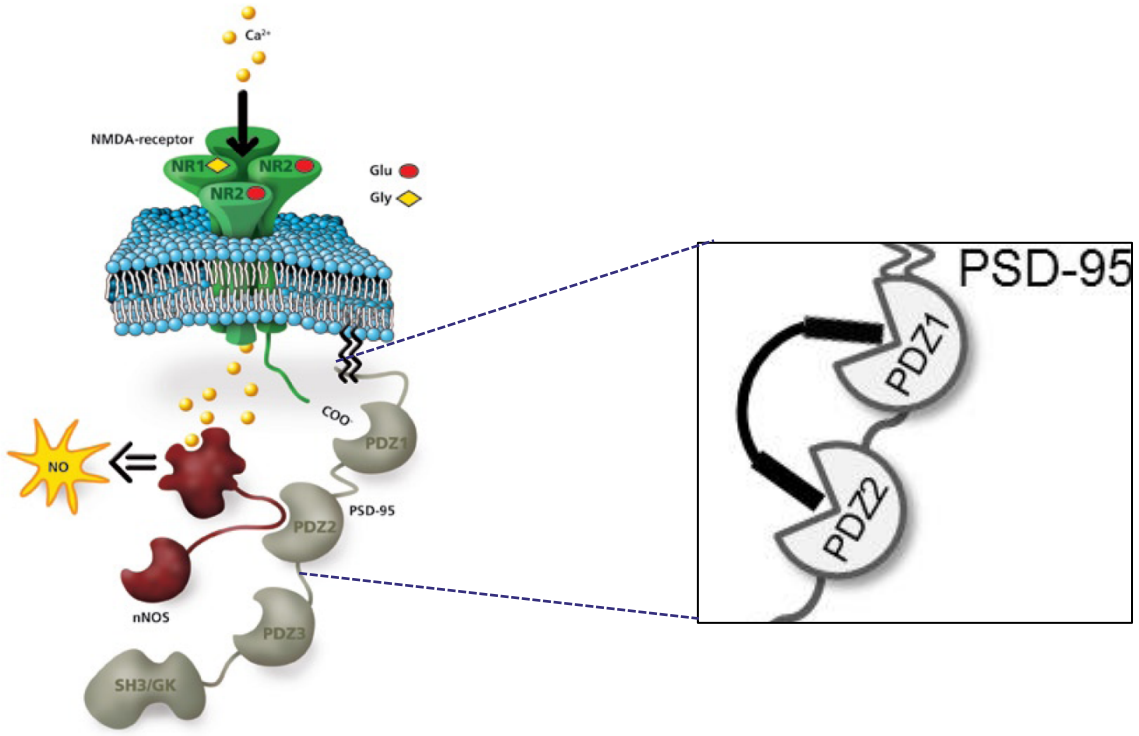
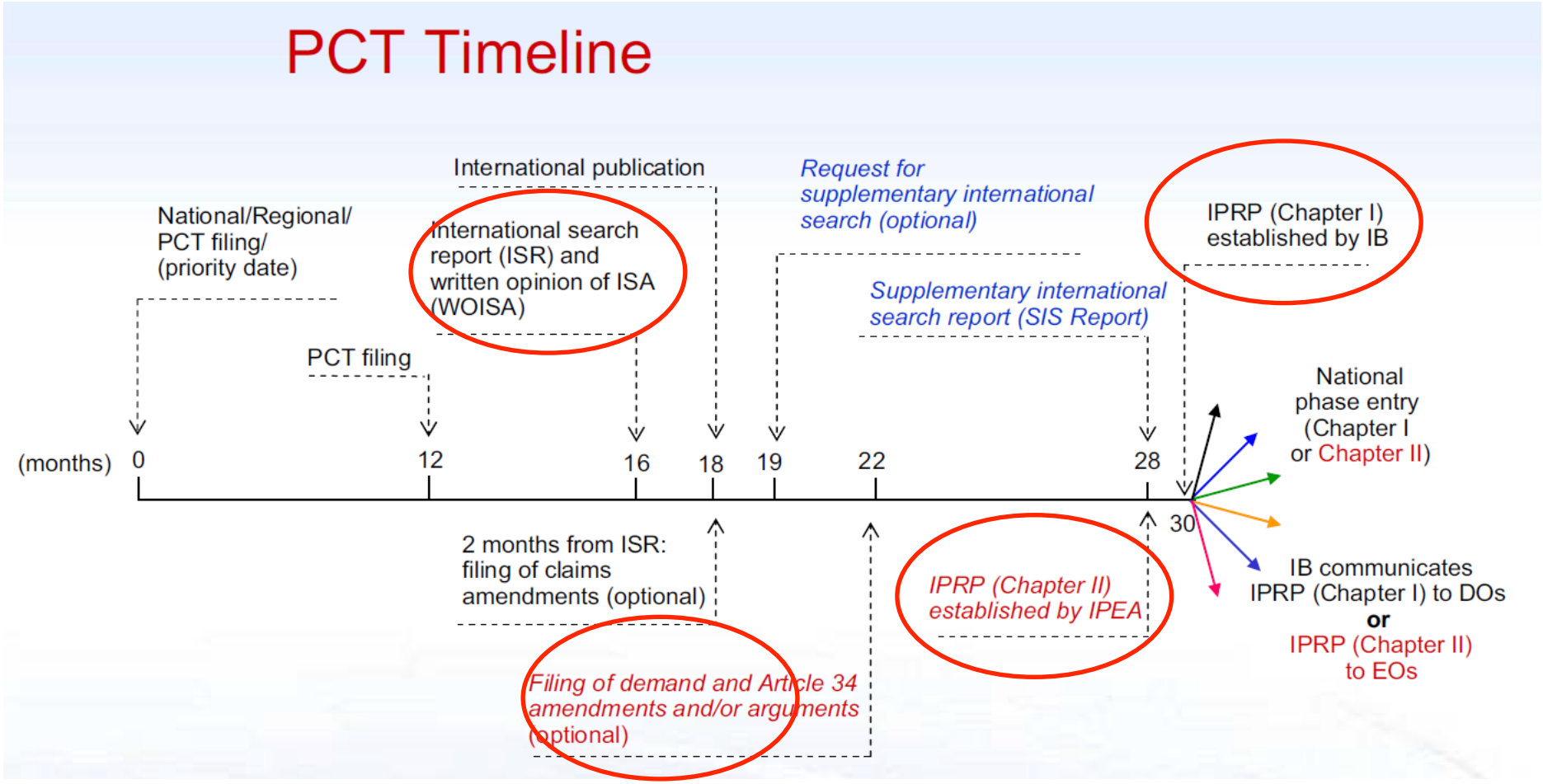
Patent Prosecution - Dimeric PSD-95 Inhibitors



