# **Supplementary Information**

Data on the clinical responses of conjugates per tumour type.

### 1. HPMA Copolymer-doxorubicin (PK1; FCE28068) [4,19]

**Table S1.** Data relating to clinical trials (Phase I [Ph-I], Phase II [Ph-II]) of PK1; [Total number of patients enrolled for the study 98 <sup>a</sup>].

	No. of patients	Cli	nical resp	onses <sup>b</sup> tot	al (Ph I/I	Ph II)	Tumour response
tumour type	per tumour total (Ph I/Ph II)	No. of SD	No. of PR	No. of MR	No. of CR	No. of NR	rate <sup>c</sup> (%) total (Ph I/Ph II)
Lung	31[(2/29(21) *]	8[-/8]	5[2/3]	-	-	10[0/10]	57[100/52]
Breast	20[3/17(14) *]	5[-/5]	3[-/3]	1[1/-]	-	8[2/6]	53[33/57]
Colon and/or rectum	24[8/16]	-	-	1[1/-]	-	23[7/16]	4[4/-]
Adenocarcinoma (Unknown primary)	5[5/-]	-	-	-	-	5[5/-]	0
Ovary	3[3/-]	-	-	-	-	3[3/-]	0
Liver	3[3/-]	-	-	-	-	3[3/-]	0
Pancreas	3[3/-]	-	-	-	-	3[3/-]	0
Urinary	3[3/-]	-	-	_	-	3[3/-]	0
Head/Neck and brain	3[3/-]	-	-	-	-	3[3/-]	0
Mesothelioma	2[2/-]	-	-	-	-	2[2/-]	0
Oesophagus, stomach and intestine	1[1/-]	-	-	-	-	1[1/-]	0

Notes: <sup>a</sup> Indicates number of patients considered for the clinical evaluation; <sup>b</sup> clinical responses is the total SD, Stable disease; PR, Partial response; MR, Minor response; CR, Complete response; NR, No response; <sup>c</sup> Tumour response rate (%) is the added responses (SD + PR + MR + CR) per tumour type; \* Indicates number of patients evaluated for the tumour responses.

#### 2. HPMA Copolymer-doxorubicin-galactosamine (PK2; FCE28069) [20]

**Table S2.** Data relating to clinical trials (Phase I [Ph-I]) of PK2; [Total number of patients enrolled for the study 31(18) <sup>a</sup>].

	No. of patients			Tumour				
Tumour type	per tumour (Ph I)	No. of No. of No. of No. of SD PR MR CR NR					response rate <sup>c</sup> (%) (Ph I)	
Liver	25	-	2	1	-	22	12	
Colon and/or rectum	6	-	-	-	-	6	0	

#### 3. Carboxymethyldextran-exatecan; DE-310 [21]

**Table S3.** Data relating to clinical trials (Phase I [Ph-I]) of DE-310; [Total number of patients enrolled for the study 29(27) <sup>a</sup>].

	No. of patients		Clinical	response	s b (Ph I)		Tumour
Tumour type	per tumour (Ph I)	No. of SD	No. of PR	No. of MR	No. of CR	No. of NR	response rate <sup>c</sup> (%) (Ph I)
Adenocarcinoma (Unknown primary)	2	1	-	-	1	0	100
Pancreas	3	2	1	-	-	0	100
Urinary	1	1	-	-	-	0	100
Cervix	1	1	-	-	-	0	100
Ovary	1	1	-	-	-	0	100
Colon and/or rectum	6	4	-	-	-	2	67
Lung	3	2	-	-	-	1	67
Skin	6	2	-	-	-	4	33
Soft tissue sarcoma	3	-	-	-	-	3	0
Oesophagus, stomach and intestine	3	-	-	-	-	3	0

Notes: <sup>a</sup> Indicates number of patients considered for the clinical evaluation; <sup>b</sup> clinical responses is the total SD, Stable disease; PR, Partial response; MR, Minor response; CR, Complete Response; NR, No response; <sup>c</sup> Tumour response rate (%) is the added responses (SD + PR + MR + CR) per tumour type.

