induction of the disease. Ongoing monitoring showed effective management of post-prandial blood sugar levels.

It is believed that MPC act in a manner that is analogous to GLP-1 agonists such as Exenatide. GLP-1 activation is associated with the inhibition of glucagon secretion as well as the stimulation of insulin secretion. Its influence on beta and alpha cell function are dependent on the presence of glucose with the effect that its effects on glucagon and insulin secretion fades as the level of glucose in the blood returns to normal. GLP-1 induces the transcription of insulin. Cardioprotective effects have been demonstrated in animal and human studies and it has been shown that GLP-1 also increases beta- cell proliferation and neogenesis, and decreases apoptosis. <sup>18</sup>

<sup>15</sup> http://www.who.int/diabetes/facts/world\_figures/en/

<sup>16</sup> http://diabetes.niddk.nih.gov/dm/pubs/statistics/index.htm#allages/

<sup>&</sup>lt;sup>17</sup> The Diabetes Market Outlook to 2014. Business Insights. 2009.

<sup>&</sup>lt;sup>18</sup> O Schmitz. Editorial: The GLP-1 Concept in the Treatment of Type 2 Diabetes – Still Standing at the Gate of Dawn? J Clin Endocrin Metab 93(2):375, 2008.



Exenatide is administered by subcutaneous injection twice daily, but longer acting GLP-1 mimetics, such as liraglutide (Victoza<sup>TM</sup>, Novo Nordisk) and albiglutide (Ondero<sup>TM</sup>, Boehringer Ingelheim), have shown promising results in clinical trials.

Table 2: Market Estimates for Angioblast Products

| Indication                     | Prevalence   | Incidence                                | Annual Growth                                   | Subset                               | Peak Market<br>Penetration | Price<br>Considerations  |
|--------------------------------|--------------|--|---|--------------------------------------|----------------------------|--|
| Congestive Heart Failure       | 6.2 million  | 670,000                                  | 7% prevalence<br>3.5% incidence                 | Ejection fraction <35%               | 20%                        | Hospitalisation<br>costs & cardiac<br>resynchronisation<br>therapy |
| Acute Myocardial Infarction    |              | 440,000                                  | 2.0%  |                                      | 30%                        | Hospitalisation costs  |
| Diabetic Macular Edema         |              | 335,000                                  | 2.0%  |                                      | 25%                        | Anti-VEGF antibodies   |
| Macular Degeneration           |              | 244,000                                  | 2.0%  |                                      | 25%                        | Anti-VEGF antibodies   |
| Bone Marrow<br>Transplantation |              | 11,700<br>autologous<br>6,000 allogeneic | 2.0% auto<br>10% - 25% allo<br>following launch |                                      | 50% auto<br>95% allo       | Hospitalisation & apheresis costs, emerging drugs                  |
| Diabetes Type 2                | 16.1 million | 900,000                                  | 2% prevalence<br>10% incidence                  | Failed<br>conservative<br>management | 20%                        | Existing & emerging diabetes drugs                                 |

#### 4.3 Indications Targeted by Mesoblast

### Osteoarthritis of the Knee

A considerable percentage of individuals suffer osteoarthritis of the knee. The prevalence of painful disabling knee osteoarthritis (OA) in people over 55 years is 10%, of whom one quarter is severely disabled. Risk factors adding to the growing incidence include obesity and aging of the population.

Approximately 800,000 patients undergo arthroscopic knee surgery annually in the US. <sup>19</sup> This procedure can temporarily relieve acute knee pain and/or instability, but it does not improve knee condition due to the lack of cartilage. <sup>20</sup> The majority of arthroscopies go to reconstruction within ten years.

In severe cases of OA, total knee reconstruction (TKR) is indicated with 542,000 primary knee arthroplasties in the US in 2006. Over the period 1997 to 2005, the volume of knee arthroplasties rose by about 69% from 328,800 to 555,800 procedures. In 2004, the mean length of hospital stay was 3.9 days at a mean cost of US\$13,200 per patient. The aggregate cost in the US for knee arthroplasty was US\$6.3 billion. One analysis projects growth of 673% from 2005 to 2030 to involve more that 3.48 million primary procedures. The actual cost of knee reconstruction is in the range US\$26,000 to US\$35,000 per operation.

Other forms of treatment for knee OA include hyaluronic acid injections with two courses often required each year. There were over 1.2 million treatments given in the US in 2006.

Competition to Mesoblast's MSC will come from Osiris's Chondrogen<sup>TM</sup> and other products which target symptomatic pain relief such as Pfizer's tanezumab, anti-nerve growth factor monoclonal antibody, which is currently in Phase III trials for OA of the knee (also under evaluation for chronic lower back pain).

<sup>&</sup>lt;sup>19</sup> Opportunities for Stem Cell Research and Commercialisation. Business Insights. March 2006.

<sup>&</sup>lt;sup>20</sup> Kirkley A, *et al.* A Randomized Trial of Arthroscopic Surgery for Osteoarthritis of the Knee. N Engl J Med 389(11):1097, 2008.

<sup>&</sup>lt;sup>21</sup> National Health Statistics Report for 2006 (published July 2008) page 16, ICD 81.54 (http://www.cdc.gov/nchs/data/nhsr/nhsr005.pdf).

<sup>&</sup>lt;sup>22</sup> Healthcare Cost & Utilization Project Statistical Brief #34. Hospital Stays Involving Musculoskeletal Procedures, 1997-2005. July 2007.

<sup>23</sup> Kurtz S, *et al.* Projections of Primary and Revision Hip and Knee Arthroplasty in the United States from 2005 to 2030. J Bone Joint Surgery 89:780, 2007.



#### 4.4 Acute Knee Injury

Mesoblast has identified an early market opportunity in acute knee injury and, although of limited revenue potential, it provides a sound entry platform for the larger OA market.

Traumatic chondral defects are currently treated by microfracture and abrasion arthroplasty of which there are an estimated 50,000 to 75,000 conducted each year in the US. It is noted that 11% of 800,000 knee arthroscopies each year show chondral damage. Competitive developments include Tigenix's ChondroCelect<sup>TM</sup> (approved in Europe, Phase III USA), Histogenics' NeoCart<sup>TM</sup> (currently in Phase II), ProChon Biotech's BioCart<sup>TM</sup> (Phase II), and Genzyme Tissue Repair's Carticell<sup>TM</sup> (approved). All of these products are autologous.

