SYNDICATED ANALYTICS | PHARMADEALS

INTELLIGENCE.™



A comprehensive assessment of valuation in the pharmaceutical sector

A PharmaDeals Report edited by Heather Cartwright & Taskin Ahmed

The Royalty Rate Report 2013

A Comprehensive Assessment of Valuation in the Pharmaceutical Sector

Edited by Heather Cartwright and Taskin Ahmed



Copyright © 2013 IMS PharmaDeals Ltd

Published by PharmaDeals Ltd, now part of IMS Health 210 Pentonville Road, London N1 9JY, UK

Contents

Preface	 	 	 8	0

Introduction	9
Introduction	9

Chapter 1

Hist	tory	16
1.1	Royalties: In the Beginning	16
1.2	Mining and Petroleum	17
1.3	Royalties: Incentives and Disincentives	17
1.4	Royalties by Industry Sector	18

Chapter 2

Tho	ught L	eadership	21
2.1	Decons	tructing Deals – Benchmarks and Effe	ctive
	Royaltie	es: The Benchmarking Challenge	21
2.2	Benchm	narking Effective Royalties	22
2.3	Develop	bing a New Methodology	26
2.4	Is the B	iotech Industry Different from Mainstr	eam
	Pharma	in its Royalty Requirements?	28
2.5	Biotech	Royalty Stacks	28
	2.5.1	Technology Royalty Stacks	32
	2.5.2	Offset Clauses in Royalty Stacks	33
2.6	The 259	% Rule of Thumb:	
	If Only I	t Was That Simple!	33
	2.6.1	What is the 25% Rule?	34
2.7	Overt o	r Covert	39
	2.7.1	Thoughts on Royalty Revelation	39

Chapter 3

Ben	chmarking and eNPV	41
3.1	Methods for Calculating Royalties	41
3.2	Return of Research and Development Costs	41
3.3	Setting Royalties: The Tools	42
3.4	Benchmarking	42
3.5	Deal Benchmarking in Practice	43
3.6	Transfer Pricing: A Hidden Distortion to Royalties	50
3.7	Expected Net Present Value (eNPV)	51

3.8	The Bas	ics of eNPV and NPV Calculation	52
	3.8.1	Cash Flows	52
	3.8.2	Relevant Costs	52
	3.8.3	Real versus Nominal Figures	53
	3.8.4	Opportunity Cost/Time Value	54
3.9	Risk		55
	3.9.1	Decision Tree Analysis	56
3.10	A Furth	er Refinement of the eNPV Model:	
	Sensitiv	ity Analysis	57
3.11	Develop	oment Cash Burn	59

Chapter 4

Disclosure of Royalties: Why the Big Secret? 64 4.1 4.2 4.3 Top 15 Big Pharma Royalty Rate Disclosure 4.4 441 4.4.2 4.4.3 AstraZeneca72 444 Novartis......74 Merck & Co......76 4.4.5 Licensing Deals in Japan: Culture and Tax 78 4.6 4.7 4.8 4.8.1 Sales Milestones: A Royalty by Any Other Name 80 Combining Sales Milestones with 4.8.2 Tiered Royalties 81 4.8.3 4.8.4 4.9 How much Value Does the Royalty Component Constitute?......95 4.10 An Analysis of Rates Used in a Phase III Deal 98 4.11 Royalties in Early-Stage Technology Deals 98 4.13 Royalties to Fund Development Costs 103 4.14 Creativity: There's More Than One Way

4.16	Royalty	Rates by Phase and Indication 108
	4.16.1	Preclinical Deal Royalties 108
	4.16.2	Phase I Deal Royalties 109
	4.16.3	Phase II Deal Royalties 110
	4.16.4	Phase III Deal Royalties 111
	4.16.5	Preregistration/Registered/
		Approved Deal Royalties 112
	4.16.6	Launched Product Deal Royalties 112
4.17	Royaltie	es and Generics:
	The Beg	ginning of the End? 113
4.18	Royaltie	es and IP Valuation 115
4.19	IP Value	and Market Cap 115
4.20	Monetis	sing the Royalty Stream 116
4.21	The Util	ity Cost of Cashing In:
	Jam Too	day or More Jam Tomorrow 117
4.22	The Cu	rrent Economic Climate and
	its Effec	t on Royalty Rates 122

Chapter 5

rmaDeals Deal-Making	
Royalty Rate Survey 2013	124
Introduction to the 2013 Survey	124
Expected Minimum and Maximum Royalty Rates	125
Platform Technologies	126
Drug Delivery Technologies	127
Type of Licensee	128
Trends for Upfront and Milestone Payments	129
Healthcare Macro-environment	130
Licensor/Licensee – Who is Favoured?	131
Tiered Royalty Rates	132
Royalties and Creativity	133
Royalties and Total Deal Values	134
Summary	135
	rmaDeals Deal-Making Royalty Rate Survey 2013 Introduction to the 2013 Survey Expected Minimum and Maximum Royalty Rates

Chapter 6

Indu	ustry Po	erceptions	136
6.1	Royaltie	s: A Review of Recent Literature	136
6.2	Auditin	g the Pharma Royalty Market	139
	6.2.1	Licensing Executives Society	139

Add	dendun	n	141
A.1	Royalty 2004 –	Rate Deals Chart: March 2013	141
A.2	Drug 'X Calcula	" Utility Cost: eNPV and Discount Rate tion	158
A.3	Royalty	Monetisers: Key Deals	159
	A.3.1	DRI Capital	159
	A.3.2	Paul Capital	160
	A.3.3	Royalty Pharma	161
A.4	Great E	xpectations: The 2011 Survey	162
	A.4.1	Introduction to the 2011 Survey	162
	A.4.2	Disclosure of Royalty Rates	163
	A.4.3	Expected Minimum and Maximum	163
	ΔΔΔ		165
	A.4.5	Perceptions on Difficulties of Doing Deals	166
	A.4.6	Licensor/Licensee – Who is Favoured?	168
	A.4.7	Trends for Upfront and Milestone Payments	168
	A.4.8	Prevalence of Commercial Milestones	169
	A.4.9	Tiered Royalty Rates	170
	A.4.10	Royalties and Creativity	172
	A.4.11	Royalties and Total Deal Values	174
~			