### 4. Delimotecan; MEN 4901/T-0128 [22]

**Table S4.** Data relating to clinical trials (Phase I [Ph-I]) of MEN 4901/T-0128; [Total number of patients enrolled for the study 22 <sup>a</sup>].

	No. of patients		Clinical	response	es b (Ph I)		Tumour
Tumour type	per tumour (Ph I)	No. of SD	No. of PR	No. of MR	No. of CR	No. of NR	response rate <sup>c</sup> (%) (Ph I)
Head/Neck and brain	2	-	1	-	-	1	50
Colon and/or rectum	7	-	1	-	-	6	14
Mesothelioma	3	-	-	-	-	3	0
Urinary	1	-	-	-	-	1	0
Skin	1	-	-	-	-	1	0
Adenoid cystic	1	-	-	-	-	1	0
Oesophagus, stomach and intestine	2	-	-	-	-	2	0
Adenocarcinoma (Unknown primary)	2	-	-	-	-	2	0
Lung	2	-	-	-	-	2	0
Kidney	1	-	-	-	-	1	0
Sarcoma (Unknown)	1	-	-	-	-	1	0

Notes: <sup>a</sup> Indicates number of patients considered for the clinical evaluation; <sup>b</sup> clinical responses is the total SD, Stable disease; PR, Partial response; MR, Minor response; CR, Complete response; NR, No response;

<sup>&</sup>lt;sup>c</sup> Tumour response rate (%) is the added responses (SD + PR + MR + CR) per tumour type.

# 5. Poly-L-glutamic acid-camptothecin; PGA-CPT; CT-2106 [23]

**Table S5.** Data relating to clinical trials (Phase I [Ph-I]) of CT-2106; [Total number of patients enrolled for the study 26(25) <sup>a</sup>].

	No of patients		Clinical	response	s b (Ph I)		Tumour
Tumour type	per tumour (Ph I)	No. of SD	No. of PR	No. of MR	No. of CR	No. of NR	response rate <sup>c</sup> (%) (Ph I)
Breast	4	1	-	-	-	3	25
Skin	14	2	-	-	-	12	14
Bone	1	-	-	-	-	1	0
Pancreas	2	-	-	-	-	2	0
Lung	3	-	-	-	-	3	0
Colon and/or rectum	1	-	-	-	-	1	0
Squamous cell carcinoma	1	-	-	_	-	1	0

# 6. Poly-L-glutamic acid-paclitaxel; PGA-PTX; CT-2103; XYOTAX; OPAXIO® [5,6,18,24-33]

**Table S6a.** Data relating to clinical trials (Phase I [Ph-I], Phase II [Ph-II]) of CT-2103 (PGA-Paclitaxel); [Total number of patients enrolled for the study 1951 <sup>a</sup>].

	No. of patients per		Clinica	l responses <sup>b</sup> to	otal (Ph I/P	h II/Ph III)		Tumour response
Tumour type	tumour total (Ph I/Ph II/Ph III)	No. of SD	No. of PR	No. of MR	No. of CR	No. of OS	No. of NR	rate <sup>c</sup> (%) total (Ph I/Ph II/Ph III)
Breast	18[-/18/-]	2[-/2/-]	4[-/4/-]	4[-/4/-]	-	-	8[-/8/-]	56[-/56/-]
Ovary	99[-/99/-]	32[-/32/-]	10[-/10/-]	-	-	-	57[-/57/-]	42[-/42/-]
Mesothelioma	3[3/-/-]	-	-	1[1/-/-]	-	-	2[2/-/-]	33[33/-/-]
Lung	1798[13/-/1785]	-	13[NA/NA/ NA]	1[NA/NA/ NA]	-	507[-/-/507]	1277[NA/NA/ NA]	30[NA/NA/NA]
Oesophagus, stomach and intestine	24[-/24/-]	-	-	1[-/1/-]	4[-/4/-]	-	19[-/19/-]	21[-/21/-]
Kidney	3[3/-/-]	-	-	-	-	-	3[3/-/-]	0
Sarcoma (Unknown)	1[1/-/-]	-	-	-	-	-	1[1/-/-]	0
Cervix	1[1/-/-]	-	-	-	-	-	1[1/-/-]	0
Adrenal	1[1/-/-]	-	-	-	-	-	1[1/-/-]	0
Unknown primary	3[3/-/-]	-	-		-	-	3[3/-/-]	0
Colon and/or rectum	8[8/-/-]	-	-	-	-	-	8[8/-/-]	0