A patient receiving Carticell can expect to be charged US\$26,950 for the treatment while microfracture averages US\$4,316.<sup>25</sup>

#### 4.5 Intervertebral Disc

The intervertebral disc is a cartilage that cushions the stress forces on the spine and enables the normal rotation of the spine. With advancing age, there is progressive loss of the proteoglycan material that gives the disc its properties, and a consequent increased risk of damage to the spine. This process, termed degenerative disc disease (DDD), affects 15-45% of the population.<sup>26</sup>

Studies examining the problem from different directions (eg. examination of volunteers and patients, imaging investigations, trials of intervention) have produced evidence implicating the intervertebral disc (IVD) in a significant proportion (at least 40%) of cases of chronic back pain, leading to the use of the term "discogenic back pain".<sup>27</sup>

Frost & Sullivan (in its analysis of Raymedica, Inc.) reports that approximately 30 million people in the US suffer from back pain. 28 "While physical therapy and medication provide a solution in most cases, a subset of approximately 15%, about 4.5 million people, still experience back pain despite such conservative therapy. For this, the next level of treatment becomes a spinal surgery involving either total disc replacement or spinal fusion. However, since spinal surgery is advocated only in severe cases of DDD, out of the 4.5 million people only 500,000 would be considered candidates for surgery. This creates a gap of about 4 million people who are currently left untreated. These patients experiencing mild to moderate DDD are normally treated with conservative procedures with significant associated morbidity and reduced productivity, until the condition worsens to a degree that warrants spinal surgery."

Since MPC produce the proteoglycan materials found in discs, Mesoblast envisages that the injection of MPC into a degenerated intervertebral disc will lead to replacement of the proteoglycan of cartilage. This approach, with its anticipated ease of application and lack of side-effects, should offer a relatively non-invasive and cost-effective therapy for patients with moderate or severe degenerative disc disease.

Mesoblast is targeting the two ends of the spectrum:

- the bulk of patients with "discogenic" chronic back pain but who are not sick enough to warrant a spinal fusion procedure; and
- the patients who get discectomies, or other surgical interventions, where the cell procedure would be adjunctive to prevent the 50-60% of surgeries that are followed by loss of disc height after this procedure.

The number of excisions and/or destructions of invertebrate discs, discectomies, in the US in 2007 were 333,000.

<sup>&</sup>lt;sup>24</sup> Arøen A, et al. Articular Cartilage Lesions in 993 Consecutive Knee Arthroscopies. Am J Sports Med. 32(1):211, 2004.

<sup>&</sup>lt;sup>25</sup> Ellison S. Cartilage Repair – Replacing Joint Arthroplasty? Pearldiver, Inc. Dec 9, 2008 (www.pearldiverinc.com).

<sup>&</sup>lt;sup>26</sup> Abdi S, *et al.* Epidural Steroids in the Management of Chronic Spinal Pain: A Systematic Review. Pain Physician 10:185, 2007.

Freemont AJ. The Cellular Pathobiology of the Degenerate Intervertebral Disc and Discogenic Back Pain. Rheumatology 48(1):5, 2009.

<sup>&</sup>lt;sup>28</sup> Frost & Sullivan Highlights Raymedica for its Pioneering Technology to Treat an Unaddressed Patient Market. April 22, 2008.



The market opportunity for a successful, minimally invasive therapy for discogenic pain, as estimated by Spinal Restoration, Inc., could conservatively exceed \$2 billion annually.<sup>29</sup> This company also estimates a potential market of about 4 million patients.

#### Spine Fusion

Over 65 million Americans suffer from back pain. Conservative therapies (anti-inflammatory medications, exercise, physiotherapy, etc.) are usually given a timeframe of two-to-three months to effectively work. However, when disc degeneration is severe, these conservative treatments can be rendered ineffective quickly. Follow-up diagnosis with X-ray, MRI, CT, myelogram, or discography is used to determine more aggressive treatment options. The elimination of motion through fusion has been the gold-standard solution to a variety of degenerative disc diseases but continues to be reserved for patients with severe degenerative disc disease.

Spinal fusion, in which two or more spinal segments are fused or mechanically locked to each other, is performed in patients with severe degenerative disc disease. It is a major surgical procedure often associated with serious complications including infection, permanent nerve damage, and recurrence or worsening of pain. In the US there are about 240,000 cervical and 280,000 lumbar spinal fusion procedures performed annually. Fusion failure (pseudoarthrosis of failure to relieve symptoms) continues to pose a significant challenge to spine surgeons, and it is estimated that up to 40% of all surgeries result in non-union.<sup>30</sup>

Biomet, Inc. estimates the 2008 market for the US spinal products market is US\$6,205 million.<sup>31</sup> Approximately 85% of revenues in this market are generated from tools used to perform procedures, rather than implants or biologics. Other sources provide similar data.

Current hospital reimbursement DRG (Medicare) for cervical spinal fusion is US\$24,000 per procedure in FY 2009 and US\$33,000 per procedure for a lumbar spinal fusion. The price of lumbar fusion implants (included in the Lumbar DRG) is \$10,000.<sup>32</sup> One state health department estimated the of cost spinal fusion at approximately \$45,000<sup>33</sup>. In comparison to these figures, MPC will be highly cost effective.

#### Non-union Long Bone Fracture

More than one million of the 5.6 million fractures occurring annually in the US are associated with healing difficulties in which repair processes stop before the break is completely repaired. Up to 10% of fractures that heal poorly require bone grafting using either the patient's own bone tissue or that from a donor. Bone grafting is not a straightforward process. It is greatly limited by a lack of blood supply to the new bone and by the limited number of regenerating bone cells in the grafted tissue.

Mesoblast's MPC technology can generate both new bone and new blood vessels, enabling greater bone regeneration. There will be no immune reaction and no donor site, so no chronic pain. Implantation of MPC at the site of poorly-healing fractures is likely to be more effective in less time, while eliminating other complications of bone grafting.

<sup>&</sup>lt;sup>29</sup> Spinal Restoration. www.spinalrestoration.com/market information/market opportunity.html.

WR Hambrecht & Co. Research Report Medical Technology. Sept 21, 2006.

