Figures relating to potential impact

Current HPV testing market worldwide	
Sales 2012	350 Mio. EUR
Growth rate:	6%

Table 1: Worldwide HPV-related diagnostic market

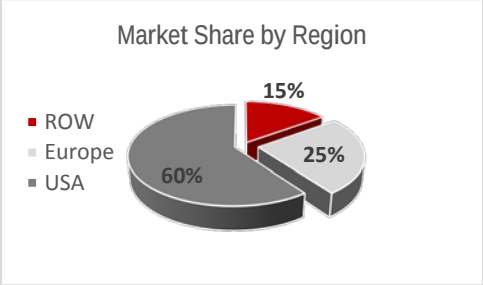

Figure 1: Market Share by Region

Test/Method	Reimbursement Number	Reimbursement in €	Description
HPV-DNA	EBM 32820, EBM 32859	34.40	only after CIN I – CIN III
HPV-DNA	private (GOÄ)(4780+4783+4785)	113.96	-
Cytology (PAP-smear)	EBM 01733	7.50	for early cancer diagnosis
Cytology (PAP-smear)	private (GOÄ) 4851+ 298	10.20	for early cancer diagnosis

Table 2: HPV reimbursement in Germany

Test name	Test system/method	Price/test in €	Weakness of previous test systems	PIPAWELL E7 test strengths
PIPAWELL E7	HPV protein based ELISA	10-15	n.a.	n.a.
ThinPrep Test (Hologic) liquid based cytology (Cytic) PAPNET (Neuromedical Systems) AUTOPAD (Neopath Inc.)	Regular PapSmear (no HPV detection)	10-60	General low sensitivities (55%) High risk of false-positive	Objective, highly cost efficient and precise test result due to molecular markers
AID GenID HPV, Roche (Amlicor, Cobas 4800, Linear Array), Quiagen (careHPV, eHC,HC2),	HPV DNA test	40-100	No discrimination between transient and persistent infection, detecting (hr, lr-) HPV	Specific detection of persistent infection;

Hologic (Cervista), BioRad (HR-HPV Dx PCR), Innogenetics (InnoLiPA), Greiner (Papillocheck), Abbott (RT HPV)			DNA in a patient is of no clinical value in predicting the regression or progression patterns of disease (CIN lesions) caused by HPV.	test identifies viral oncoprotein which drive cervical carcinogenesis; the E7 ELISA test allows for subsequent prediction of cancer.
Aptima (GenProbe), OncoTest (InCellDx), PreTect Proofer (Norchip)	HPV mRNA test	100-150	No discrimination between transient and persistent infection	Specific detection of persistent infection
Multiplex HPV Genotyping Kit (Multimetrix)	HPV genotyping	280	Indirect marker of progression, based on the epidemiologically defined “malignant potential” of each high-risk type	Direct and specific progression marker, based on the increased expression of E7 oncoprotein
E6 protein, strip assay (Arbor Vitae),	HPV protein	60	Strip assay; low sensitivitiy; two hrHPV types only	High sensitivity; available for up to 12 hrHPV types
CINtec plus (mtm Roche), ProExC (Becton Dickinson)	Celluar proteins	28	Dependence on costly and time consuming immuno- cytology technique and surrogate markers	independent of cytology, ELISA-based robust technology