Figures

1.1	Effective royalty calculation (scenario A)14
1.2	Adjusted royalty calculation (scenario B) 14
1.3	Royalty scenario comparison 15
2.1	Diamyd [®] model 1 scenarios
2.2	Diamyd [®] model 2 scenarios
2.3	Xiaflex [®] model scenarios25
2.4	'Biomol-x', Phase I effective royalty model 28
2.5	Biologics royalty rates from 2007 to 2012
2.6	Non-biologics royalty rates from 2007 to 2012
3.1	PharmaDeals® v4 Agreements database search engine
3.2	Pharmaceutical product decision tree
4.1	Royalty disclosure rates of licensing deals from mid-1996 to 2012
4.2	Royalty disclosure rates of royalty-bearing deals from mid-1996 to 2012
4.3	Big pharma licensing deals in the period 2008–2012
4.4	Disclosed royalty rates of deals involving top 15 pharma companies from mid-1996 to 2012 67
4.5	Pfizer's licensing activity in the period 2008–2012
4.6	GlaxoSmithKline's licensing activity in the period 2008–2012 70
47	Volibris [®] (ambrisentan) model scenarios 70
4.8	AstraZeneca's licensing activity in the period 2008–2012
4.9	Novartis' licensing activity in the period 2008–2012
4.10	Merck & Co.'s licensing activity in the period 2008–2012
4.11	Pexiganan effective royalty model (scenario A). 82
4.12	Pexiganan adjusted royalty model (scenario B). 82
4.13	Pexiganan adjusted royalty without sales milestones model (scenario B)
4.14	Promacta® (eltrombopag) sales forecasts for the period 2008–2017
4.15	Promacta [®] (eltrombopag) royalties forecast by tier for the period 2008–2017
4.16	'Steptrin' sales forecast
4.17	'Steptrin' flat royalties
4.18	'Steptrin' escalating royalties

4.19	'Steptrin' reducing royalties
4.20	'Steptrin' cumulative royalties
4.21	Percentage of licensing deals declaring royalty tiers 2008–2012
4.22	'Biomol-y' effective royalty model (scenario A)
4.23	'Biomol-y' adjusted royalty model (scenario B)
4.24	Comparison of cash flow at sales of US\$1.5 B 102
4.25	Comparison of cash flow at sales of US\$0.5 B 103
4.26	Upfront value trends in licensing deals 105
4.27	Milestone value trends in licensing deals 105
4.28	Royalty value trends in licensing deals 106
4.29	Upfront payments and milestones as a
	percentage of total payments in licensing deals 107
4.30	Deal A vs. Deal B, apparent values
1 7 1	of upfront payments and milestones
4.31	payments and milestones
4.32	Preclinical royalty rates by therapy area for the period 2007–2012 109
4.33	Phase I royalty rates by therapy area for the period 2007–2012 110
4.34	Phase II royalty rates by therapy area for the period 2007–2012 110
4.35	Phase III royalty rates by therapy area for the period 2007–2012 111
4.36	Preregistration/Registered/Approved royalty rates by therapy area
	for the period 2007–2012 112
4.37	Launched product royalty rates by therapy area for the period 2007–2012 113
4.38	Expected licensor's eNPV share by phase 117
4.39	Licensing deal numbers and mean upfront values
5.1	Mean expected minimum and maximum royalty rates by development phase
5.2	Licences for 'disruptive' platform technologies have a royalty range of' (mean values) 126
5.3	In your view, how do royalty rates for drug delivery technologies today compare with 5 years ago?
5.4	'In your experience, does the royalty rate agreed depend upon the type of licensee?' 128

5.5	'Over the past 5 years, I believe that upfront payments have'
5.6	'Big pharma is keen to keep royalty rates down even at the expense of higher milestones' 129
5.7	Concern around healthcare costs and future price limitations is pushing royalty rates down? 130
5.8	'In my view the current market for deals favours'
5.9	'How do you expect tiered royalties to change with increasing sales?'
5.10	'What term best describes your company's attitude to tiered royalties?'
5.11	'Have you seen any examples of creativity in royalty structures?'
5.12	'Would you consider using alternative deal structures to royalties?'
5.13	Perceived contribution of royalties to total deal value (mean values)
A.1	'What type of deal were you involved in over the last 5 years?'
A.2	'We prefer royalty rates in our deals to be made public'
A.3	Mean expected minimum and maximum royalty rates by development phase (all respondents)
A.4	Mode of expected minimum and maximum royalty rates by development phase (all respondents)
A.5	Mode of expected minimum and maximum royalty rates by development phase (Pharma respondents)
A.6	Mode of expected minimum and maximum royalty rates by development phase (Biotech respondents) 165
A.7	'Royalty rates agreed depend on the type of licensee'
A.8	'Over the past 5 years doing deals has' (All respondents) 167
A.9	'Over the past 5 years doing deals has' (Biotech respondents)
A.10	'In my view the current market for deals favours' (All respondents)
A.11	'In my view the current market for deals favours'
A.12	'Over the past 5 years, I believe that upfront payments have'
A.13	'Big pharma is keen to keep royalty rates down even at the expense of higher milestones' 169
A.14	'How prevalent are deals involving commercial milestones compared with 5 years ago?' 170

A.15	'How prevalent are deals involving tiered royalties compared with 5 years ago?'
A.16	'How do you expect tiered royalties to change with increasing sales?'
A.17	'What term best describes your company's attitude to tiered royalties?'
A.18	'Have you seen examples of creativity in royalty structures?'
A.19	'Would you consider using alternative deal structures to royalties?'
A.20	Perceived contribution of royalties to total deal value (modal values)
A.21	Perceived contribution of royalties to total deal value (mean values)
A.22	Respondents by job function 175