<sup>&</sup>lt;sup>31</sup> Biomet Corporate Presentation 2009 (www.biomet.com).

<sup>&</sup>lt;sup>32</sup> Morgan Stanley. Synthes. Feb 4, 2009.

<sup>&</sup>lt;sup>33</sup> Minnesota Department of Health, March 2001 (www.health.state.mn.us/htac/idet.htm).



**Table 3: Market Estimates for Mesoblast Products** 

| Indication                          | Prevalence   | Incidence | Annual<br>Growth            | Subset                                    | Market<br>Share | Price Considerations  |
|-------------------------------------|--------------|-----------|-----------------------------|---|-----------------|---|
| Osteoarthritis of the Knee          | 33.5 million | 528,000   | 2.0% preval.<br>3.0% incid. | Radiographic<br>evidence &<br>severe pain | 25%             | Total knee reconstruction,<br>hyaluronic acid, anti-<br>arthritic drugs, antibodies |
| Acute Knee Injury                   |              | 70,000    | 5.0%                        |   | 20%             | Microfracture surgery   |
| Intervertebral Disc<br>Regeneration |              | 660,000   | 5.0%                        |   | 20%             | Discectomy, bone<br>morphogenic protein,<br>intradiscal electrothermal<br>therapy   |
| Cervical Spine Interbody<br>Fusion  |              | 120,000   | 2.0%                        |   | 25%             | Cost of fusion procedures   |
| Lumbar Spine Interbody<br>Fusion    |              | 280,000   | 2.0%                        | Modelled on<br>ALIF<br>procedures<br>only | 20%             | Cost of fusion procedures   |
| Non-union Fracture Repair           |              | 60,000    | 2.4%                        | Modelled on tibial fractures only         | 25%             | Hospitalisation, surgery & Bone morphogenic protein                                 |

### 5. Status of Development programs

#### 5.1 Angioblast Product Development Programs

Congestive Heart Failure

The safety of the proprietary adult stem cell technology using a patient's own (autologous) MPC has been shown in pilot clinical trials conducted in Australia.

A Phase II clinical trial for CHF using allogeneic MPC has completed forty of a planned sixty patients. This is the world's first clinical use of allogeneic, or "off-the-shelf", adult stem cells from an unrelated donor to treat patients with congestive heart failure. The multi-centre, placebo-controlled trial is testing the safety and effectiveness of Revascor<sup>TM</sup>. Revascor<sup>TM</sup> is delivered to damaged areas of the heart by a minimally invasive cardiac catheterization procedure performed under local anaesthesia while the patient is awake. Patients undergoing the procedure are released from the hospital within 24 hours.

The first cohort of patients, those receiving the lowest dose along with controls, commenced treatment in October 2008 and were completed in early 2009. Interim three month efficacy results released in May 2009 showed a mean 37% improvement in cardiac function with allogeneic MPC treatment compared to a mean 11% fall in the control group. These patients will continue to be monitored but, to date, no adverse events have been reported.

The second group of 20 patients has recently completed treatment at a higher dose and an additional group of 20 is currently being recruited for the highest proposed dose in the study.

The company has initiated a Phase II clinical trial to evaluate the safety and effectiveness of Revascor<sup>™</sup> for improving heart muscle function in patients with the most severe, or class IV, end-stage form of heart failure. The clinical trial will be performed across multiple medical centers in the US and will involve 80 patients who are waiting to receive a heart transplant from an appropriate donor and are being kept alive temporarily by a Left Ventricular Assist Device (LVAD).

#### Acute Myocardial Infarction

An autologous MPC Phase Ib human clinical trial for Acute MI has been completed in Australia. This study successfully met the primary six-month endpoint of safety in patients suffering from severe coronary artery disease and heart muscle damage. Heart muscle recovery was seen in all six patients within three months of cell



implantation. Four of the six were assessed as having a reduced class of heart failure symptoms as defined by the New York Heart Association scale for congestive heart failure. Three out of three patients with reduced heart function before cell implantation, as defined by ejection fraction, demonstrated sustained improvement at three and/or six months. Five of the patients had reduction in angina symptoms and use of angina medications.

A Phase II trial of allogeneic MPC in 25 patients is currently enrolling patients at multiple sites in the US. Patients receive either placebo or one of 3 progressively increasing doses of MPC.

This is the 1st trial in the world to evaluate an allogeneic, or "off-the-shelf", stem cell therapy injected directly into damaged heart muscle by cardiac catheter.

#### Eye Diseases

The potential for MPC in diabetic retinopathy and wet age-related macular degeneration (AMD) has been demonstrated in a recently completed trial in 42 non-human primates. The results of the preclinical trial showed that a single intra-ocular injection of the Company's adult stem cells was as effective at reducing blood vessel leakage after laser-induced damage as Genentech's Lucentis, the most effective FDA approved anti-VEGF agent in use. The trial showed similar effectiveness with each of the three escalating cell doses used, without any cell-related adverse events.

More importantly, the trial showed that combining Lucentis with a single injection of MPC resulted in a highly synergistic and significantly superior outcome to Lucentis alone in preventing development of severe blood vessel leakage, preventing disease recurrence, reducing formation of new blood vessels, and preventing retinal detachment.

The results of the primate study, together with earlier preclinical results, will form the basis of an IND submission to the FDA to commence a Phase II clinical trial in combination with an anti-VEGF agent, with the objective to show improvement in vision, long-term disease remission, and reduction in frequency of intraocular anti-VEGF maintenance injections.

#### Bone Marrow Transplantation

To address the two BMT market opportunities, Angioblast is currently executing two complementary clinical programs for product registration:

- Phase I/II trial in up to 30 patients conducted at the University of Texas M. D. Anderson Cancer Center. The trial is funded through a grant awarded by the US National Institutes of Health (NIH). On the basis of the excellent results obtained to date, Angioblast anticipates that upon completion of the first ten patients it will enter into discussions with the FDA to commence an accelerated Phase III trial in approximately 100 patients. Such an accelerated program may see Angioblast's product generating revenues as early as 2012. By both increasing overall BMT success rates using cord blood and reducing by as much as two weeks the time spent in intensive care-type settings through accelerated engraftment and bone marrow reconstitution, Angioblast expects that its therapy will reduce hospital costs by as much as US\$75,000/patient, thereby justifying significant reimbursement for this procedure.
- A clinical program in autologous BMT showing that autologous bone marrow can be expanded by Angioblast's MPC to generate sufficient haematopoietic and stem cell progenitors for successful BMT, thereby totally eliminating the need for any mobilisation agents and repeat apheresis procedures.