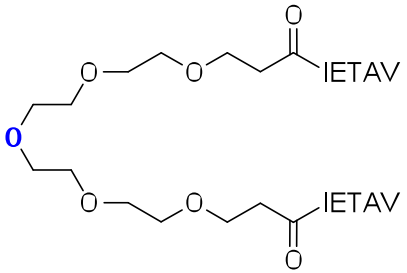
Anders Bach
Exercise (February 2, 2017)
Innovation and intellectual property rights in biotechnology


PCT Timeline
International publication
Request for supplementary international search (optional)
IPRP (Chapter I) established by IB
National/Regional/ PCT filing/ (priority date)
International search report (ISR) and written opinion of ISA (WOISA)
Supplementary international search report (SIS Report)
PCT filing
National phase entry (Chapter I or Chapter II)
(months) 0 12 16 18 19 22 28 30
2 months from ISR: filing of claims amendments (optional)
IPRP (Chapter II) established by IPEA
IB communicates IPRP (Chapter I) to DOs
or
IPRP (Chapter II) to EOs
Filing of demand and Article 34 amendments and/or arguments (optional)

Patents

Patent 1 (WO 2010/004003):

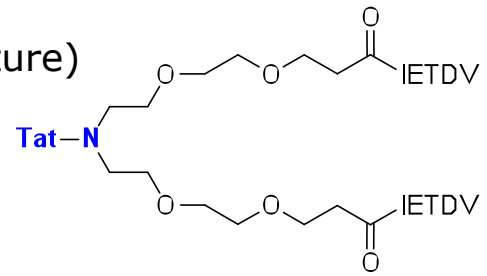
- Dimeric peptide inhibitors based on PEG linkers
- High affinity, medium stability (No BBB permeability)
- Inventors: Anders Bach, Kristian Strømgaard



UCCB01-125

Patent 2 (WO 2012/156308):

- Dimeric peptide inhibitors based on *N*PEG linkers (a novel structure)
- High affinity, high stability, BBB permeability
- Inventors: Anders Bach, Kristian Strømgaard



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(Tat = YGRKKRRQRRR)

Competitor compound – NA1 (Tymianski, NoNO):

- Tat-NR2B9c
- Aarts et al, 2002, Science
- Patent applications from 2005 and 2008

YGRKKRRQRRRKLSSIESDV

NA-1

WO2010/004003
WO2012/156308

Prosecution – PCT Phase

Were our 2 PCTs considered patentable during the PCT phase?

What kind of documents and arguments (if any) were raised against us?
- and how would you deal with these?

Hints: 1) International search report (ISR)
2) Written Opinion of the International Search Authority (WOISA)
3) International Preliminary Report on Patentability (IPRP) (Chapter I/II)
(page 50-54 in text book)

WO2010/004003
1) 3 A docs
2) Novelty, Inv Step: YES
3) Novelty, Inv Step: YES (Chapter I)
- Lack of Unity?
- Claim 16-19?