Tables

1.1	Distribution of royalty rates by industry 1	19
2.1	Biologics royalty rates from 2007 to 2012	30 32
2.2	Encerve royary range by development phase.	2
3.1	Benchmarking sources	17
3.2	Websites useful as sources of royalty data 2	17
3.3	Benchmarking our deal	18
3.4	Refining our benchmarks	19
3.5	Probability of success by phase of development	56
3.6	Variables in development costs: impact on royalties	59
3.7	Example of a basic eNPV calculation for our 'demodrug'6	51
3.8	Licensor share for our 'demodrug' as royalties . 6	52
3.9	Licensor share for our 'demodrug' as upfront payments, milestones and royalties	52
4.1	Statistical analysis of disclosed royalty rates from deals involving top 15 pharma companies	ו 58
4.2	Promacta [®] (eltrombopag) royalty tier contributions forecast for 2017	37
4.3	'Steptrin' escalating royalty tiers	39
4.4	'Steptrin' reducing royalty tiers	90
4.5	Participation rates by development stage	99
4.6	Original licence and sublicence deal terms 10	01
4.7	NPV of Deals A and B 10)8
4.8	Utility cost and share of eNPV for drug 'X' 11	18
4.9	Utility cost and share of eNPV for drug 'X' at a lower sales forecast	19
4.10	Risk factors for late-stage and in-market drugs12	20
A.1	Chart detailing the financial details of deals recorded in the PharmaDeals® v4 Agreements from 2004 to March 2013143–15	57
A.2	Drug 'X' utility cost calculation 15	58
A.3	DRI Capital's biopharma royalty interests 15	59

A.4 Paul Capital's biopharma royalty interests 160

OK, so Pfizer's Lipitor[®] (as atorvastatin is better known) was a special case, but many of today's deals are for Phase II drugs for which a minimum 5% royalty rate is not uncommon – in fact, many rates are in the double-digit range, as you will discover in this report. The hope is that many of these drugs will achieve blockbuster status. At US\$1 B a year in sales, that 5% is worth US\$50 M for every year that the US\$1 B sales level is maintained: not an upfront payment, not a milestone, but a year-on-year stream. Deals are definitely big business, and royalties are definitely a big deal! For late development phase candidates, licensing deal royalties can typically comprise 50-80% of the expected Net Present Value (NPV) of the deal from the licensor's perspective: the highest value – but often the lowest visibility profile – in deal-making public relations.

Overview of the Report

The Royalty Rate Report 2013: A Comprehensive Assessment of Valuation in the Pharmaceutical Sector covers new ground in the analysis and interpretation of royalty information. It introduces methods for calculating useful financial data that are missing from the public domain, but are essential for dealmakers in benchmarking, and in determining deal value and its relationship with eventual royalty streams.

Chapter 1 deals with the history of royalties, its relevance to the biotech/pharma arena and the psychology of royalty structures.

In Chapter 2, topics of thought leadership are covered. These include the concept of 'effective royalties' as an aid in the analysis of deal structures, royalty issues in biotechnology, a critique of the oft-quoted 25% rule of thumb and its relevance – or lack of relevance – in pharmaceutical deals, and key opinion leader thoughts on the public disclosure of royalty rates.

Chapter 3 covers the practical aspects of royalty calculation, with a focus on benchmarking and expected Net Present Value (eNPV) skills.² These tools will give dealmakers a complete understanding of the value intrinsic to their products, and of the relationship between royalties and other deal components.

Market data and current trends are covered in Chapter 4, which looks at actual royalty rates by indication, product type and phase of development. The emerging area of royalty monetisation is covered in detail, along with an analysis of the utility cost of that process.

² Expected Net Present Value (eNPV) is widely used in capital budgeting and investment decision making. It means the current worth of future cash flows as discounted backwards with an industrystandard rate of return (or cost of capital), adjusted for the risks that the project faces.

Chapter 5 presents the results of PharmaDeals' Deal-Making and Royalty Rate Survey 2013, which provide insight into the attitudes and expectations of dealmakers with regard to royalties and deal structuring.

Chapter 6 looks at current thinking on royalty rates and includes a review of recent literature on royalties.

The comprehensive Addendum includes the results of a survey of industry executives conducted by PharmaDeals in 2011 in order to uncover information on royalty rates from active dealmakers and a listing of royalty reporting deals between 2004 and March 2013.

And throughout the report, you will find case histories, deal analysis and opinion leader comment, all relating to the quest for better and more usable royalty data.

Effective Royalties

Throughout this report, we will be using the concept of 'effective royalties' to analyse and explain various deal scenarios. Royalties are often viewed in isolation from other factors related to intellectual property (IP) licensing. Too much time (and too much energy) is spent searching for meaning within what little royalty evidence exists in the public domain. The truth is more complex than the superficiality of royalty values alone. Without insight into the value of other deal components, such as upfront payments or milestone payments, two seemingly similar royalty percentages may be seen as indicative of a trend or average when, in reality, they are components of deals which might have vastly dissimilar values and structures aside from this one coincidental component.

'Effective royalty' is a value concept that allows all those other deal components to be factored into a valuation, which is then expressed as a single component: a royalty. The effective royalty rate answers the question: if there were no other structural components included in this deal, what would the royalty be? In other words, what is the size of the royalty if all the value due to the licensor were incorporated into it? For dealmakers, this can be very valuable, as it allows benchmarking and comparison without the confusion caused by the complexity of reported deal structures.

Effective royalty becomes a theoretical starting point for the value return to an IP licensor, as a function of (future) sales. If all deals were based on marketed products with flat sales, and all licensors sought a regularised cash flow from their licensees' sales revenues, with no upfront lump sum licence fee, then royalty data alone would be comparable. Furthermore, if expressed as a percentage of sales, royalty data would reflect the true share of value. Knowledge of that profit margin would allow estimation of the share of value between the licensor, via royalty (thus answering the oft-posed question – 'As licensor what can I expect to get?'), and the licensee, via margin minus that royalty (so answering the licensee's equivalent question – 'After paying appropriate royalties, what benefit will the deal bring to my business?').

Deals are rarely as straightforward as that, however. More likely there will be complications with regard to product status. In the years pre-launch: at which clinical development stage is the product? And in the commercial years post-launch: at which stage is the product in the life cycle? Then there will be lump sum deal components (upfront payments, development milestone payments, equity investments, sales milestones), all of which will attempt to confound the derivation of value and the share of it between the parties. The estimation of value is, therefore, a key element in understanding effective royalty and, thereafter, actual royalty rates. In our experience, value in the biotech/pharmaceutical field is best derived by a discounted cash flow methodology (what is tomorrow's money worth today?) incorporating decision tree analysis (what are the chances or risks of reaching specific points of progress on the road to that future flow of tomorrow's money?). When project or product financial data are forecast, then expressed as today's value (NPV), we can consolidate all these data into one single figure, the eNPV. This subject is covered in greater detail in Chapter 3.