Angioblast received orphan drug designation to treat patients with hematologic malignancies who need a bone marrow transplant. This allows for an accelerated review process by the FDA and seven-year market exclusivity in the US upon obtaining marketing authorization.



#### 5.2 Mesoblast Products Development Programs

#### Osteoarthritis of the Knee

Australian institutional ethics approval has been received to begin the first human trial of MSC for prevention of knee osteoarthritis after an acute traumatic knee injury and anterior cruciate ligament reconstruction.

#### Acute Knee Trauma

A trial of 40 patients, including microfracture controls, taking six months to achieve significance of the primary end-point and 12 months to demonstrate durability, could commence once IND approval has been obtained. Based on patient numbers used in current autologous chondrocyte development programs, we anticipate that a Phase III trial will require no more than 120 patients. The product will be administered during arthroscopy along with a matrix in which the MPC can grow.

#### Intervertebral Disc

Mesoblast conducted a study in sheep to evaluate the effect of allogeneic MPC on degenerated intervertebral discs. The sheep were injected with chondroitinase to initiate a process of progressive degeneration with changes to the intervertebral disc equivalent to moderate DDD in humans (25-50% disc height reduction, water content reduction and histopathology and biochemical changes). The discs were then treated with two doses of MPC in a hyaluronic acid carrier, hyaluronic acid carrier alone or no treatment. Treatment with MPC and hyaluronic acid significantly increased disc height, improved water content as determined by MRI and improved the histologic appearance to that of undegenerated discs (untreated control discs). These results provide a strong indication that MPC may be an effective treatment for mild to moderate DDD, where there is no currently available effective therapy.

Mesoblast is in the process of designing a Phase II clinical trial in the US for mild to moderate DDD. Patients that have failed 3 months conservative care would be included in the study. The proposed study will evaluate two doses of MPC delivered via an injection to the disc compared to a control placebo treatment, mock injection. The primary endpoint will be safety at 6 months. Potential efficacy would be assessed as a clinically significant reduction in pain and/or function at 6 months. Additionally, patients would be followed through 2-3 years to evaluate the duration of effect of the MPC and incidence of surgical intervention in both groups with the goal of demonstrating a reduction in the progression to surgical intervention, which is estimated to be approximately 20% or more.

#### Spinal Fusion

Animal (sheep) studies have shown that MPC inserted in an interbody cage achieved a statistically significant improvement in cervical fusion compared to Medtronic's Mastergraft<sup>TM</sup> osteoconductive bulking agent.

Significantly, no cell-related adverse events were noted throughout the study. Animals receiving MPC at two dosages levels had earlier and more robust fusion than autograft or the bone graft substitute as demonstrated by:

- CT scan at three months, 9/12 cell-treated animals had continuous interbody bony bridging compared with only 1/6 autograft and 2/6 with bone graft substitute;
- Functional x-rays at three months showed that cell-treated subjects had significantly reduced flexion/extension at the C3/4 level compared with the other groups indicating significantly superior fusion outcomes.

Mesoblast has started a Phase II clinical trial in anterior cervical interbody fusion and a Phase II trial for lumbar spinal fusion. As reported in February 2009, the lumbar continues with good safety profile.



#### Non-union Long Bone Fracture

Phase I studies have demonstrated the safety of autologous MPC and it is anticipated that, for this indication, a Phase III study is all that is required. As reported on 26 February 2009, the non-union long bone fracture repair trial concluded with excellent outcome.

#### 6. Modelling the Applications

#### 6.1 Congestive Heart Failure

Based on Angioblast's clinical and pre-clinical trials to date, the company expects that a single injection of its allogeneic MPC may result in sustainable and significant improvement of heart muscle function for at least twelve months. Therefore, the company believes that its Phase III trial for product registration will more closely resemble Pivotal trials for devices than drugs. In this regard, we have modelled its Phase III trial size, primary end-points, post-registration market uptake, penetration and pricing on the successful recent history of cardiac resynchronisation therapy devices for patients with CHF.

We have assumed that the pivotal trial will commence prior to 2011 and run for three years and with a further 12 months for FDA deliberations leading to marketing approval, Revascor<sup>TM</sup> could be marketed in the first quarter of 2015.

The target market for MPC therapy is CHF patients in NYHA class II to IV with ejection fraction less than 35%. The incidence of CHF in the US is 670,000 patients a year and prevalence 6.2 million. The US National Heart Lung and Blood Institute estimates that at any given time 35% of patients with heart failure are in functional NYHA class II, 25% in class III and 5% in class IV. Forty one percent have ejection fraction less than 35%. We have used this fraction in determining the relevant sub-set for treatment of the existing patients but taken 30% of the newly diagnosed on the basis that diagnosis will occur earlier in the disease's progression.

The estimated market size is currently 2.5 million patients (41% of 6.2 million pre-existing sufferers) and 201,000 newly diagnosed (30% of 670,000) each year. The model allows for a decline in prevalence due to death, and effective treatment by MPC and competitive therapies (assumed to have treatment rates equivalent to MPC therapy).

The valuation term is to 2024 with current patents expiring in March 2024 (PCT/AU2004/000416 and 000417). No provision is made for extension of patent term, which may be possible under the Hatch-Waxman Act<sup>36</sup> and/or the recently passed United States Patient Protection and Affordable Care Act, or the ongoing sale of product.

Modelling includes provision for the payment of milestones and royalties to MedVet Sciences.

Sales of Revascor commence in 2014, take four years to reach a peak penetration of 20% of eligible patients and hold at this level of penetration for a further four years.

Projected cash flows are adjusted in accordance with probabilities applied to the completion of the various phases of development. The probabilities used are 65% likelihood of successfully completing the current trial, 57% for Phase 3 and 80% for FDA approval. The cumulative probability, or likelihood of a product being launched in the USA is therefore approximately 30%.

For this, and all indication, we have assumed that Angioblast, or Mesoblast, receives a 15% royalty on net sales or 50% of an estimated, pre-tax profit margin.