**Table S6b.** Cont. [Total number of patients enrolled for the study 22 <sup>a</sup>].

Т	No. of patients per tumour		Cli	T			
Tumour type		No. of SD	No. of PR	No. of MR	No. of CR	No. of NR	Tumour response rate ° (%)
Solid tumours *	23	12	3	-	-	12	65

Notes: \* Solid tumours includes-Lung (6); Head/Neck and brain (6); Ovary (3); Pancreas (2); Oesophagus, stomach and intestine (1); Breast (1); Kidney (1); Unknown primary (1); Colon and/or rectum (2); <sup>a</sup> Indicates number of patients considered for the clinical evaluation; <sup>b</sup> clinical responses is the total SD, Stable disease; PR, Partial response; MR, Minor response; CR, Complete response; NR, No response; <sup>c</sup> Tumour response rate (%) is the added responses (SD + PR + MR + CR) per tumour type.

# 7. HPMA Copolymer-carboplatin; HPMA-Carboplatin; AP5280 [34]

Table S7. Data relating to clinical trials (Phase I [Ph-I]) of AP5280; [Total number of patients enrolled for the study 29(19) <sup>a</sup>].

Т	No. of patients		Cl	inical responses	Tumour response rate <sup>c</sup>		
Tumour type	per tumour (Ph I)	No. of SD	No. of PR	No. of MR	No. of CR	No. of NR	(%) (Ph I)
Lung	4	2	-	-	-	2	50
Ovary	2	1	-	-	-	1	50
Colon and/or rectum	12	2	-	-	-	10	17
Kidney	3	-	-	-	-	3	0
Oesophagus, stomach and intestine	3	-	-	-	-	3	0
Head/Neck and brain	1	-	-	-	-	1	0
Pancreas	2	-	-	-	-	1	0
Skin	2	-	-	-	-	2	0

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# 8. HPMA Copolymer-platinate; HPMA-Pt; AP5346 [35]

**Table S8.** Data relating to clinical trials (Phase I [Ph-I]) AP5346; [Total number of patients enrolled for the study 26 <sup>a</sup>].

T	No. of patients		Clinic	al responses b	(Ph I)		Tumour response rate <sup>c</sup>
Tumour type	per tumour (Ph I)	No. of SD	No. of PR	No. of MR	No. of CR	No. of NR	(%) (Ph I)
Cervix	1	1	-	-	-	0	100
Oesophagus, stomach and intestine	1	1	-	-	-	0	100
Skin	5	1	1	-	-	3	40
Ovary	4	-	1	-	-	3	25
Breast	4	-	-	-	-	4	0
Adenocarcinoma (Unknown primary)	3	-	-	-	-	3	0
Prostate	2	-	-	-	-	2	0
Lung	1	-	-	-	-	1	0
Pancreas	1	-	-	-	-	1	0
Kidney	1	-	-	-	-	1	0
Head/Neck and brain	1	-	-	-	-	1	0
Bone	1	-	-	-	-	1	0
Urinary	1	-	-	-	-	1	0

# 9. HPMA copolymer-paclitaxel; HPMA-PTX; PNU166945 [36]

**Table S9.** Data relating to clinical trials (Phase I [Ph-I]) PNU166945 (HPMA-PTX); [Total number of patients enrolled for the study 12 <sup>a</sup>].

T	No. of patients	Clinical responses b (Ph I)					Tumour response rate <sup>c</sup>
Tumour type	per tumour (Ph I)	No. of SD	No. of PR	No. of MR	No. of CR	No. of NR	(%) (Ph I)
Solid tumours *	12	2	1	-	-	9	25

Notes: \* Solid tumours includes-Ovary (4); Breast (2); Colon and/or rectum (2); Lung (1); others (3); <sup>a</sup> Indicates number of patients considered for the clinical evaluation; <sup>b</sup> clinical responses is the total SD, Stable disease; PR, Partial response; MR, Minor response; CR, Complete response; NR, No response; <sup>c</sup> Overall tumour response rate (%) is the added responses (SD + PR + MR + CR) per tumour type; A clinical response per tumour type has not been mentioned in this respective study.