Value Calculation

Familiarity with eNPV calculation and utility will be of major advantage in maximising the use of this report, and in extrapolating the lessons learned into future deal analysis.

By combining our 'effective royalty' and 'eNPV' approaches, we can simplify complex deal structures, and we can assess the impact of those lump sum payments (one-off value payments, such as milestones) on the royalty rate (the regularised or repeat-value payments).

The Visualisation of Deals

Here, we will show three types of deal structures diagrammatically.

Our first diagram (*Figure 1.1*) visualises the outputs from eNPV/effective royalty calculations.

Project Name Topcure	
Input	Output
Entering Phase II	Total eNPV of Project US\$M 188 - 306
Peak Year Sales US\$M 400 – 600	Licensor : Licensee Ratio 1: 3.50
	Effective Royalty 12.3 – 13.4%
	eNPV to Licensor US\$M 42 - 68
Here we show the range o royalties that generate our estimate of the licensee's s of the eNPV.	f Based on our modelled hare assumptions, this represents the typical range of eNPVs for the licensor.

Figure 1.1 – Effective royalty calculation (scenario A).

Figure 1.2 shows an alternative structure for deals where upfront and milestone payments exist, and demonstrates their impact on royalties, thus producing an 'adjusted' royalty.

Project Name To	pcure				
Input		Output			
Entering Phase	Phase II	Total eNPV of Project	US\$M	188 – 306	
Peak Year Sales US\$M	400 - 600	Licensor : Licensee Ratio	1:	3.50	
		Adjusted Royalty		8.9 - 11.1%	
		eNPV to Licensor	US\$M	42 – 68	
		Total Upfront + Milestones (und	iscounted) US\$M	29	
The adjusted	d rovaltv rang	e takes			
into accoun	t any upfront	and The u	pfront and m	nilestone paym	ients
milestone pa reduce the r	ayments that rovalty stream	will are sl exact	hown here at ly as they wo	their face valu uld appear in	Ie,
	cyarty stream	the d calcu adjus	eal announce lation will disc t this 'total'.	ement. The eN count and risk	PV



Introduction

Figure 1.3 provides a third visual summary for a more complex analysis that uses many more specific variables (which are either taken from available data, or modelled/estimated). The diagram depicts the same two scenarios of effective royalty (scenario A) and adjusted royalty (scenario B).

Project Name Supercure



When viewing these summaries, it should be remembered at all times that the use of eNPV calculations including decision tree analysis is a valuable comparative method, but does not relate to a future reality, only to our present estimate of value. An analogy might be to value two different sized piles of lottery tickets before the draw, either based on the totals of their face value, or, more accurately, based on total payout divided by ticket numbers; the future reality after the draw will change those values significantly – most will be worthless, while some will have far greater value than their initial price. However, before the draw, the value assessment is based on the best possible available information.

Chapter 2 Thought Leadership

2.1

Deconstructing Deals – Benchmarking and Effective Royalties: The Benchmarking Challenge

The process of seeking out specific information from deals that are substantially similar to your own in order to uncover the typical royalty rates enjoyed by similar deal parties is known as benchmarking. The closer deals are to your own in the nature of the product, the market involved, the territory covered and the stage of drug development, the more useful will be the comparison. The PharmaDeals® v4 Agreements database contains more than 49,000 deals recorded in the biotech and pharmaceutical industry since 1996, and is the definitive, most comprehensive source of financial information for current deals. Sadly though, less than 1% of the deals in the database have disclosed royalty rates. Currently, that is just over 400, compared with 2350+ deals with specific upfront payment values disclosed and 1800+ with total milestone payments revealed. The chance of finding good royalty benchmarks is exceedingly slim. With at least four development-phase options, eight therapy areas, ten product types and three geographic combinations, we get 960 possibilities; add in three time periods (pre-2001, 2001-06, 2007 onwards) to derive a timeliness or trend relevance, and that escalates to over 2800 possibilities! Finding a selection of good matches from 400 complex royalty-revealing deals that's not just a slim chance, it's a catwalk-wiggling double zero of a chance!

What may be of greater utility as a benchmarking approach would be to benchmark against prospective partners' activity. Knowledge of the deal-making history of prospective partners may help to reveal preferred deal structures, and possibly even to narrow down the wide industry ranges seen at the macro level.

As we show in this report, a more analytical approach might be to use the power of eNPV calculations to derive effective royalty rates. The 99% of deals in the database that do not have specific royalty rates reported are a much better source for a benchmark than the 1% that do. Many of these will have current and archived analysts' sales forecasts available, and these will help us to generate 'effective' royalty rates.

Thought Leadership

Case History

TriLink's RNAi Chemistries

On 10 September 2007, CytRx's majorityowned subsidiary, RXi Pharmaceuticals, entered into an agreement with privately held TriLink Biotechnologies to license exclusively three RNA interference (RNAi) chemistry technologies for all therapeutic RNAi applications (Deal no. 28271). The agreement includes rights to sublicense a patented RNA linker technology, a patent application on novel RNAi compositions, and a novel, undisclosed chemistry approach that has potential applications in improving existing RNAi compounds. Terms of the licence agreement include upfront and yearly minimum licensing payments, royalties of 1% or less from RXi to TriLink on sales of therapeutic products developed from technologies included in the licence agreement, and payments based on the achievement of certain clinical milestones.

2.5.2 Offset Clauses in Royalty Stacks

As we have highlighted, in the modern biotech/pharma industry there is a concern about the impact of the cumulative burden that royalties might impose. The final licensee therefore generally tries to include clauses to limit royalty stacking, or at least to limit its impact. This is often achieved through the use of royalty offset clauses. Such clauses allow the licensee to reduce the amount of royalty it will pay to one licensor, if it is also required to pay royalties to another licensor. Of course, licensors will not accept the loss of all their future royalty, so such clauses usually have a licensor-negotiated floor below which the royalty cannot fall. Also, the right to offset other royalty payments may be limited to other patents of a similar type.