<sup>35</sup> Cardiac Resynchronization Therapy. JP Morgan, 2007.

<sup>34</sup> J Heart Lung Transplant 13(7):S107, 1993.

<sup>&</sup>lt;sup>36</sup> A patent extension is available in the USA under the Drug Price Competition and Patent Restoration Act (1984) also known as the Hatch-Waxman Act. The Act added Section 156 to the Patent Act permitting patent term extension for patents on products (or processes for making or using the same) that are human drugs, and other products, subject to regulation under the Federal Food, Drug and Cosmetic Act. The Act restores a portion of the patent term during which the patentee is unable to sell or market a product while awaiting government approval, such as the FDA's review of a prescription drug.



#### 6.2 Acute Myocardial Infarction

It is anticipated that the current Phase Ib/IIa trial will be completed within 3 years and followed by a Phase III study of two years duration, and 12 months for regulatory approval. A product launch in 2016 is achievable.

The initial target for MPC is the approximately 50% of the annually 880,000 surviving heart attack patients with left anterior descending coronary disease - being the group with poorest prognosis. The aim of trials will be demonstration of reduction in death or infarct recurrence at 30 days.

The cumulative probability of a successful launch is 24%.

#### 6.3 Diabetic Macular Oedema

Angioblast anticipates completion of a Phase I/II study within two years to be followed by a further three years for a Phase III and one year for registration. A product could be launched by 2016.

In addition to the patents licensed from MedVet Science, two international patent applications have been lodged in the name of Angioblast claiming the use of MPC in the treatment of excessive neovascularisation and ocular disease. These provide a revenue horizon to 2027.

Revenue projections are based on 335,000 cases each year of which 25% are amenable to MPC treatment. In estimating the selling price into this indication consideration was given to the potential need for concomitant anti-VEGF antibody treatment.

The likelihood of this product getting to market is around 22%.

#### 6.4 Macular Degeneration

The market has been based on an estimated of 244,000 procedures in 2010 extrapolated to launch date in 2016 with a market penetration of 25%. The time lines are similar to those projected for DME. The estimated likelihood of a product reaching market is 22.4%.

#### **6.5** Bone Marrow Transplantation

The current cord blood trial will be completed in the first half of this year and will be followed by a Phase III pivotal trial for an estimated product launch in mid-2013 with fast track and orphan status.

In the US, there are approximately 12,000 autologous and 6,000 allogeneic procedures performed annually. Our opinion is that neither group will grow significantly without major breakthroughs (current endogenous growth is of the order of 2% p.a.). MPC in our models achieves 50% penetration of the autologous market. Once MPC have been demonstrated to provide effective treatment, numbers of allogeneic procedures will grow to exceed 20,000 by our estimate at the time of peak penetration.

The assumed cumulative likelihoods of success are 43% for autologous and 41.0% for allogeneic BMT.

## 6.6 Diabetes Type 2

The company expects that an IND may be lodged with the US FDA within 24 months following further animal studies. A Phase Ib/IIa study will require 2 years and a Phase III, 2 years. A product as primary therapy or in conjunction with oral antidiabetic agents could be available by 2016.

The model assumes a US prevalence market of 17.9 million diabetics of whom 90% are type 2. We have assumed that only 50% of these require interventional therapy and that 25% are prescribed either GLP-1 therapy (as forecast



by Business Insights) or MPC. The incidence rate is 900,000<sup>37</sup> and again 50% are prescribed treatment of which 50% are prescribed GLP-1 or MPC which will be the drugs of choice for newly presenting patients. We have then estimated a market share for MPC as 20% on the basis that there could be several well performing GLP-1 agonists on the market. It should be noted that GLP-1 drugs will not reduce the prevalence of the disease as they are not curative. However, we have assumed that MPC are administered only once and that the patient pool declines as a consequence of effective treatment (this is a conservative assumption as current thought is that patients may require ongoing cell therapy) with at least one other curative product on the market capturing equivalent market share.

Following launch sales take four years to reach a peak penetration of 20% of eligible patients. Projected cash flows are adjusted in accordance with probabilities applied to the completion of the various phases of development for a cumulative probability, or likelihood of a product being launched in the USA, of 8%.

**Table 5: Development Assumptions for Angioblast Products** 

| Indication                                | Status   | Est. Launch                        | Product Life<br>(years) | Time to Peak<br>(years) | Cumulative<br>Likelihood |
|---|--|------------------------------------|-------------------------|-------------------------|--------------------------|
| Congestive Heart Failure                  | Forty of 60 patients in Phase Ib/IIa study under IND complete. Recruiting patients under IND for Class IV CHF study. | 2015                               | 9                       | 3                       | 29.5%                    |
| Acute Myocardial<br>Infarction            | Early Phase II study under IND underway.   | 2016                               | 8                       | 3                       | 23.6%                    |
| Diabetic Macular Edema                    | Primate study complete. IND in preparation.  | 2016                               | 12                      | 3                       | 22.4%                    |
| Macular Degeneration                      | IND in preparation.  | 2016                               | 12                      | 3                       | 22.4%                    |
| Allogeneic Bone Marrow<br>Transplantation | Late Phase Ib/IIa study under IND.   | 2014 autologous<br>2015 allogeneic | 10<br>9                 | 2 auto<br>4 allo        | 43.2% auto<br>41.0% allo |
| Diabetes Type 2                           | Proof-of-principle obtained in rats.<br>Primate study planned.   | 2016                               | 15                      | 3                       | 7.9%                     |

#### 6.7 Osteoarthritis of the Knee

Assuming that a Phase II study can be commenced in 2012, a product could be launched in by 2016.

The target population for clinical trials is individuals with advanced disease (Kellgren-Lawrence grade 3+) who, without MPC treatment, are candidates for knee arthroplasty. Clinical trials will aim to demonstrate slowed progression in radiographic damage and improvement in pain. A report by D'Ambrosia provides an overall adult prevalence of Kellgren-Lawrence grades 3 and 4 of 15.7% with 40% of this population reporting symptoms. This would suggest an existing pool of 13.8 million American adults. Between 20% and 30% of those with radiological evidence have severe disease and will be candidates for total knee replacement within a half to two years. The target market in the US is therefore 8.6 million persons (220 million adults x 15.7% OA of the knee x 25% with severe pain).