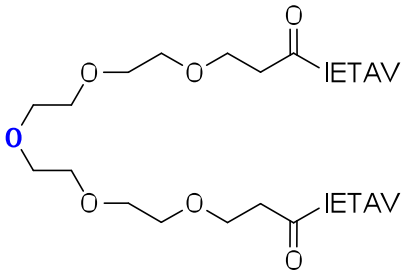
WO2012/156308
1) X (WO2010004003)
Y (2xTymianski)
2) Novelty: YES
Inv Step: NO
3) Novelty: YES
Inv Step: YES
(IPRP: Chapter II)

Demand*

**Demand for International Preliminary Examination (Extra fees, incl. interaction between applicant and Examiner) => IPRP, Chapter II*

WOISA – Arguments (Patent 2)

Patent 1 (X)



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\+

NA1 (Y)

YGRKKRRQRRRKLSSIESDV

NA-1

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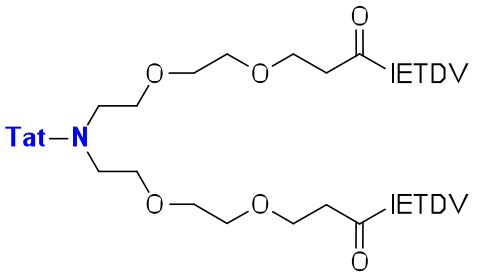
Patent 2



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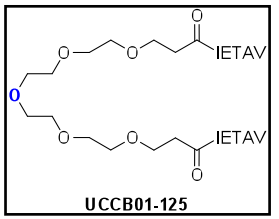
Demands - Arguments

1. It is not obvious how and where to attach the Tat
2. *N*PEG linker is different from PEG
3. *N*PEG and design leads to unexpected (positive) properties:
   - Affinity, stability, In vivo efficacy

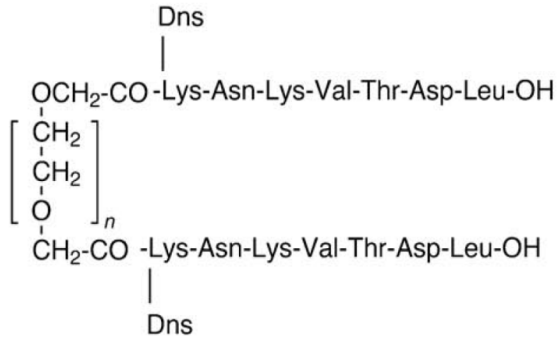
=> Inventive Step

Prosecution – US Region (Patent 1)



Paduch et al, ChemBioChem 2007:

- Dimeric ligands with PEG and peptide
- Peptides are longer and different sequence
- PEG-linkers are polydisperse and longer
- Target is different (artificial PDZ-PDZ)



	Bivalent peptide PEG(K(Dns)NKVTDL)$_2$ [μM]			Monovalent peptide
	32 atom PEG	35 atom PEG	38 atom PEG	Dns–EEVENKVTDL [μM]
mΔPDZ^{PRG}	35.0 ± 2	34.0 ± 0.5	34.0 ± 0.5	29.0 ± 0.5
dΔPDZ^{PRG}	2.6 ± 0.2	2.0 ± 0.4	1.7 ± 0.2	13.0 ± 3
mPDZ^{LARG}	19.8 ± 0.2	21.0 ± 0.5	19.8 ± 0.5	19.0 ± 2
dPDZ^{LARG}	6.0 ± 0.2	7.4 ± 0.4	8.2 ± 0.6	21.0 ± 0.5

Lu et al (WO 03/014303 A2):

- Claiming peptide sequences (incl. IETAV, IETDV) for targeting PDZ domains

Paduch + Lu = Patent 1 (???)

1. Technical arguments about definition of PEG length (units vs atoms)
2. Paduchs target not relevant/predictive for our case
3. **Limit our claims so not to overlap (substantially) with Paduch**

IP position

Patent Application 1 (WO 2010/004003)

- Title: Modified peptides as potent inhibitors of the PSD-95/NMDA receptor interaction
- Priority date: July 9, 2008
- Positive IPRP (International Preliminary Report on Patentability) from the PCT phase
- US approved; Validated in 11 European countries

Patent Application 2 (WO 2012/156308)

- Title: High-affinity, dimeric inhibitors of PSD-95 as efficient neuroprotectants against ischemic brain damage and for treatment of pain
- Priority date: May 13, 2011
- Positive IPRP (International Preliminary Report on Patentability) from the PCT phase
- US and China approved; Validated in 11 European countries
- National/regional phase in AU, BR, CA, IN, IL, JP, KR, MX, SG

Patent Application 3 (PCT/DK2014/050402)

- Title: Fatty acid derivatives of dimeric inhibitors of PSD-95
- Priority date: December 1, 2013
- Positive IPRP