For example, a company may be required to pay a royalty of 3% for access to a drug target patent. However, it may be allowed to offset some of that 3% if it also finds that it has to pay royalties to a third party for a similar technology: for instance, if it is discovered that the drug affects another patented biological pathway. The floor may be 1.5%, so if a 1% royalty is paid to the third party, the licensee would still pay a 2% royalty to the first licensor. If, however, it was compelled to pay 1.75% to the third party, it would still have to pay 1.5% to the first licensor, making a total of 3.25% -still better from its viewpoint than 1.75%+ 3% = 4.75%. Additional terms might clarify that a requirement to pay royalties on patents covering production processes or delivery technologies would not be deductible from those due on the target.

2.6 The 25% Rule of Thumb: If Only It Was That Simple!

We have already referred to the fact that the 25% rule is cited by some as 'a useful starting point' in negotiating or calculating royalties. In deals in which upfront and milestone payments are present, we should consider the rule in relation to 'effective royalties' first, before calculating an actual royalty that would need to take into account the value of those lump sum payments. With that single royalty figure, we can then see if the rule of thumb has any approximation in pharmaceutical deal making.

Despite our inherent suspicion of business folklore measures with regard to their 'normative' usefulness, the 25% rule does have some redeeming features, and it also has legal endorsement, which makes it a valid distillation of some commonsense issues, at least in the general business environment. But can it apply to the complex risk-hurdled environment of pharmaceutical development? In our opinion it cannot, and an approach to simplify the royalty calculation in this way will create a bad deal for one or both parties.

Chapter 3 Benchmarking and eNPV

In this chapter, we focus on the two most commonly used valuation methodologies in the pharmaceutical and biotechnology industry. Royalties are a component or expression of value that should not be viewed in isolation from other valuebearing components. It follows, then, that calculations to derive possible royalty rates should first employ methodologies that calculate total value, thereafter apportioning that value to deal components such as upfront payments, milestones and royalties.

3.1 Methods for Calculating Royalties

A variety of methods are available that claim to provide valuations or royalty rates for products and/or technologies that include suitable deal terms. These methods range from arbitrary or traditional rules of thumb (such as the fatalistic, and, in the context of pharmaceuticals, wholly inappropriate 25% rule), through more rigorous analyses that can illuminate the value creation process, to somewhat esoteric methods, such as the Black–Scholes model,¹⁴ which have little (if any) practical utility. Our focus here is on those methods that we believe relevant and proven in the pharmaceutical industry.

'Most of our negotiation around royalties and milestones is based on benchmarking, with eNPV used more to compare a couple of deals that are on the table.'

Business Analyst, Biotech, UK¹⁵

¹⁴ For more on Black-Scholes, visit – http://en.wikipedia.org/ wiki/Black_Scholes

¹⁵ Personal communication.

3.2 Return of Research and Development Costs

Despite the general acceptance that R&D costs are, once incurred, sunk costs, and therefore have no influence on any eNPV calculation and no role to play in calculating royalties, R&D costs do have an influence on royalties for pipeline products for which much of the R&D spend has yet to be incurred.

First, they influence the split between upfront and milestone payments, as each of these deal components removes a discrete chunk of cash from the eNPV calculation, thereby leaving less to be accounted for in the eventual royalty stream. Although development cost averages are widely proclaimed within the industry, there are very different costs associated with different therapy areas and drug types. Generally, a

Case History

GlaxoSmithKline and Myogen

On 6 March 2006, **GlaxoSmithKline** (GSK) and **Myogen** entered into a two-part collaboration in pulmonary arterial hypertension (PAH) (Deal no. 23627). Myogen licensed the commercialisation rights for ambrisentan, its selective endothelin receptor antagonist (ERA), then in Phase III development, to GSK in all territories outside the US.

Under the terms of the ambrisentan licence agreement, Myogen received an upfront payment of US\$20 M and, subject to the achievement of specific milestones, was eligible to receive up to an additional US\$80 M in milestone payments. In addition, Myogen would receive stepped royalties on product sales, with an estimated average royalty in the mid-20% range. GSK was to take responsibility for all regulatory and commercial expenses in its licensed territories. The companies were to share the costs of certain additional clinical development activities for ambrisentan.

On 10 April 2006, following positive results in the second Phase III trial evaluating ambrisentan, Myogen received a US\$5.25 M milestone payment from GSK.

Case History

'Participation' in the GSK/ Tolerx Deal

As a result of the licence agreement between Tolerx and GlaxoSmithKline in October 2007 (Deal no. 28750), BTG, from which Tolerx licensed otelixizumab (as TRX4) in 2001 (Deal no. 29052), received a payment of US\$10 M, being the relevant share of the initial US\$70 M received by Tolerx. Furthermore. BTG is entitled under the terms of its licence agreement with Tolerx to receive 50% of any future milestone payments received by Tolerx in respect of the successful development, approval and commercialisation of TRX4 in all indications. BTG also has rights to receive royalties on product sales.

The royalty participation cascade runs further back still, as BTG will share around half of any amounts received with the original sources of the licensed patents. GSK signed three deals during 2008 with some useful disclosed financial information. One deal was the February 2008 licensing agreement with **EUSA Pharma** (a **Vaccinex** collaboration partner) for OP-R003, a human anti-interleukin-6 antibody discovered by Vaccinex (Deal no. 29696). The deal involved a consideration of up to US\$44 M and required GSK to pay an upfront licence fee, development milestones and royalties on product sales. Vaccinex was to share 50% of the fees.

The second deal was with **Valeant Pharmaceuticals International** in August 2008 under which the two companies formed an exclusive worldwide collaboration for retigabine (Deal no. 31115), a first-in-class neuronal potassium channel opener that had completed two Phase III trials for treatment of adult epilepsy patients with refractory partial onset seizures. Valeant received an upfront payment of US\$125 M and was eligible to receive up to US\$545 M based on the achievement of certain regulatory, development and commercialisation milestones and the development of additional indications for retigabine. Valeant was to co-commercialise with GSK and share up to 50% of net profits within the US, Canada, Australia, New Zealand and Puerto Rico, and would receive up to a 20% royalty on net sales of retigabine outside of these regions.