The incidence of OA of the knee with both radiographic and symptomatic evidence has been conservatively estimated at 0.24% - 528,000 new cases annually.

Our modelling assumes a prevalence starting number, less those treated by all procedures, less deaths (2% in the prevalence group and 1% in the incident group), plus untreated incidence. Numbers of knee replacement

<sup>&</sup>lt;sup>37</sup> The CDC estimate incidence of 1 in 340 or 798,000 (www.wrongdiagnosis.com/d/diabets/incidence-types.htm

<sup>&</sup>lt;sup>38</sup> D'Ambrosia R. Epidemiology of Osteoarthritis. Orthopedics 28(2 Suppl):s201, 2005 (http://www.orthosupersite.com/print.asp?rID=2167).

<sup>&</sup>lt;sup>39</sup> Waddell D, *et al.* Cost Implications of Introducing an Alternative Treatment for Patients with Osteoporosis of the Knee in a Managed Care Setting. Am J Managed Care 7(10):981, 2001.



procedures grows from current numbers at 9% p.a. until MPC are approved. This corresponds to the actual growth rate for the past 8 years 40 and provides projections comparable to those available from other sources 41. Arthroplasty thereafter declines as the preferred procedure until it, or a competitive treatment, is utilised at the same level as MPC.

Clinical trials under IND will commence in 2010 with 2 years for a Phase Ib/IIa study, 3 years for a Phase III study and 1 year for approval by the FDA. MPC have a peak market penetration of 25%. We have priced treatment as similar to TKR and assumed only one course of therapy (although annual injections may be indicated).

The cumulative probability of a product reaching market is 17%.

#### 6.8 **Acute Knee Injury**

Our models assume that MPC treatment achieves 20% replacement of the 70,000 microfracture operations undertaken in the US each year. The numbers of relevant injuries grows at 5% per annum such that at Mesoblast's peak penetration MPC are used in around 20,000 procedures. We anticipate a launch in 2014.

The cumulative probability of success of 24%. The development timeframes are one and two years for Phase I/II and Phase III trials respectively and a further year for regulatory approval.

#### 6.9 **Intervertebral Disc**

Our conservative modelling is based on an estimate of lower back pain sufferers who have failed epidural steroid injections (ESI). Based on data presented by Friedly et al, 2.5 million Americans had ESIs in 2001 of which approximately 1.5 million had two or more. 42 Many of these are given for indications such as spinal stenosis and herniated disc, but 44% are given for degenerative disc and radiculopathy. Thus, approximately 660,000 people are potential candidates for MPC therapy having received little or no benefit from an epidural.

The model assumes that MPC achieve 20% market penetration in the fourth year following product launch in 2017. The cumulative probability is estimated to be 22.4%.

#### 6.10 **Spinal Interbody Fusion**

Modelling of cash flows for cervical spinal fusion starts with the 2006 numbers of fusions undertaken in the US and assumes that 50% of cervical patients are amenable to this treatment. Incidence increase at 2% per annum. MPC treatment cost is assumed to be US\$9,500, on average, for multi level treatment, based on current fusion

A product can be launched in 2016 with sales reaching peak penetrations of 25% after 4 years. We have assumed 52% likelihood of completing Phase I/II trials, 57% Phase III and 80% for regulatory approval.

The pivotal Phase III trial for lumbar is expected to start in 2011, with 400 patients. The trial will require three years.

Modeling is based on 280,000 lumbar procedures currently performed in the US increasing at 2% p.a. MPC treatment cost is assumed to be US\$5,000 for a single level treatment and US\$9,500, on average, for multi level with 52% of procedures multilevel.

<sup>&</sup>lt;sup>40</sup> Merrill C & Elixhauser A. Hospital Stays Involving Musculoskeletal Procedures, 1997-2005. Healthcare Cost and Utilization Project.

Statistical Brief #34. Agency for Healthcare Research and Quality. July 2007.

41 Kurtz S, *et al.* Projections of Primary and Revision Hip and Knee Arthroplasty in the United States from 2005 to 2030. J Bone Joint Surg Am 89:780, 2007.

<sup>42</sup> Friedly J, et al. Increases in Lumbosacral Injections in the Medicare Population 1994 to 2001. Spine 32(16):1754, 2007.



A lumbar product launched in 2016 may reach peak sales of just under US\$500 million, at a penetrations of 20% (competing against bone morphogenic protein currently selling in excess of US\$1 billion annually) after 4 years. The cumulative probability assumed is 24%.

#### 6.11 Non-union Long Bone Fracture

We anticipate that a product for this indication can be launched by 2015. There are an estimated 60,000 non-union fractures of the tibia in the US annually (it is an assumption that any approval is likely to be bone-specific and the tibia is the obvious first target) with MPC obtaining 25% of this market. The likelihood of successful launch is 32%.

**Table 6: Development Assumptions for Mesoblast Products** 

| Indication                          | Status   | Est. Launch | Product Life<br>(years) | Time to Peak<br>(years) | Cumulative<br>Likelihood |
|-------------------------------------|--|-------------|-------------------------|-------------------------|--------------------------|
| Osteoarthritis of the Knee          | IND in preparation   | 2016        | 8                       | 3                       | 17.2%                    |
| Acute Knee Injury                   | Phase II study has commenced under CTN. 2014                     |             | 10                      | 3                       | 23.6%                    |
| Intervertebral Disc<br>Regeneration | Animal study complete and IND in preparation.                    | 2017        | 7                       | 3                       | 22.4%                    |
| Cervical Spine Interbody<br>Fusion  | Phase II study under CTN recently started.                       | 2016        | 8                       | 4                       | 23.6%                    |
| Lumbar Spine Interbody<br>Fusion    | Early Phase II study under IND.                                  | 2015        | 9                       | 3                       | 23.6%                    |
| Non-union Fracture Repair           | Autologous study complete and IND for allogeneic in preparation. | 2015        | 9                       | 3                       | 31.8%                    |

#### 7. Risk Assessment

There are significant risks inherent in the development of the MPC technology along with a suite of others that are applicable to the pharmaceutical and biotechnology industries generally. These have been considered in the preparation of cash flow forecasts.

