DATAMONITOR Healthcare

PRM-151

Product Analysis

Ref Code: DMKC0145465
Publication Date: 15/10/2015
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Reference: DMKC0145465
First published: 15/10/2015

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PRM-151 : Idiopathic pulmonary fibrosis

PRODUCT PROFILE

Analyst Outlook

Although Promedior's lead product PRM-151 demonstrated the ability to improve forced vital capacity (FVC) in its small Phase I study, overall results of the trial were somewhat mixed and open to interpretation. Nonetheless, the results were positive enough for the company to progress it to a Phase II trial. Depending on the results of this study, Bristol-Myers Squibb may choose to exercise its option to acquire Promedior and add PRM-151 to its growing portfolio of anti-fibrosis therapies. This would largely improve PRM-151's commercial prospects and would be likely to expedite its development.

Drug Overview

PRM-151 is an intravenous formulation of recombinant human pentraxin-2 in development for idiopathic pulmonary fibrosis (IPF) and myelofibrosis. Pentraxin-2, also referred to as serum amyloid P, has been found to inhibit apoptosis, airway inflammation, pulmonary fibrocyte accumulation, and collagen deposition driven by transforming growth factor beta-1 (Murray et al., 2011). Pentraxin-2 also promotes macrophages associated with increased expression of interleukin-10 and interferon gamma-induced protein-10, which both possess anti-fibrotic properties (Duffield et al., 2013; Promedior press release, 2011).

Table 1: PRM-151 drug profile

Molecule	n/a
Phase of development	Phase II
Mechanism of action	Recombinant human pentraxin-2 protein
Originator	Promedior
Marketing company	Promedior/Bristol-Myers Squibb*
Targeted indication	First-line or previously treated mild to moderate IPF
Formulation	Intravenous
Pricing strategy	10% premium to average cost of Esbriet and Ofev
Dosing frequency	10mg/kg every four weeks
Estimated approval date	Q3 2021 (US), Q4 2021 (5EU), Q2 2022 (Japan)
Alternative names	n/a
*Bristol-Myers Squibb has the exclusive option to acquire Promedior.	
5EU = five major EU markets (France, Germany, Italy, Spain, and the UK); IPF = idiopathic pulmonary fibrosis	

Source: Datamonitor Healthcare; BioMedTracker, Copyright 2015, reprinted with permission; Bristol-Myers Squibb press release, 2015; Medtrack, October 2015, Copyright Informa UK; Pharmaprojects ®, 2015; Citeline; Promedior press release, 2015

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DEVELOPMENT OVERVIEW

The tables below summarize the design of PRM-151's Phase I and Phase II studies.

Table 2: PRM-151 Phase I data in idiopathic pulmonary fibrosis

Trial	Sample size	Target patients	Study design	Dosing tested and duration	Results	Reference
NCT01254409 (Phase I)	20	Diagnosed IPF patients	Randomized, double-blind, parallel-assignment, multiple-dose, safety study	Arm 1: PRM-151 1mg/kg Arm 2: PRM-151 5mg/kg Arm 3: PRM-151 10mg/kg Arm 4: placebo Duration: 57 days	Mean change from baseline in absolute FVC: Arm 1: 58ml Arm 2: 60ml Arm 3: 78ml Arm 4: -63ml; Mean change from baseline in predicted DLCO: Arm 1: 0.2% Arm 2: -4.0% Arm 3: -1.5% Arm 4: -2.3%; Mean change from baseline in predicted FEV1:	Van Den Blink et al., 2013

Table 2: PRM-151 Phase I data in idiopathic pulmonary fibrosis

Trial	Sample size	Target patients	Study design	Dosing tested and duration	Results	Reference
					Arm 1: 2.6% Arm 2: 2.4% Arm 3: 0.3% Arm 4: -1.7%; Mean change from baseline in 6MWT distance: Arm 1: -11.2m Arm 2: 5.8m Arm 3: 34.8m Arm 4: -10.5m	

6MWT = six-minute walk test; DLCO = diffusion capacity of the lung for carbon monoxide; FEV1 = forced expiratory volume in one second; FVC = forced vital capacity; IPF = idiopathic pulmonary fibrosis