The third deal was with **Ligand Pharmaceuticals** in December 2008, under which GSK licensed worldwide exclusive rights to Ligand's LGD-4665 product candidate and its other thrombopoietin (TPO)-related molecules (Deal no. 31946). LGD-4665 was in Phase II for the treatment of thrombocytopaenia. Under the terms of the agreement, GSK would pay Ligand US\$5 M as an upfront licence fee, up to US\$158 M in development and commercial milestones and a 16% royalty on net sales. In the first year of sales, royalties would be one-half of the regular royalty rate, in recognition no doubt of the additional marketing costs associated with product launch.

Case Histories

Regeneron Pharmaceuticals' Identical Deal Terms in Two Technology Deals Involving Royalties

Licence Agreement with AstraZeneca UK

'In February 2007, we [**Regeneron Pharmaceuticals**] entered into a non-exclusive license agreement with **AstraZeneca UK Limited** that allows AstraZeneca to utilize our VelocImmune[®] technology in its internal research programs to discover human monoclonal antibodies (Deal no. 26482). Under the terms of the agreement, AstraZeneca made a \$20.0 million non-refundable, up-front payment to us. AstraZeneca is required to make up to five additional annual payments of \$20.0 million, subject to its ability to terminate the agreement after making the first three additional payments or earlier if the technology does not meet minimum performance criteria. We are entitled to receive a mid-single-digit royalty on any future sales of antibody products discovered by AstraZeneca using our VelocImmune technology.'

Licence Agreement with Astellas Pharma

'In March 2007, we [**Regeneron Pharmaceuticals**] entered into a non-exclusive license agreement with **Astellas Pharma Inc.** that allows Astellas to utilize our VelocImmune technology in its internal research programs to discover human monoclonal antibodies (Deal no. 26894). Under the terms of the agreement, Astellas made a \$20.0 million non-refundable, up-front payment to us. Astellas is required to make up to five additional annual payments of \$20.0 million, subject to its ability to terminate the agreement after making the first three additional payments or earlier if the technology does not meet minimum performance criteria. We are entitled to receive a mid-single-digit royalty on any future sales of antibody products discovered by Astellas using our VelocImmune technology.'

Source: Regeneron Pharmaceuticals, 10-K SEC filing, 27 February 2008.

4.8 Royalties and Deal Structures

How much of a deal value resides in royalties compared with other deal components? What drives the decision to bias the split of value?

Despite the solid appearance of bar chart averages, there is no one right answer to deal structures, as witnessed by the noise, or range, within deal databases. The decision as to how much should go where is a function of dealmakers' needs and the compromise agreed through each party's understanding of the other's requirements.

4.8.1

Sales Milestones: A Royalty by Any Other Name

It is not uncommon to see deal structures that include sales milestone payments. Although these may be included in deal announcements as part or all of milestone payment components, they can be considered as royalty lump sums, as they are directly linked to sales volumes. The July 2007 deal between **Genaera** and **MacroChem** is an example of such a deal structure (see *Case History*).

Chapter 5 PharmaDeals Deal-Making and Royalty Rate Survey 2013

5.1 Introduction to the 2013 Survey

During the first quarter of 2013 PharmaDeals undertook an online survey in preparation for The Royalty Rate Report 2013 in order to understand the attitudes and expectations of dealmakers with regard to deal terms and to royalty rates in particular.

This section sets out the results of this recent survey and compares the data with a similar survey conducted by PharmaDeals in 2011 (see Addendum, section A.4) to identify any shifting trends. More than 30 respondents completed the survey, approximately 70% of which were from biotech or pharmaceutical companies, with the remainder spread across a variety of related areas such as academia and venture capital.

We were keen to uncover up-to-date information on royalty rates from active dealmakers, and over 60% of the respondents confirmed their involvement in deal making within the past 5 years, with half of these having experience as both a licensor and a licensee. These active dealmakers were predominantly business development or licensing professionals, with the remainder having senior management roles. Those respondents that had been inactive in deal making over the period were filtered out to allow a focus on current dealmakers.

Chapter 6 Industry Perceptions

We have developed our opinions and understanding of royalties from experience and analysis. Little practical information exists in the public domain. Publications are few and far between, and, in our view, often reflect the desire for data rather than interpretation. In this section, we look at some industry papers and surveys to see what others have said or done in the field of biotech/pharmaceutical (biopharma) royalties.

6.1 Royalties: A Review of Recent Literature

There follows a review of recent publications relating to royalties in the biopharma licensing area.

Year:	2012
Title:	How to Determine Fair License Terms: No Need for Rules of Thumb Anymore
Resource:	Les Nouvelles, September 2012
Author(s)/Editor(s):	Ralph Villiger
Publisher:	Licensing Executive Society International

Relevant information

This paper supports our view that the 25% rule is an inappropriate method for calculating pharmaceutical royalty rates and describes a virtual company model for the design of licensing deal terms that attributes value to a project at each value inflection point. This model assumes that the licensor sets up a virtual company and puts a project into that company as its own asset. The goal is then to sell this company to the licensee at a fair price.

Addendum

structure: is it an up tier, or is it a down tier? It starts at 15% for 20 months, falls to 5% thereafter, but climbs back to 15% based on sales levels. The deal is reported as a 15% royalty, but the reality is more complex. On the one hand, the analyst entering the data will interpret 'mid-double digit' as meaning 15%, which may or may not be what the dealmakers understand by the phrase, as double digit can mean a whole lot more (or less);³⁶ on the other hand, 'mid-teens' is a safer bet to be entered as 15%. Be immediately suspicious of '15%' and '50%'; further research is advised – does the original reference refer to 'double digit', does it refer to profit rather than sales?

The chart presented here (*Table A.1*) is best used to source deal parties for further research and analysis into the significance of the numbers concerned. Company websites, SEC filings and search engines may bring greater insight into the values and deal structures outlined. Finally, remember the effective royalty calculation methodology. With the agreements listed here, a great deal more information is available compared with the norm, including that 'adjusted' royalty rate, so it should be possible to model the effective rates within more accurate limits.