#### 7.1 MPC Specific Risks

Studies have also shown that MPC do not initiate an immune response in recipients in both animal and human studies. The numbers of humans who have received these cells is still small and, although indications are highly encouraging, there remains a possibility that adverse events may occur in larger study groups or where delivery routes are different to those used to date. If it is not possible to use MPC in an allogeneic mode, the economic viability of the technology may be drawn into question. At the least, the Company's main competitive advantage will be lost.

It should be noted that the issue of safety is not just confined to the MPC themselves. The cells are separated from a mixture of cells recovered from one or more humans. There is a remote possibility that other cells, which may be immunogenic or cancerous, or even capable of initiating an immune response against the recipient, are carried over into the final formulation. The MPC are isolated from the cellular milieu through the use of magnetic beads to which the MPC-specific monoclonal antibodies are attached. The antibodies are obtained from mouse cells and are immunogenic to humans, ie. the body will recognise them as foreign and mount a defence against them. Although every effort is made to prevent carry-through of the antibodies to the final formulation, it is possible that minute amounts may be delivered to the patient. A single administration of MPC with residual murine antibody may not be detrimental, but multiple injections could lead to serious complications.



Neither autologous human implantation nor the Phase I/II studies conducted to date have shown no adverse effects due to these potential contaminants.

The other stem cell specific area of risk relates to the fact that it is evolving technology and the regulatory framework is still being developed. A specific concern of regulatory agencies is the fact that, unlike conventional drug therapy (where the drug is broken down in the body and the effect reduces with time), the effect of cell therapy may increase with time as the cell population propagates *in vivo* with no clearly defined end point. Another concern of regulatory agencies is the lack of specifications regarding the cells to be used for therapy.

Guidelines are under development in most western countries and, barring a major setback as occurred with gene therapy, procedures and safeguards are not likely to be problematic. An unlikely outcome may be a delay in market approvals.

#### 7.2 General Industry Risks

Mesoblast and Angioblast share other risks that are common to the biotechnology industry. These include a dependence on patents, growing competition, the high cost of drug development and often constrained ability to raise the necessary capital.

#### 8. Information Sources

To assist in the preparation of our report, we were provided with the following documents by Mesoblast and Angioblast:

- Angioblast Systems, Incorporated. Strategic Plan.
- Deed of Confirmation between Angioblast Systems, Inc and Medvet Science Pty Ltd and Institute of Veterinary and Medical Science. Dated 1 October 2004.
- Intellectual Property Assignment Deed between Medvet Science Pty Ltd and Angioblast Systems, Inc. Dated 4 October 2004.
- Licence Agreement, between Angioblast Systems, Inc. and Mesoblast Limited. Dated 12 November 2004.
- Agreement between Cordis Corporation and Angioblast Systems, Inc. Dated 1 November 2005.
- Services Agreement between Avid BioSciences and Mesoblast Limited. Dated 31 August 2005.
- Process Development and Manufacturing Services Agreement between Cambrex Bio Science Walkerville and Mesoblast Limited. Dated August 24, 2005.
- Quality Agreement between Cambrex Bio Science Walkerville and Mesoblast Limited. Dated August 24, 2005.
- Consulting and Cell Processing Agreement between Mesoblast and Cell Therapies Pty Ltd. Dated 14
  February 2005.
- A listing of all patent applications as at February 2010 accessed through the FB Rice & Co client website. Current information on patents was derived from searches of patent databases.
- Angioblast Systems, Inc. Revascor (Allogeneic Mesenchymal Precursor Cells). Investigational New Drug Application. SN 0000. Dated March 29, 2007.

#### 9. Qualifications & Declarations

Acuity is a consultancy firm that advises on R&D and its commercialisation with a particular emphasis on healthcare and biotechnology. Acuity undertakes technology and market assessments of projects and provides advice to the developers of high technology products and processes on intellectual property protection, commercialisation and cash flow forecasting. The author of this report, Dr David Randerson, has over 35 years experience as a practicing biomedical engineer and research adviser. He has managed commercial and academic research programs, taught science and engineering at tertiary institutes and worked in the medical device and pharmaceutical industries. He has conducted over 300 IP evaluations in the Biotechnology field.



The financial modelling prepared for Deloitte Corporate Finance makes certain assumptions in relation to the revenue prospects. The projections prepared by Acuity derive, in part, from information that we have obtained from Mesoblast and Angioblast, a number of publicly available sources and our own judgement in relation to projections based on this information.

In presenting these figures, we are making no representation that further research and development will be successful, or that market growth and penetration will be realised. We consider that the projections are based on reasonable assumptions with regards to the markets and that, following adjustment for risk, provide a sound basis for the preparation of a valuation.

Neither Acuity nor its principals have any pecuniary interest in Mesoblast or Angioblast that could be regarded as affecting the ability to provide an unbiased opinion of the matters contained in this report. Acuity will receive a professional fee for the preparation of this report.

This report was submitted in draft form to Mesoblast for comment on factual accuracy prior to finalisation.

Yours Sincerely

D H RANDERSON, PhD Managing Director

## **Appendix 5: Source of information**

In preparing this report we have had access to the following principal sources of information:

- Draft Mesoblast Notice of Meeting
- Merger implementation agreement dated 3 May 2010
- annual report for Mesoblast for the year ended 30 June 2009
- unaudited financial statements for Mesoblast for the six month period ended 31 December 2009
- audited financial statements for Angioblast for the two years ended 30 June 2008 and 2009
- unaudited balance sheet and profit and loss statement for Angioblast for the six month period ended 31 December 2009
- internal management documents provided by Mesoblast
- probability weighted projected cash flows for Mesoblast and Angioblast prepared by Acuity
- company websites for Mesoblast, Angioblast and comparable companies
- publicly available information on comparable companies published by ASIC, Thompson research, Capital IQ, SDC Platinum and Mergermarket
- IBIS company and industry reports
- other publicly available information, media releases and brokers reports on Angioblast, Mesoblast, comparable companies and the biotechnology industry.

In addition, we have had discussions and correspondence with certain directors and executives, including Professor Silviu Itescu, Founder and Director, Mesoblast and Jenni Pilcher, CFO, Mesoblast in relation to the above information and to current operations and prospects.