#### 10. HPMA Copolymer-camptothecin; HPMA-CPT; PNU166148 [37–39]

**Table S10.** Data relating to clinical trials [(Phase I [Ph-I]) PNU166148 (HPMA-PTX); [Total number of patients enrolled for the study 48(40) <sup>a</sup>].

T	No. of patients		Clin	Tumour response rate c			
Tumour type	per Tumour (Ph I)	No. of SD	No. of PR	No. of MR	No. of CR	No. of NR	(%) (Ph I)
Solid tumours *	40	5	-	1	-	34	15

Notes: \* Solid tumours includes-Colon and/or rectum (18); Ovary (2); Oesophagus, stomach and intestine (4); Unknown primary (4); Head/Neck and brain (2); Lung (6); Kidney (3); Adrenal (1); Cervix (1); Bone (1); Mesothelioma (1); Prostate (1); Sarcoma (3); <sup>a</sup> Indicates number of patients considered for the clinical evaluation; <sup>b</sup> clinical responses is the total SD, Stable disease; PR, Partial response; MR, Minor response; CR, Complete response; NR, No response; <sup>c</sup> Overall tumour response rate (%) is the added responses (SD + PR + MR + CR) per tumour type; A clinical response per tumour type has not been mentioned in this respective study.

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# 11. Polyethylene-camptothecin; PEG-CPT; EZN246; Pegmaotecan; Prothecan™ [40–42]

**Table S11.** Data relating to clinical trials (Phase I [Ph-I], Phase II [Ph-II]) of PEG-CPT; [Total number of patients enrolled for the study 64(63) <sup>a</sup>].

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T	No. of patients per tumour		Clinical re	esponses b total	l (Ph I/Ph II)		Tumour response rate <sup>c</sup>
Tumour type	total (Ph I/Ph II)	No. of SD	No. of PR	No. of MR	No. of CR	No. of NR	(%) total (Ph I/Ph II)
Bone	1[1/-]	-	-	1[1/-]	-	0[0/-]	100[100/-]
Oesophagus, stomach and intestine	42[7/35]	14[-/14]	5[-/5]	3[2/1]	-	20[5/15]	52[29/57]
Unknown primary	5[5/-]	-	-	1[1/-]	-	4[4/-]	20[20/-]
Lung	7[7/-]	-	1[1/-]	-	-	6[6/-]	14[14/-]
Colon and/or rectum	25[25/-]	-	-	-	-	25[25/-]	0
Liver	3[3/-]	-	-	-	-	3[3/-]	0
Head/Neck and brain	2[2/-]	-	-	-	-	2[2/-]	0
Mesothelioma	1[1/-]	-	-	-	-	1[1/-]	0
Ovary	1[1/-]	-	-	-	-	1[1/-]	0
Pancreas	4[4/-]	-	-	-	-	4[4/-]	0
Sarcoma (Unknown)	2[2/-]	-	-	-	-	2[2/-]	0
Breast	1[1/-]	-	-	-	-	1[1/-]	0
Lymphoma	1[1/-]	-	-	-	-	1[1/-]	0
Skin	2[2/-]	-	-	-	-	2[2/-]	0
Leiomyosarcoma	2[2/-]	-	-	-	-	2[2/-]	0
Leiomyosarcoma	Z[Z/-]	-	-	-	-	2[2/-]	0

#### 12. Polyethylene Glycol-Paclitaxel; PEG-PTX [43]

**Table S12.** Data relating to clinical trials (Phase I [Ph-I]) of PEG-PTX; [Total number of patients enrolled for the study 13 <sup>a</sup>].