Table 3: Human papillomavirus (HPV) based tests offered by competitors

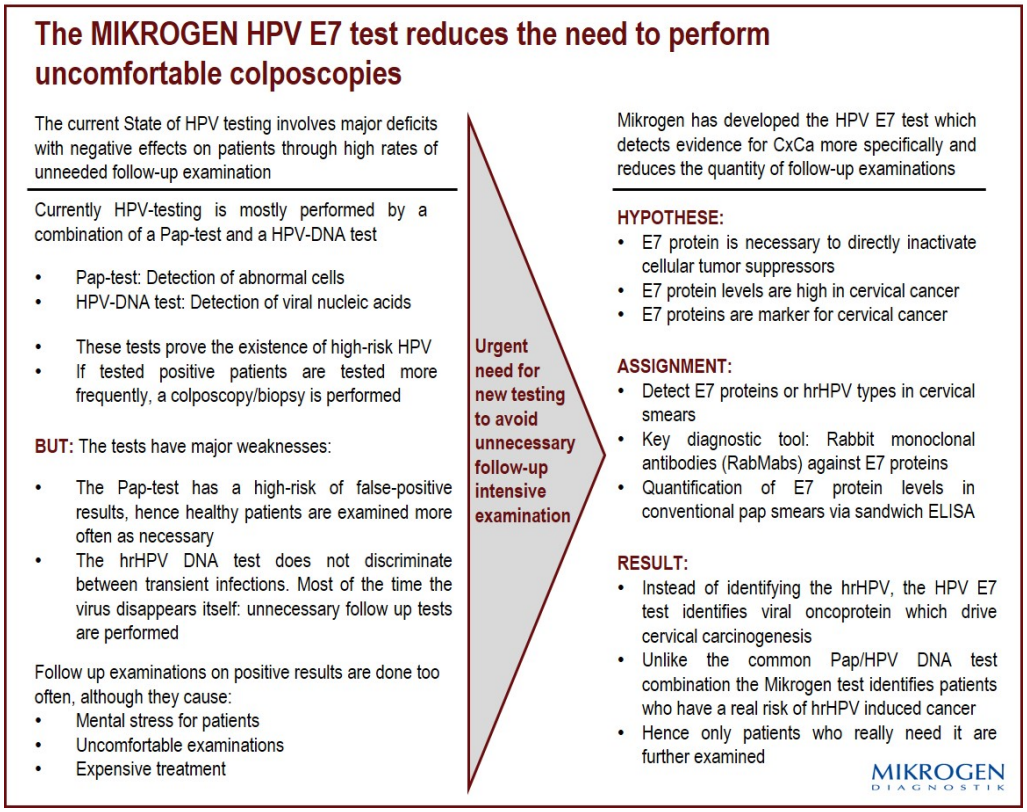

Figure 2: Unique Selling Proposition (USP) of PIPAWELL diagnostic kits

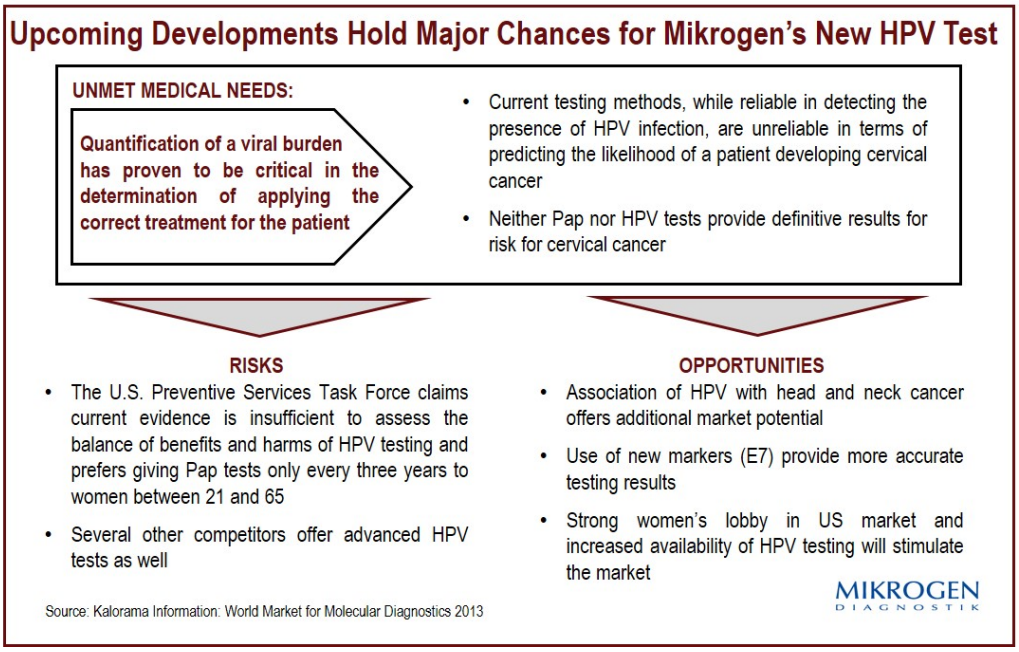

Figure 3: Market entry barriers and opportunities

		Europe	USA	Asien/SA
Relevant market	• Total Population	739	313	1.921
	• Women aged 20-60 years (27%)	200	85	519
Testing rate	• ASCUS Triage	2%	2%	0,1%
	• Adjunct screening	15%	40%	5%
	• Primary screening	20%	60%	6%
Total sales volume in market	• Qty. of tests	73.826.100	86.200.200	57.572.370
Calculation of Mikrogen sales	• Average market share Mikrogen	0,86%	0,71%	0,92%
	• Price per test	10 €	15 €	10 €
	• Years in market	12	8	11
	Total Sales (in Mio. EUR)	**76,2**	**73,4**	**58,3**
				207,9

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Figure 4: Projected PIPAWELL sales over 14 years