## **Appendix 6: Qualifications, declarations and consents**

The report has been prepared at the request of the Independent Directors of Mesoblast and is to be included in the Mesoblast Notice of Meeting to be given to Non-Associated Shareholders for approval of the Proposed Transaction in accordance with the ASX Listing Rule 10 and Chapter 2E and Section 611 of the Corporations Act. Accordingly, it has been prepared only for the benefit of the Independent Directors and those persons entitled to receive the Mesoblast Notice of Meeting in their assessment of the Proposed Transaction outlined in the report and should not be used for any other purpose. We are not responsible to you, or anyone else, whether for our negligence or otherwise, if the report is used by any other person for any other purpose. Further, recipients of this report should be aware that it has been prepared without taking account of their individual objectives, financial situation or needs. Accordingly, each recipient should consider these factors before acting on the Proposed Transaction. This engagement has been conducted in accordance with professional standard APES 225 Valuation Services issued by the APESB.

The report represents solely the expression by Deloitte Corporate Finance of its opinion as to whether the Proposed Transaction is fair and reasonable for the purpose of the ASX Listing Rule 10.1 and Chapter 2E and Section 611 of the Corporations Act. Deloitte Corporate Finance consents to this report being included in the Mesoblast Notice of Meeting.

Statements and opinions contained in this report are given in good faith but, in the preparation of this report, Deloitte Corporate Finance has relied upon the completeness of the information provided by Mesoblast and its officers, employees, agents or advisors which Deloitte Corporate Finance believes, on reasonable grounds, to be reliable, complete and not misleading. Deloitte Corporate Finance does not imply, nor should it be construed, that it has carried out any form of audit or verification on the information and records supplied to us. Drafts of our report were issued to Mesoblast management for confirmation of factual accuracy.

In recognition that Deloitte Corporate Finance may rely on information provided by Mesoblast and its officers, employees, agents or advisors, Mesoblast has agreed that it will not make any claim against Deloitte Corporate Finance to recover any loss or damage which Mesoblast may suffer as a result of that reliance and that it will indemnify Deloitte Corporate Finance against any liability that arises out of either Deloitte Corporate Finance's reliance on the information provided by Mesoblast and its officers, employees, agents or advisors or the failure by Mesoblast and its officers, employees, agents or advisors to provide Deloitte Corporate Finance with any material information relating to the Proposed Transaction.

Deloitte Corporate Finance has also relied on the probability weighted projected cash flows for Mesoblast and Angioblast prepared by Acuity. Deloitte Corporate Finance has received consent from Acuity for reliance in the preparation of this report.

To the extent that this report refers to prospective financial information we have considered the prospective financial information and the basis of the underlying assumptions. The procedures involved in Deloitte Corporate Finance's consideration of this information consisted of enquiries of Acuity and analytical procedures applied to the financial data. These procedures and enquiries did not include verification work nor constitute an audit or a review engagement in accordance with standards issued by the AUASB or equivalent body and therefore the information used in undertaking our work may not be entirely reliable.

Based on these procedures and enquiries, Deloitte Corporate Finance considers that there are reasonable grounds to believe that the prospective financial information for Mesoblast and Angioblast included in this report has been prepared on a reasonable basis. In relation to the prospective financial information, actual results may be different from the prospective financial information of Mesoblast and Angioblast referred to in this report since anticipated events frequently do not occur as expected and the variation may be material. The achievement of the prospective financial information is dependent on the outcome of the assumptions. Accordingly, we express no opinion as to whether the prospective financial information will be achieved.

Deloitte Corporate Finance holds the appropriate Australian Financial Services licence to issue this report and is owned by the Australian Partnership Deloitte Touche Tohmatsu. The employees of Deloitte Corporate Finance principally involved in the preparation of this report were Stephen Reid, Director, MAppFinInv, B.Ec, F.Fin, CA, Tapan Parekh, Director, BBus, MCom, CA, F Fin, Jennifer Liu, Associate Director, CFA, B.Com (Hons), Alexandra White, Senior Analyst, B.Com, CA. Stephen and Tapan have many years experience in the provision of corporate financial advice, including specific advice on valuations, mergers and acquisitions, as well as the preparation of expert reports.

Neither Deloitte Corporate Finance, Deloitte Touche Tohmatsu, nor any partner or executive or employee thereof has any financial interest in the outcome of the proposed transaction which could be considered to affect our ability to render an unbiased opinion in this report. Deloitte Corporate Finance will receive a fee of AUD 97,500 exclusive of GST in relation to the preparation of this report. This fee is based upon time spent at our normal hourly rates and is not contingent upon the success or otherwise of the Proposed Transaction. Over the past two years, Deloitte Corporate Finance has provided other services to Mesoblast. These services include the preparation of previous independent expert's reports, for which Deloitte Corporate Finance received fees of AUD 75,000, and other taxation services, for which Deloitte Touche Tohmatsu received fees of AUD 80,000.

#### Consent to being named in disclosure document

Deloitte Corporate Finance Pty Limited (ACN 003 833 127) of 550 Bourke Street, Melbourne VIC 3000 acknowledges that:

- Mesoblast proposes to issue a Mesoblast Notice of Meeting in respect of the Proposed Transaction whereby Mesoblast will acquire all of the shares in Angioblast that it does not already own
- the Mesoblast Notice of Meeting will be issued in hard copy and be available in electronic format
- it has previously received a copy of the draft Mesoblast Notice of Meeting for review
- it is named in the Mesoblast Notice of Meeting as the 'independent expert' and the Mesoblast Notice of Meeting includes its independent expert's report in Appendix D of the Mesoblast Notice of Meeting.

On the basis that the Mesoblast Notice of Meeting is consistent in all material respects with the draft Mesoblast Notice of Meeting received, Deloitte Corporate Finance Pty Limited consents to it being named in the Mesoblast Notice of Meeting in the form and context in which it is so named, to the inclusion of its independent expert's report in Appendix D of the Mesoblast Notice of Meeting and to all references to its independent expert's report in the form and context in which they are included, whether the Mesoblast Notice of Meeting is issued in hard copy or electronic format or both.

Deloitte Corporate Finance Pty Limited has not authorised or caused the issue of the Mesoblast Notice of Meeting and takes no responsibility for any part of the Mesoblast Notice of Meeting, other than any references to its name and the independent expert's report as included in Appendix D.

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