T	No. of patients		Tumour response rate <sup>c</sup>				
Tumour type	per tumour (Ph I)	No. of SD	No. of PR	No. of MR	No. of CR	No. of NR	(%) (Ph I)
Solid tumours *	13		N	ÍΑ	NC	NC	

Notes: \* Solid tumours includes-Colon and/or rectum (3); Breast (2); Neuroendocrine (2); Lung (1); Prostrate (1); Others (4); <sup>a</sup> Indicates number of patients considered for the clinical evaluation; <sup>b</sup> clinical responses is the total SD, Stable disease; PR, Partial response; MR, Minor response; CR, Complete response; NR, No response; <sup>c</sup> Tumour response rate (%) is the added responses (SD + PR + MR + CR) per tumour type; NA-Not available; NC-Not calculated.

#### 13. Multiarm-Polyethylene-SN38; EZN-2208 [44,45]

Table S13. Data relating to clinical trials (Phase I [Ph-I], Phase II [Ph-II]) of PEG-CPT; [Total number of patients enrolled for the study 264(196) <sup>a</sup>].

Т	No. of patients per tumour		Clinical re	Tumour response rate <sup>c</sup>			
Tumour type	total (Ph I/Ph II)	No. of SD	No. of PR	No. of MR	No. of CR	No. of NR	(%) total (Ph I/Ph II)
Urinary	1[1/-]	1[1/-]	-	-	-	0[0/-]	100[100/-]
Oesophagus, stomach and intestine	3[3/-]	2[2/-]	-	-	-	1[1/-]	67[67/-]
Breast	3[3/-]	2[2/-]	-	-	-	1[1/-]	67[67/-]
Lung	2[2/-]	1[1/-]	-	-	-	1[1/-]	50[50/-]
Pancreas	3[3/-]	1[1/-]	-	-	-	2[2/-]	33[33/-]
Colon and/or rectum	236[25/211(192) *]	32[12/20]	4[-/4]	_	-	181[13/168]	17[48/13]
Carcinoid	1[1/-]	-	-	-	-	1[1/-]	0
Ovary	1[1/-]	-	-	_	-	1[1/-]	0
Prostate	1[1/-]	-	-	-	-	1[1/-]	0
Soft tissue sarcoma	1[1/-]	-	-	-	-	1[1/-]	0

### 14. Multiarm-Polyethylene glycol-Pacliaxtel; PEG-PTX; NKTR-102 [46-48]

**Table S14.** Data relating to clinical trials (Phase I [Ph-II], Phase II [Ph-II]) NKTR-102; [Total number of patients enrolled for the study 127(125) <sup>a</sup>].

T	No. of patients per tumour		Clinical re	Tumour response rate <sup>c</sup>			
Tumour type	total (Ph I/Ph II)	No. of SD	No. of PR	No. of MR	No. of CR	No. of NR	(%) total (Ph I/Ph II)
Solid tumours *	125[32/68]	28[-/28]	24[7/17]	6[6/-]	2[2/-]	65[8/23]	48[47/66]

Notes: \* Solid tumours includes-Ovary; Breast; Adrenal; Oesophagus, stomach and intestine; Lymphoma; Lung; Cervix; Head/Neck and brain; Urinary; <sup>a</sup> Indicates number of patients considered for the clinical evaluation; <sup>b</sup> clinical responses is the total SD, Stable disease; PR, Partial response; MR, Minor response; CR, Complete response; NR, No response; <sup>c</sup> Tumour response rate (%) is the added responses (SD + PR + MR + CR) per tumour type; A clinical response per tumour type has not been mentioned in this respective study.

## 15. Multiarm-Polyethylene glycol-docetaxel; NKTR-105 [50]

NKTR-105 was clinically evaluated in [Phase-I] trials involving 17 patients with different solid tumours. The data of this study was not available.

**Table S15.** Data on clinical trials ([Phase I [Ph-I]) NKTR-105; [Total number of patients enrolled for the study 17 <sup>a</sup>].

Tumoun tumo	No. of patients		Cli	Tumour response rate <sup>c</sup>			
Tumour type	per tumour (Ph I)	No. of SD	No. of PR	No. of MR	No. of CR	No. of NR	(%) (Ph I)
NA	17	NA	NA	NA	NA	NC	NC

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### 16. PHF-Camptotecin; PHF-CPT; MER-1001; XMT-1001 [51]

**Table S16.** Data relating to clinical trials (Phase I [Ph-I]) XMT-1001; [Total number of patients enrolled for the study 49(46) <sup>a</sup>].