Good luck!

 ³⁶ dou·ble-dig·it adj., Being between 10 and 99 percent: The American Heritage[®] Dictionary of the English Language, Fourth Edition, ©2000 (updated 2003); Houghton Mifflin Company.

D3D Description Optimization Description Descrip <thdescription< th=""> <thdescri< th=""><th>e deal ounced</th><th>Principal company</th><th>Partnering company</th><th>Deal type</th><th>Deal indications</th><th>Total (potential) deal value (US\$ M)</th><th>Upfront payment (US\$ M)</th><th>Equity investment (US\$ M)</th><th>Total I Milestones (US\$ M)</th><th>Royalties value (%)</th><th>Product brand name</th><th>Product generic name (or synonym)</th><th>Product development status</th></thdescri<></thdescription<>	e deal ounced	Principal company	Partnering company	Deal type	Deal indications	Total (potential) deal value (US\$ M)	Upfront payment (US\$ M)	Equity investment (US\$ M)	Total I Milestones (US\$ M)	Royalties value (%)	Product brand name	Product generic name (or synonym)	Product development status
0001 Understanding Destination of the function of the	2/2004	Nuvelo Inc.	Dendreon Corp.	Rights; Licensing	Neoplasms		4.00			10			
2010 Biothermatic methodenession Biothermatic meth	2/2004	Longport Inc.	US Medical Systems, Inc.	Distribution/Marketing		1.02				5			
30.1 Understands Grout Boarden(U) Bard Boarden(U	2/2004	Elan Corporation plc	Valeant Pharmaceuticals International	Rights; Licensing	Diseases of the nervous system	10.00				12.5	Zelapar®, Permax®	Zydis [®] selegiline; pergolide	Launched
301 Tutu	2/2004	DOV Pharmaceutical Inc.	Neurocrine Biosciences Inc.; Wyeth	Licensing	Diseases of the nervous system					2		indiplon; ocinaplon; bicifadine	Phase 2; Phase 3
3000 Browner for which and an element of the second method method of the second method method of the second method of the second method method of the second method me	13/2004	GTx Inc.	Johnson & Johnson Pharmaceutical Research & Development LLC, Ortho Biotech Products L.P.	Co-promotion, Marketing; Collaborative R&D Licensing	Diseases of the nervous system; Symptoms, signs and abnormal clinical and laboratory findings, nor elsewhere classified; Diseases of the genitourinary system; Diseases of the musculoskeletal system and connective tissue		6.00			20		andarine	Phase 1
4000KomenterionioMonteriorio <td>3/2004</td> <td>Skinvisible Pharmaceuticals Inc.</td> <td>Dermal Defense Inc.; JD Nelson & Associates</td> <td>Distribution/Marketing; Rights; Licensing</td> <td>Certain infectious and parasitic diseases; Diseases of the skin and subcutaneous tissue</td> <td>1.00</td> <td>0.25</td> <td></td> <td></td> <td>5</td> <td></td> <td></td> <td></td>	3/2004	Skinvisible Pharmaceuticals Inc.	Dermal Defense Inc.; JD Nelson & Associates	Distribution/Marketing; Rights; Licensing	Certain infectious and parasitic diseases; Diseases of the skin and subcutaneous tissue	1.00	0.25			5			
4700 Stehande, Beduchander, Bezeichte nervousstem: 710 Politypier, Stepander, Stepander, </td <td>4/2004</td> <td>Xechem International Inc.</td> <td>Alembic Ltd</td> <td>Manufacture/Supply: Distribution/ Marketing: Rights; Licensing; Equity Investment</td> <td>Diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism</td> <td>3.64</td> <td>0.64</td> <td>0.64</td> <td></td> <td>30</td> <td>Nicosan[™], Hemoxin[™], Niprisan[®]</td> <td>Nix 0699</td> <td>Phase 3</td>	4/2004	Xechem International Inc.	Alembic Ltd	Manufacture/Supply: Distribution/ Marketing: Rights; Licensing; Equity Investment	Diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism	3.64	0.64	0.64		30	Nicosan [™] , Hemoxin [™] , Niprisan [®]	Nix 0699	Phase 3
47001 Biolewy Sciences Genetic and character of paces 7 Pionearia Pionearia 47001 Renatorial directions Genetic and practic of paces Pionearia Pionearia Pionearia Pionearia Pionearia 47001 Names Medica Medica Relativity concertencia Pionearia	4/2004	SkyePharma plc	Medeus Pharma Ltd	Distribution/Marketing	Diseases of the nervous system; Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified	121.30				50	DepoMorphine [®]	sustained-release injectable morphine	Registration pending
47:004Intermediation, decident workerstand, departmentation, AssetReplanse soft the gentourinary1.800.301.502.66No 1.50No 1.50 <td>4/2004</td> <td>BioDelivery Sciences International Inc.</td> <td>Accentia Inc.</td> <td>Royalty monetisation; Asset acquisition; Rights; Licensing</td> <td>Diseases of the respiratory system; Certain infectious and parasitic diseases</td> <td></td> <td></td> <td></td> <td></td> <td>7</td> <td>BioNasal[™] encochleated amphotericin B</td> <td>topical encochleated amphotericin B</td> <td>DNI</td>	4/2004	BioDelivery Sciences International Inc.	Accentia Inc.	Royalty monetisation; Asset acquisition; Rights; Licensing	Diseases of the respiratory system; Certain infectious and parasitic diseases					7	BioNasal [™] encochleated amphotericin B	topical encochleated amphotericin B	DNI
4/2004Stepharma pic fisherIndexterisionBisaese of the skin and subcutaneous fisher20.0010105/2004Stepharma pic (coponationInst Horizon Pharmaceutial Marketing, Rights diseasesMandacue/Supply, Distribution diseasesDiseases of the circulatory system; diseases55.0050.00251010105/2004ATJ Gupdino TuxtOther see detailsDiseases of the circulatory system; diseases55.0050.0012710	4/2004	Inverness Medical Switzerland GmbH	Antisoma plc	Royalty monetisation; Asset acquisition; Rights	Neoplasms; Diseases of the genitourinary system	1.80	0.30		1.50	2.66		R 1549; Monoclonal antibody HMFG1(R 1550)	Phase 1; Phase 3
5/2004SkePharma plc for for the first Horizon Phamaceutical CorporationMandacture/Skephy: Diseases of the circulatory system; diseases5.005.0020101010105/2004ATS Liquidating Tustken Tissue Therapeutics Inc.Other see detailsDiseases of the circulatory system; diseases0.00100.0 <td>4/2004</td> <td>SkyePharma plc</td> <td>Trigenesis Therapeutics Inc.</td> <td>Rights; Licensing</td> <td>Diseases of the skin and subcutaneous tissue</td> <td>20.00</td> <td></td> <td></td> <td></td> <td>10</td> <td></td> <td></td> <td></td>	4/2004	SkyePharma plc	Trigenesis Therapeutics Inc.	Rights; Licensing	Diseases of the skin and subcutaneous tissue	20.00				10			
5/20d. ATS Liquidating Tinst len Tissue Therapeutics Inc. Other: see details Diseases of the circulatory system; 0.20 1.20 3 Anginera [®] 6/20d. XIL Cubist Pharmaceuticals Inc. Licensing: Clinical and commercial Diseases of the digestive system; 6.00 3.00 17 HepeX-B [®] 6/20d. Ethicon Endo-Surgery Immed Comportion Diseases of the digestive system; 6.00 3.00 17 HepeX-B [®] 6/20d. Ethicon Endo-Surgery Immed Corporation Licensing Diseases 17.25 17.25 7.5 6/20d. Ethicon Endo-Surgery Immed Corporation Licensing Diseases of the digestive system; 17.25 17.25 7.5	5/2004	SkyePharma plc	First Horizon Pharmaceutical Corporation	Manufacture/Supply; Distribution/ Marketing; Rights	Diseases of the circulatory system; Endocrine, nutritional and metabolic diseases	55.00	5.00		50.00	25	Triglide®	fenofibrate IDD-P	Preregistration
105/2004 XTL Cubict Pharmaceuticals Inc. Licensing: Clinical and commercial Diseases of the digestive system; 6.00 3.00 17 HepeX-B [®] Biopharmaceuticals Lud Cubict Pharmaceuticals Inc. Certain infectious and parasitic diseases; 6.00 3.00 17 HepeX-B [®] Rolocrine, nutritional and metabolic diseases Endocrine, nutritional and metabolic 17.25 17.25 7.5 1nc. Inc. Tional and metabolic Diseases of the digestive system; 17.25 17.25 7.5	15/2004	ATS Liquidating Trust	Iken Tissue Therapeutics Inc.	Other: see details	Diseases of the circulatory system		0.20		1.20	œ	Anginera®		Preclinical
17.25 17.25 7.5 Findo-Surgery Inamed Corporation Licensing Diseases of the digestive system; 17.25 17.25 7.5 Endocrine, nutritional and metabolic diseases diseases	16/2004	XTL Biopharmaceuticals Ltd	Cubist Pharmaceuticals Inc.	Licensing; Clinical and commercial	Diseases of the digestive system; Certain infectious and parasitic diseases; Endocrine, nutritional and metabolic diseases	6.00	3.00		3.00	17	HepeX-B [®]		Phase 2
	6/2004	Ethicon Endo-Surgery Inc.	Inamed Corporation	Licensing	Diseases of the digestive system; Endocrine, nutritional and metabolic diseases	17.25	17.25			7.5			