Source: see above

Table 3: PRM-151 Phase II trial in idiopathic pulmonary fibrosis

Trial	Sample size	Target patients	Study design	Treatment arms	Primary endpoints	Start date/primary completion date
NCT02550873 (Phase II)	117	Mild to moderate IPF patients (predicted FVC ≥50% and ≤90%; predicted DLCO ≥25% and ≤90%; minimum 6MWT distance of 150m; FEV1/FVC ratio >0.7)	Randomized, double-blind, parallel-assignment, safety/efficacy study	Arm 1: PRM-151 10mg/kg days 1, 3, and 5, then once every four weeks Arm 2: placebo Duration: 28 weeks	Change from baseline in predicted FVC	August 2015/March 2017

6MWT = six-minute walk test; DLCO = diffusion capacity of the lung for carbon monoxide; FEV1 = forced expiratory volume in one second; FVC = forced vital capacity; IPF = idiopathic pulmonary fibrosis

Source: ClinicalTrials.gov

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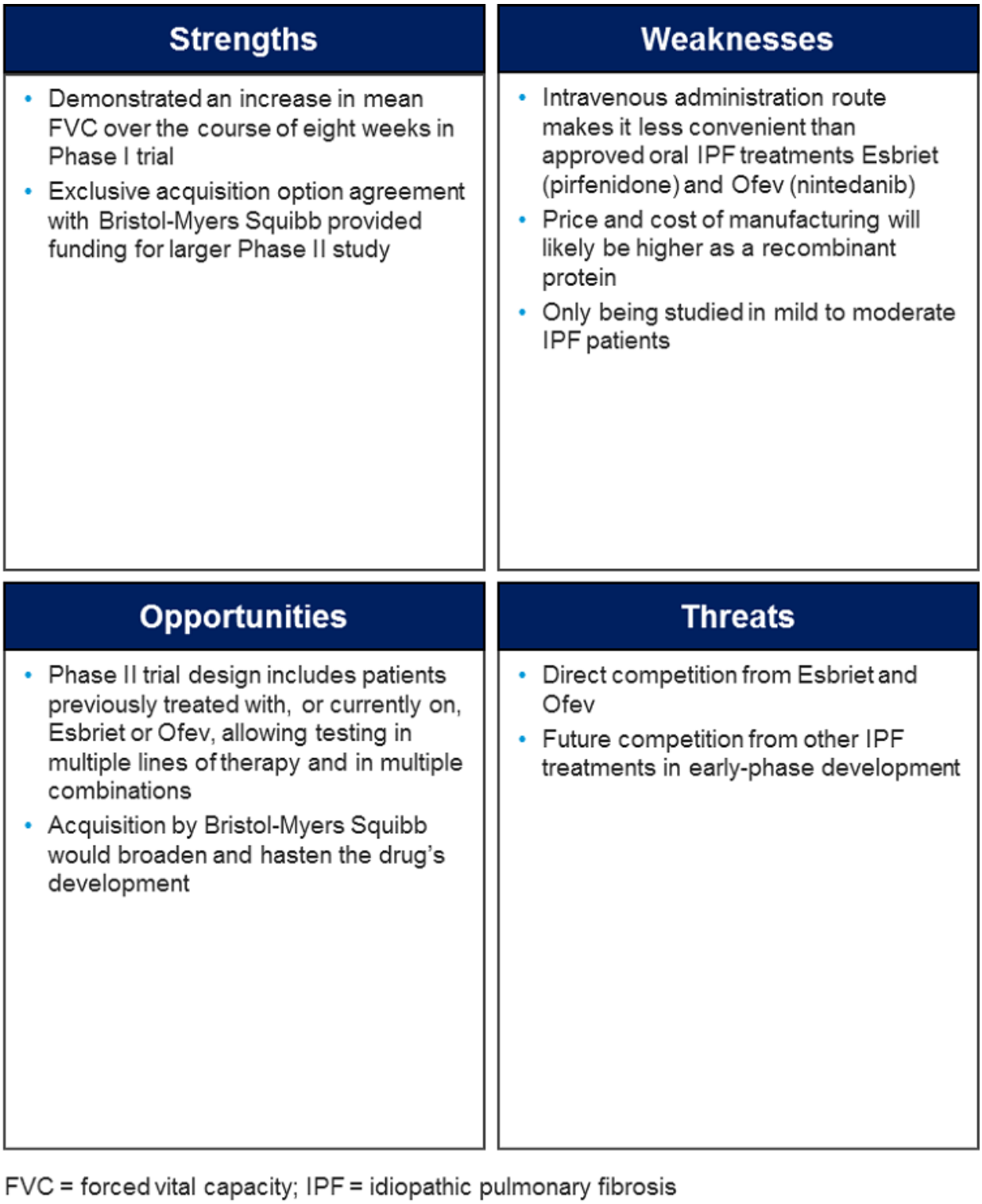
SWOT ANALYSIS