T 4	No. of patients		Clinica	Tumour response rate <sup>c</sup>			
Tumour type	per tumour (Ph I)	No. of SD	No. of PR	No. of MR	No. of CR	No. of NR	(%) (Ph I)
Skin	2	1	-	-	-	1	50
Lung	7	3	-	-	-	4	43
Solid tumours (Unspecified)	8	3	-	-	-	5	38
Ovary	3	1	-	-	-	2	33
Oesophagus, stomach and intestine	3	1	-	-	-	2	33
Colon and/or rectum	11	2	-	-	-	9	18
Pancreas	9	1	-	-	-	8	11
Breast	4	-	-	-	-	4	0
Unknown primary	2	-	-	-	-	2	0

Notes: <sup>a</sup> Indicates number of patients considered for the clinical evaluation; <sup>b</sup> clinical responses is the total SD, Stable disease; PR, Partial response; MR, Minor response; CR, Complete response; NR, No response; <sup>c</sup> Tumour response rate (%) is the added responses (SD + PR + MR + CR) per tumour type.

# 17. Cyclodextrin-Camptothecin; CRLX101; IT-101 [52]

Table S17. Data relating to clinical trials (Phase I [Ph-I]) IT-101; [Total number of patients enrolled for the study 62 <sup>a</sup>].

T	No. of patients		Tumour response rate <sup>c</sup>				
Tumour type	per tumour (Ph I)	No. of SD	No. of PR	No. of MR	No. of CR	No. of NR	(%) (Ph I)
Lung	27	16	-	-		11	59
Solid tumours *	35	28	-	-	-	7	80

Notes: \* Solid tumours includes-Pancreas (11); Head/Neck and brain (4); Kidney (4); Ovary (3); Breast (3); Cervix (2); Colon and/or rectum (1); Oesophagus, stomach and intestine (1); Liver (5); Urinary (1); <sup>a</sup> Indicates number of patients considered for the clinical evaluation; <sup>b</sup> clinical responses is the total SD, Stable disease; PR, Partial response; MR, Minor response; CR, Complete response; NR, No response; <sup>c</sup> Tumour response rate (%) is the added responses (SD + PR + MR + CR) per tumour type.

### 18. Hyaluronic Acid-Paclitaxel (ONCOFID-P<sup>TM</sup>) [53]

Table S18. Data relating to clinical trials (Phase I [Ph-I]) ONCOFID-P<sup>TM</sup>; [Total number of patients enrolled for the study 16(15) <sup>a</sup>].

T	No. of patients		Clini	Tumour response rate <sup>c</sup>			
Tumour type	per tumour (Ph I)	No. of SD	No. of PR	No. of MR	No. of CR	No. of NR	(%) (Ph I)
Urinary	15	-	-	-	9	6	60

Notes: <sup>a</sup> Indicates number of patients considered for the clinical evaluation; <sup>b</sup> clinical responses is the total SD, Stable disease; PR, Partial response; MR, Minor response; CR, Complete Response; NR, No response; <sup>c</sup> Tumour response rate (%) is the added responses (SD + PR + MR + CR) per tumour type.

#### 19. Oxidized Dextran-Doxorubicin; OXD-DOX (AD-70) [54]

**Table S19.** Data relating to clinical trials (Phase I [Ph-I]) AD-70 (OXD-DOX); [Total number of patients enrolled for the study 13 <sup>a</sup>].

Tumour type	No. of patients		Tumour response rate <sup>c</sup>				
	per tumour (Ph I)	No. of SD	No. of PR	No. of MR	No. of CR	No. of NR	(%) (Ph I)
Colon and/or rectum	6	1	-	-	-	5	17
Oesophagus, stomach and intestine	2	-	-	-	-	2	0
Lung	2	-	-	-	-	2	0
Urinary	1	-	-	-	-	1	0
Head/Neck and brain	1	-	-	-	-	1	0
Skin	1	-	-	-	-	1	0