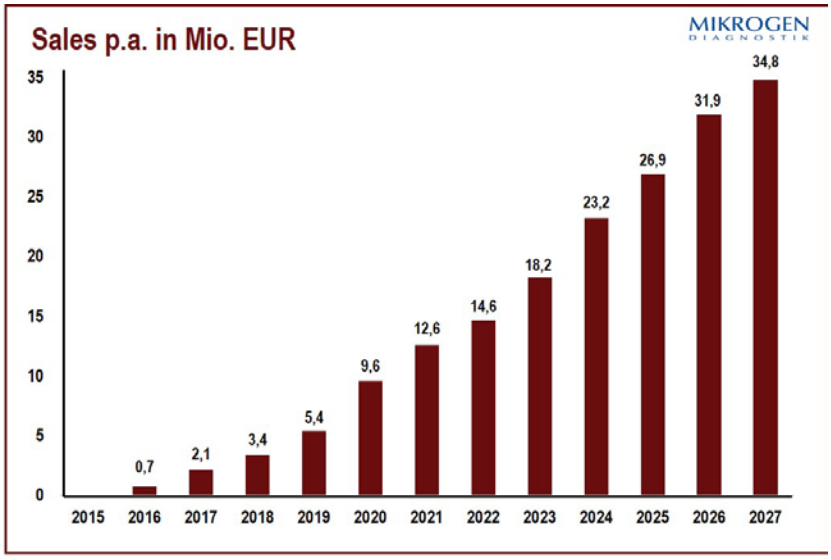

Figure 5: PIPAWELL sales projections for 2016-2017

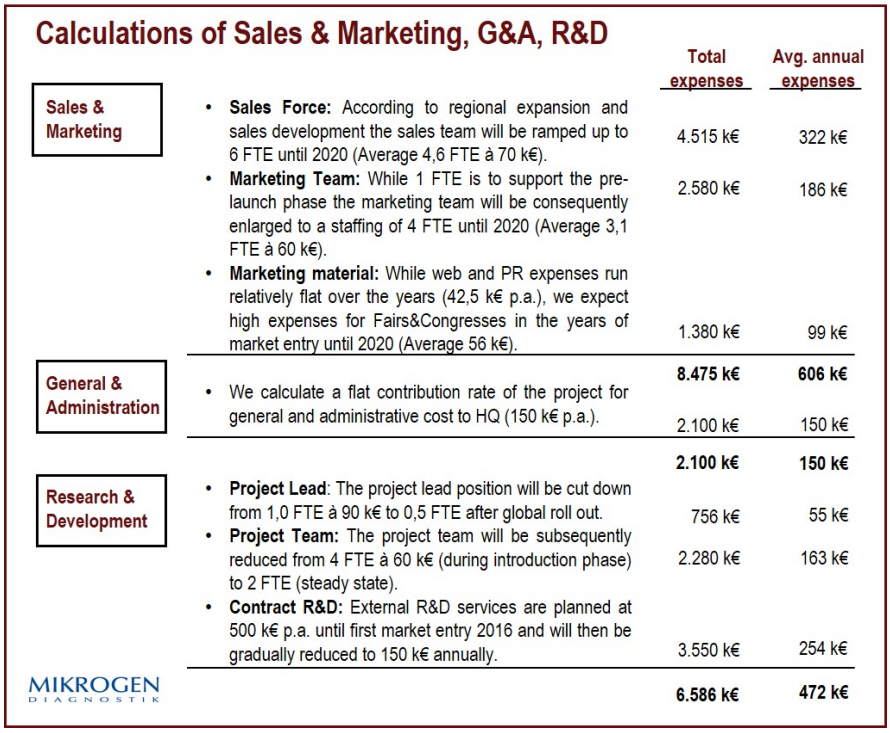

Figure 6: Calculations of Sales&Marketing, G&A, R&D

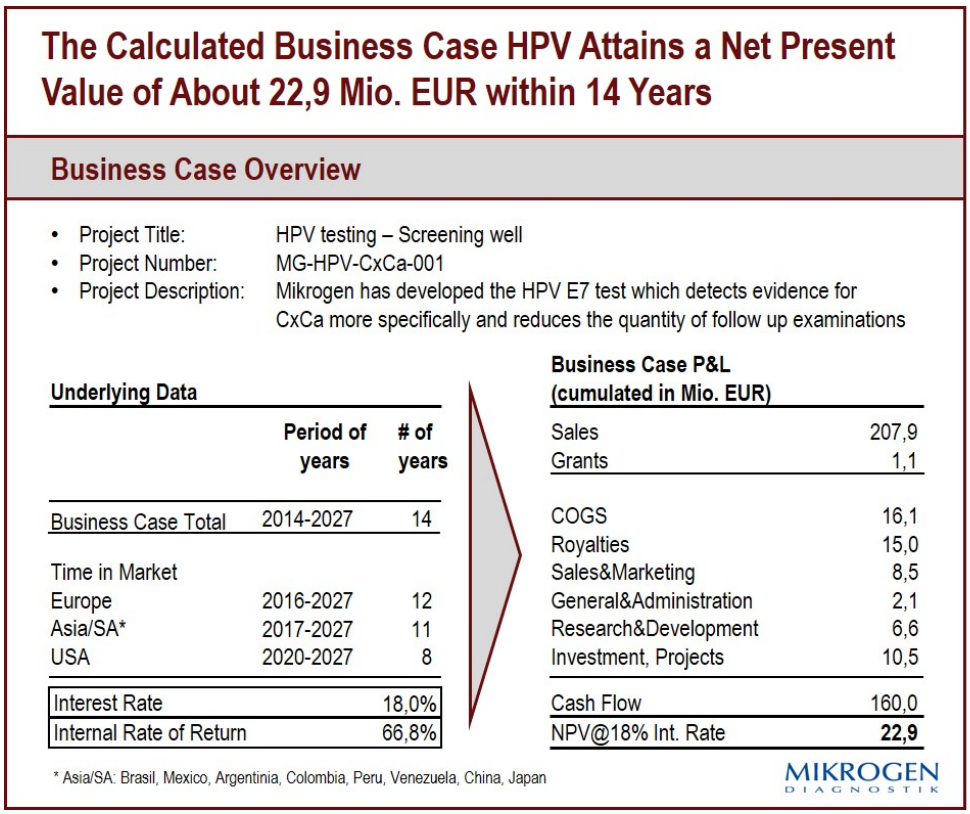

Figure 7: Business Case Overview

4.1.5 The address of the project public website, if applicable as well as relevant contact details.

www.pipavir.com

Annex I: List of participants and contact details

Beneficiary Number	Beneficiary name	Beneficiary short name	Country	Date enter project	Date exit project
1 (CO)	Universitaet Innsbruck PI: Pidder Jansen-Dürr Tel.: +43 512 507 50844 pidder.jansen-duerr@uibk.ac.at	UIBK	Austria	1	36
2	Mikrogen GmbH PI: Oliver Böcher Tel.: +49 89 54801 190 boecher@mikrogen.de	MIKROGEN	Germany	1	36
3	Biosynex SA PI: Thierry Paper Tel.: +33 3 88 77 57 01 paper@biosynex.com	BIOSYNEX	France	1	36
4	Charite- Universitaetsmedizin Berlin PI: Andreas M. Kaufmann Tel.: +49 30-8445-2756 andreas.kaufmann@charite.de	CHARITE	Germany	1	36
5	Aristotelio Panepistimio Thessalonikis PI: Theodoros Agorastos Tel.: +30 2310 892140 agorast@auth.gr	AUTH	Greece	1	36