Addendum

 Table A.1 – Chart detailing the financial details of deals recorded in the PharmaDeals® v4 Agreements database from 2004 to March 2013.

 (Source: PharmaDeals® v4 Agreements database).

A.3.3 Royalty Pharma

Royalty Pharma has royalty interests in 37 approved and marketed products, including Abbvie's Humira® (adalimumab), Johnson & Johnson's Remicade® (infliximab), Merck & Co.'s Januvia® (sitagliptin), Pfizer's Lyrica® (pregabalin) and Genentech's Rituxan® (rituximab). In addition to the diversified and predictable revenue streams provided by its marketed products, Royalty Pharma expects further revenue growth and diversification from its five products in clinical trials and/or under review with the US FDA.³⁸ The company had unaudited revenue of US\$1.39 B for the 2012 financial year and unaudited EBITDA of US\$1.35 B for the same period. In February 2013, Royalty Pharma made an indicative proposal to acquire the entire issued and to be issued share capital of Elan for US\$11 per share. Earlier in the same month, Elan agreed to restructure its 50:50 collaboration with Biogen Idec for Tysabri® (natalizumab), giving Biogen Idec complete ownership of the asset in return for an upfront payment of US\$3.25 B and a double-digit tiered royalty structure (see *Case History* on page 78). Details of Royalty Pharma's philosophy are given in Chapter 4 (Section 4.20).

³⁸http://www.royaltypharma. com/index.php?option=com_ content&view=article&id=55&l temid=11

IMS HEALTH®

ASIA-PACIFIC JAPAN **EUROPE & WORLDWIDE** THE AMERICAS 210 Pentonville Road IMS Health Asia Toranomon Towers Office 4-1-28 200 Campus Drive London N1 9JY Collegeville, PA 19426 8 Cross Street #21-01/02/03 Toranomon, Minato-ku United Kingdom **PWC Building** Tokyo 105-0001 USA Tel: +44 (0)20 3075 5888 Tel: +1 610 244-200 Singapore 048424 Japan Tel: 81-3-5425-9000 Tel: 65-6227-3006

For all office locations, visit: www.imshealth.com/locations

ABOUT IMS

IMS Health is the leading provider of information services for the healthcare industry around the world. The company draws on its global technology infrastructure and unique combination of in-depth, sophisticated analytics, on-shore and off-shore commercial services, and consulting platforms to help clients better understand the performance and value of medicines. With a presence in 100+ countries and more than 55 years of industry experience, IMS Health serves leading decision makers in healthcare, including pharmaceutical manufacturers and distributors, providers, payers, government agencies, policymakers, researchers and the financial community. Additional information is available at http://www.imshealth.com