Figure 1: PRM-151 for idiopathic pulmonary fibrosis – SWOT analysis



FVC = forced vital capacity; IPF = idiopathic pulmonary fibrosis

Source: Datamonitor Healthcare; Bristol-Myers Squibb press release, 2015; Van Den Blink et al., 2013

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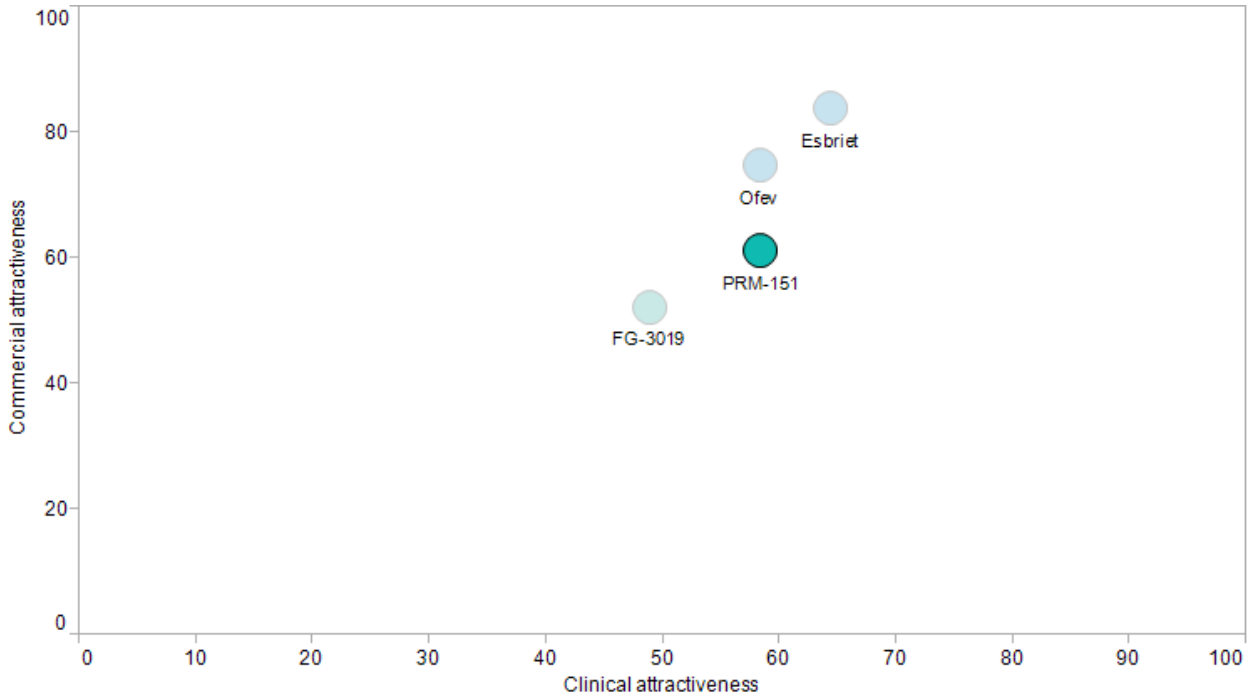
CLINICAL AND COMMERCIAL ATTRACTIVENESS

The figure below depicts Datamonitor Healthcare's drug assessment summary for PRM-151 in IPF.