6	Oesterreichische Akademie der Wissenschaften	OEAW	Austria	1	1

Figures relating to Description of the main S&T results/foregrounds

Work Package 2

Parameter	Achieved (Yes/No)	Comments
Test format choice	Yes	"uncommon" Immunochromatography with a liquid conjugate allowing a sample/conjugate pre-incubation for better sensitivity
Antibodies conjugation to particles	Yes	Validation of RabMab Klon 42-3 and 143-7 for HPV16, 18 and 45-E7 detection Validation of the use of Gold particles amongst various markers (Biotin, Latex beads, HRP-Magnetic, etc)
Reproducibility of conjugation	Yes	Validated with all available batches of antibodies from different supplier
Membrane choice	Yes	Test of various porosity ➔ 8µm porosity chosen
Test calibration	Yes	Validation of a mix of Goat 1 and 2 (Affinity + G200 purified) for test line and of Goat anti-Rabbit in Control line
Test protocol	Yes	Validation of two buffers: the Buffer A and B and a upgraded version for the buffer with the addition of two chemical components in buffer B to help migration of problematic samples

Table: Resume of rapid test development task:

Antigen	1rst test version	Improved test version
HPV16-E7	1 ng/mL	0,1 ng/mL
HPV18-E7	1 ng/mL	0,1 ng/mL
HeLa cell lysis	25 000 cells/test	5 000 cells/test

Table: Comparison of the detection limits before and after improvement.

Study	2nd smears	1rst smears
Cure CxCa	9	12
Cure HSIL	485	463
Screening	627	1577
Self Sampling	189	190
Triage Cyto+	166	180
Triage HPV+	98	289
	1574	**2917**

Table: number of samples tested with the rapid test per Study.

Parameter	Achieved (Yes/No)	Comments
Self-sampling buffer	No	Due to other technical problems during the hrE7-Rapid test development this has not been investigated

Development of self-sampling test (below)

Antigen	Detection limit (ng/mL)
Recombinant HPV-16 E7	1-5
Recombinant HPV-18 E7	0.5
Recombinant HPV-45 E7	1-5
Recombinant HPV-11 E7	100
Recombinant HPV-33 E7	Not detected
Recombinant HPV-35 E7	1000
Recombinant HPV-51 E7	1000
Recombinant HPV-52 E7	Not detected
Recombinant HPV-56 E7	1000
Recombinant HPV-58 E7	Not detected
Recombinant HPV-59 E7	10

Cell name	HPV type	Detection limit (cells/test)
Caski	16	100 000
SiHa	16	Not detected
HeLa	18	10 000
MS 751	45	25 000
MS 180	Other	Not detected
Cerv 215	45	25 000
C33a	Negative	Not detected