Figure 2: Datamonitor Healthcare's drug assessment of PRM-151 for idiopathic pulmonary fibrosis



Source: Datamonitor Healthcare

The figure below provides a breakdown of how Datamonitor Healthcare scored PRM-151's clinical and commercial attractiveness. The weighting given to each attribute is also shown.

Figure 3: Datamonitor Healthcare's drug assessment of PRM-151 for idiopathic pulmonary fibrosis

Source: Datamonitor Healthcare

Despite mixed results, early studies show PRM-151's potential to improve FVC

Although results of PRM-151's initial Phase I trial were somewhat mixed, the drug did show the potential to improve lung function in IPF patients, and therefore warrants further testing in larger Phase II studies. The Phase I trial enrolled 20 IPF patients who were treated with one of three different doses of PRM-151 or placebo. Results showed that PRM-151 improved both FVC and six-minute walk test distance in a dose-dependent fashion. Patients receiving PRM-151 also saw marginal increases in percent-predicted forced expiratory volume in one second; however, patients receiving smaller doses saw larger improvements, decreasing confidence in this endpoint's outcome. Changes in percent-predicted diffusion capacity of the lung for carbon monoxide also varied, with two treatment cohorts performing better than placebo, and the other performing worse. Nonetheless, overall results of these lung function tests trended in favor of PRM-151, especially when data for all treatment cohorts are pooled (Promedior press release, 2013; Van Den Blink et al., 2013). Although imbalanced baseline characteristics could have skewed results, the unmet needs within IPF make these results positive enough to proceed to Phase II trials, which initiated in August 2015 (ClinicalTrials.gov identifier: NCT02550873).

The design of Phase II studies will gauge PRM-151's efficacy in multiple settings

Due to the broad enrollment criteria of its Phase II trial, PRM-151 will be tested in multiple lines of therapy and in multiple combinations, broadening the drug's potential range of clinical applications, which can then be explored further in Phase III studies. The Phase II trial will enroll treatment-naïve patients, as well as patients who have received Esbriet (pirfenidone; Roche/Shionogi) or Ofev (nintedanib; Boehringer Ingelheim) and have stopped treatment at least four weeks prior to initiating

the study. Therefore, PRM-151 will technically be tested in the first, second, and potentially third lines of therapy. Furthermore, the trial will also include patients currently being treated with Esbriet or Ofev who have been on a stable dose for at least three months without an increase in predicted FVC on two consecutive pulmonary function tests. This will test PRM-151's viability as an add-on therapy for IPF patients who are not responding particularly well to Esbriet or Ofev alone (ClinicalTrials.gov identifier: NCT02550873).

Although patients in all of these different settings will be included in the study, it remains to be seen whether Promedior will stratify patients according to all of these segmentations. Furthermore, the size of the study (current estimated enrollment of 117 patients) may not be powered to detect significant differences in such narrowly defined patient segments (ClinicalTrials.gov identifier: NCT02550873). Nonetheless, if results are positive, this broad approach will be useful in guiding the design of PRM-151's Phase III program.

Bristol-Myers Squibb may add PRM-151 to its growing portfolio of anti-fibrosis drugs

Bristol-Myers Squibb may choose to acquire Promedior in order to add PRM-151 to its growing portfolio of early-stage drugs addressing fibrotic diseases. In August 2015, the two companies reached an agreement in which Bristol-Myers Squibb paid $150m upfront in exchange for exclusive rights to acquire Promedior. This payment will help Promedior fund Phase II trials in both IPF and myelofibrosis, after which Bristol-Myers Squibb can exercise its option with an additional fee (Bristol-Myers Squibb press release, 2015). Bristol-Myers Squibb already has a similar agreement with Galecto Biotech AB in order to gain exclusive rights to its lead product TD139, an inhalable galectin-3 inhibitor in Phase I/II development for IPF (Bristol-Myers Squibb press release, 2014). Along with Bristol-Myers Squibb's own lysophosphatidic acid 1 receptor antagonist, BMS-986020, these three products may allow the company to become a key player in the future IPF market.

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